Cheng-Hua Luo
Editor

Retroperitoneal Tumors

Clinical Management

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Foreword 1

The book *Surgery of Primary Retroperitoneal Neoplasm: Principle and Practice* edited by Professor Cheng-Hua Luo and me in 2006 is the first retroperitoneal tumor monograph in Chinese with both pictures and illustrations. We present four biological characteristics of retroperitoneal tumors: (1) expansive growth and noninvasiveness, (2) intact capsules, (3) low occurrence of distant metastasis, and (4) being prone to local recurrence. Since publication, the book has been highly praised by surgical colleagues over the past decade. It has benefited Chinese patients by improving the diagnostic and therapeutic understanding of primary retroperitoneal tumors.

In 2011, Dr. Cheng-Hua Luo held the 1st Retroperitoneal Tumor Symposium in China (RTSC) in Beijing. In 2016, his team also organized the 2nd Retroperitoneal Tumor Symposium in Beijing, and on June 26, 2016, the Society for Retroperitoneal and Pelvic Floor Disease of the Chinese Research Hospital Association was established. Dr. Cheng-Hua Luo took this unique opportunity to publish this book in English together with over a dozen Chinese surgeons in this field. The work is based on their rich experience in the diagnosis and treatment of retroperitoneal tumors and will help integrate Chinese approach to the diagnosis and therapy of retroperitoneal tumors into the world's literature and thus promote academic exchange. We believe that Chinese scholars in cooperation with international researchers have much to offer in terms of contributing to development in the diagnosis and therapy of retroperitoneal tumors.

Beijing, China
January 2017

Yanyong Jiang

Foreword 2

Retroperitoneal sarcoma is an exceedingly rare clinical entity that comprises approximately 0.1% of all adult solid tumors. The overall survival for these lesions is a disappointing 10% at 10 years and points to the difficulties in dealing with high-risk, massive tumors that are growing in an anatomically constrained location. Because of their rarity, few centers have the ability to provide contemporary, cutting-edge clinical care that encompasses accurate pathologic diagnosis, radiologic depiction, systemic therapies, organ-sparing radiotherapy, and the incisive multispecialty surgical care needed to maximize the likelihood long-term survivorship. Experience in managing these complex tumors is critical, especially in counseling patients on prognosis, surveillance, detection of early recurrence, and selection of adjuvant treatment strategies. Given these needs, patients and physicians alike should be encouraged to pursue referral to centers of excellence in the management of these diseases *prior* to the deployment of irrevocable interventions—even if this means travel over long distances with logistical inconvenience.

Dr. Luo and colleagues at Peking University International Hospital have prepared a comprehensive textbook of retroperitoneal sarcoma multidisciplinary management. This is a very sorely needed addition to the sarcoma oncology literature and is unique in the available compendia available for the practicing sarcoma specialist. This effort is based on one of the largest sarcoma clinical practices worldwide, as is provided under the auspices of the Peking University International Hospital. The experience presented is predictably a valuable learning opportunity for all of us who are dedicated students of this challenging disease. Working together we will make the situation better for our patients afflicted with this malignancy, and I am delighted to be able to have Dr. Luo and his associates as my colleagues and friends!

Raphael Pollock
Professor of Surgical Oncology, Director
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Preface

Retroperitoneal tumors are a group of neoplasms that occur in the retroperitoneal area of the abdomen and pelvis. The retroperitoneum is not an organ but a large space, so the term "retroperitoneal tumor" is different from tumors classified according to the organs of origin, such as the breast, bladder, etc. The retroperitoneal space is complex with its contents being diverse such that retroperitoneal tumors are best characterized by pathological subtypes, of which soft tissue sarcoma is dominant.

Retroperitoneal tumors are relatively rare and accurate incidence is not available. For example, retroperitoneal sarcoma only accounts for 15% of systemic soft tissue sarcomas. Clinical studies on retroperitoneal tumor are often limited to single cases or reports of a small group of cases. Up to now, the largest (n>500) studies on retroperitoneal sarcoma were reported by the Memorial Sloan Kettering Cancer Center (New York, USA), the Instituto Nazinonale Tumori (Milan, Italy), and the Multicenter French Sarcoma Group.

Retroperitoneal tumors are generally asymptomatic in their early stage. When symptoms such as abdominal pain and abdominal distention appear, they lack specificity. Symptoms often are not linked to "retroperitoneal tumor" by either the patients or doctors until the tumor has grown large. The American Joint Committee on Cancer (AJCC) staging for retroperitoneal sarcoma was derived from extremity soft tissue sarcoma. Surgical resection is the primary treatment for retroperitoneal tumor. At present, no widely accepted guidelines or consensus has yet been reached regarding retroperitoneal soft tissue sarcoma staging, treatment options, and surgical methods. At the time of surgery, most of retroperitoneal tumors involve or invade large vessels, nerves, the digestive system, the urinary system, the reproductive system, and skeletal muscles, and multiple-organ resection is often required. Treatment is best in comprehensive centers in large general hospitals dedicated to the treatment of retroperitoneal tumors, which requires expert multidisciplinary collaboration due to the complexity of the operations. There is no definite consensus on whether radiotherapy is beneficial for retroperitoneal sarcoma or whether (adjuvant or neoadjuvant) chemotherapy exerts significant effects on the regression and prolonged survivals. Although progress on new surgical technology, treatment, and medication for retroperitoneal tumor has been slow, we were pleasantly surprised that worldwide scholars and physicians have begun to pay increasing attention to retroperitoneal sarcoma. The Trans-Atlantic RPS Working Group that was founded in 2013 with the

aim of sharing institutional experience has come to an agreement on the treatment of retroperitoneal sarcoma through pooled multi-institutional case series. The National Retroperitoneal and Pelvic Disease Committee founded in China in 2016 holds the Annual China Retroperitoneal Tumor Forum, publishes expert consensus on retroperitoneal liposarcoma, and has launched multicenter prospective studies on retroperitoneal liposarcoma surgery. This committee will closely work with international collaborators engaged in the studies on retroperitoneal tumors, to jointly promote the development of technology in the treatment of retroperitoneal tumors.

The Department of Retroperitoneal Tumor Surgery at Peking University International Hospital is the largest treatment and research center for retroperitoneal tumors among the eight hospitals that perform more than 100 retroperitoneal tumor surgeries annually in China. This center performs 500–600 surgeries annually, has published three professional books on retroperitoneal tumors in Chinese, has trained more than 200 surgical experts in the field of retroperitoneal tumors, and has proposed the new concept of total ipsilateral retroperitoneal fat resection in the treatment of retroperitoneal liposarcomas. To the best of the author's knowledge, no monograph on retroperitoneal tumors has been published in English. To fill gaps in knowledge and based on his three retroperitoneal tumor monographs, the author has edited this book together with many famous Chinese experts in the field of retroperitoneal tumors. With the publication of this book, the authors wish to share their experience with international colleagues who are engaged in the diagnosis, therapy, and research of retroperitoneal tumors, so as to spur common interests of international community to this relatively rare disease.

This book crystallizes the knowledge and experience of Chinese authors in the diagnosis, treatment, and research of retroperitoneal tumors and reflects the latest international research as faithfully as possible. The book consists of three parts: Part 1 summarizes basic knowledge of retroperitoneal tumors and provides a comprehensive introduction to diagnosis and treatment; Part 2 focuses on the surgical techniques used for retroperitoneal tumors and describes general procedures of operation on retroperitoneal tumors at different sites; and Part 3 details the etiology, pathology, evaluation, treatment, and prognosis of retroperitoneal tumors according to pathological subtypes.

Chapter 1 summarizes retroperitoneal and pelvic anatomy, focusing on retroperitoneal and pelvic organs closely related to retroperitoneal tumor surgery as well as abdominal and pelvic anatomical structures. Chapter 2 provides an overview of the etiology, clinical manifestations, and biological characteristics of retroperitoneal tumors and explains the author's perspective on ipsilateral total retroperitoneal lipectomy in the treatment of retroperitoneal liposarcoma based on its pathogenesis. Chapters 3 and 4 demonstrate the role of CT and MRI, respectively, in the diagnosis of retroperitoneal tumors. Chapter 5 illustrates pathologic diagnosis of retroperitoneal tumors. Chapter 6 outlines key points of anesthesia for retroperitoneal tumors, including anesthesia risk assessment, intraoperative monitoring and transfusion-free techniques, as well as anesthesia in retroperitoneal tumor cases complicated with endocrine and metabolic disorders. Chapter 7 describes preoperative preparation and perioperative management of retroperitoneal tumors. Chapter 8

provides an overview on therapeutic strategies of various complications after operation of retroperitoneal tumors. Chapter 9 describes the surgery of the left upper retroperitoneal tumors and also provides details of typical surgical procedures for retroperitoneal tumors including the operative techniques involving the spleen, pancreatic body and tail, left kidney, and other organs in the left upper abdomen. Common surgical treatment of corresponding organs involved by the tumor is discussed in this chapter. The surgery of retroperitoneal tumors in the right upper quadrant, lower abdomen, and pelvis is illustrated in Chaps. 10, 11, and 12, respectively. Chapter 13 focuses on the surgical techniques in the management of retroperitoneal tumors involving major blood vessels, such as the abdominal aorta and inferior vena cava.

Retroperitoneal tumors of different histological origin have been included in this book from Chap. 14. Common histology is described as follows: retroperitoneal liposarcoma in Chap. 14, retroperitoneal leiomyosarcoma in Chap. 15, leiomyosarcoma of the inferior vena cava in Chap. 16, retroperitoneal rhabdomyosarcoma in Chap. 17, idiopathic retroperitoneal fibrosis in Chap. 18, retroperitoneal fibromatosis in Chap. 19, retroperitoneal fibrosarcoma in Chap. 20, retroperitoneal gastrointestinal stromal tumor (GIST) in Chap. 21, Castleman's disease in Chap. 22, retroperitoneal lymphangioma in Chap. 23, retroperitoneal angiosarcoma in Chap. 24, benign and malignant retroperitoneal hemangiopericytoma in Chap. 25, retroperitoneal neurofibroma in Chap. 26, retroperitoneal schwannoma in Chap. 27, retroperitoneal paraganglioma in Chap. 28, retroperitoneal neuroblastoma in Chap. 29, retroperitoneal teratoma in Chap. 30, retroperitoneal extragonadal germ cell tumor in Chap. 31, retroperitoneal endodermal sinus tumor in Chap. 32, retroperitoneal synovial sarcoma in Chap. 33, malignant peritoneal mesothelioma in Chap. 34, malignant retroperitoneal lymphoma in Chap. 35, and retroperitoneal lymph node metastasis in Chap. 36.

The publication of this book has been strongly supported by my mentor, Professor Yanyong Jiang, a pioneer in the diagnosis and treatment of retroperitoneal tumors in China who has devoted himself to this area since the 1980s. I would like to thank my wife and children for their full support, as their warmth in the process of writing this book endowed me with passion. Finally, this work has been supported by grants Z111107067311063 and Z161100000516025, which are funded by the Beijing Municipal Science and Technology Commission.

Beijing, China
January 2017

Cheng-Hua Luo

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Dr. Xiaoqun Dong's team, from the USA, made English correction for the book, and Bing Hu of Springer China made valuable suggestions on how to optimize the content.

Finally, thanks are given to my co-workers for their assistance in the ward and theater.

Without their contribution, none of this will be possible.

Contents

Surgical Anatomy of the Retroperitoneal and Pelvic Extraperitoneal Space

1

Xianzhong Shi and Cheng-Hua Luo

1 Surgical Anatomy of the Retroperitoneal Space

1.1 Overview

The retroperitoneal space (retroperitoneum) is a potential space in the posterior peritoneal cavity that lies between the parietal peritoneum internally and the fascia of posterior abdominal wall externally. The space extends from the diaphragm superiorly to the sacral promontory and to the arcuate line inferiorly, which communicates with the pelvic extraperitoneal space inferiorly, with mediastinal connective tissue superiorly through the lumbocostal triangles, as well as with extraperitoneal fat bilaterally. Therefore, a primary tumor located in the retroperitoneal space may spread or invade to the posterior mediastinum, lateral abdominal wall, or pelvic extraperitoneal space. The retroperitoneal space can be divided into left lumbar region (left flank), right lumbar region (right flank), prevertebral region, left iliac fossa (RIF), and right iliac fossa (LIF) areas.

The flank is the surrounding area that originates from the level of the 12th thoracic vertebrae and the 12th rib and extends downward to the sacral promontory and iliac crest. The left flank is continuous with the right flank through the prevertebral area. The longitudinal groove located at the outer edge of erector spinae marks its exterior boundary. When viewing from the abdominal cavity, the exterior edge of the quadratus lumborum defines its exterior boundary. Retroperitoneal tumors usually can extend beyond the abovementioned exterior boundaries or cause displacement of quadratus lumborum by pushing them outward. The base of the flank and iliac fossa is formed by the quadratus lumborum and psoas major whose surfaces are covered by fascia. The psoas major is connected downward to the iliac fascia and thus constitutes the posterior wall of retroperitoneal space (Serio and Tenchini 1998).

The retroperitoneal space contains abundant loose connective tissue and adipose tissue. Retroperitoneal tissue is divided into three layers: (a) outer layer of transversalis fascia, close to the inner surface of the posterior abdominal muscles; (b) inner layer, peritoneal basement membrane, constructed by an inner connective tissue layer located directly at the deeper peritoneal surface; and (c) middle layer positioned between the abovementioned two layers. Its thickness varies with the individual's body weight as well as its surrounding organs or structures. Retroperitoneal tissue either fills in the space between the muscle and organs, such as the duodenum, ascending colon, and descending colon, or encapsulates the kidney, renal vessels, ureter, abdominal aorta, inferior vena cava,

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iliac artery, lumbar sympathetic trunk, lymph nodes, etc. The organs and urinary system in the retroperitoneal space are shown in Fig. 1.1. As retroperitoneal tumors may involve the abovementioned structures, the surgical treatment of these tumors becomes extremely complex (Nishino et al. 2003).

1.2 Kidney

1.2.1 Shape and Location of Kidney

Kidneys are horse bean-shaped organs located on both sides of the spine. Each of them has anterior vs. posterior surfaces, upper vs. lower poles, and lateral vs. medial borders. The upper pole of the kidney is wide and thin, while the lower pole is narrow and thick. The kidneys lie in the superior part of the retroperitoneum on either side of the spine with upper poles slightly tilted toward the spine. The superior pole of the right kidney is adjacent to the liver, typically making it lower in position than the left kidney. The left kidney therefore lies at a position approximately between vertebral levels T_{11}-L_2, whereas the right kidney occupies an area approximately between vertebral levels T_{12}-L_3. Kidneys move with respiratory movements of the diaphragm within the range of no more than one vertebra (Rohen et al. 1998).

The renal outer edge is convex, whereas the inner edge is concave. The renal hilus is located in the center of the concave area, serving as the point of entry and exit of the renal vein and artery, renal pelvis, nerves, and lymphatic vessels. The structures at the renal hilus of the kidney from the front backward are the renal vein, renal artery, and renal pelvis and from above downward are the

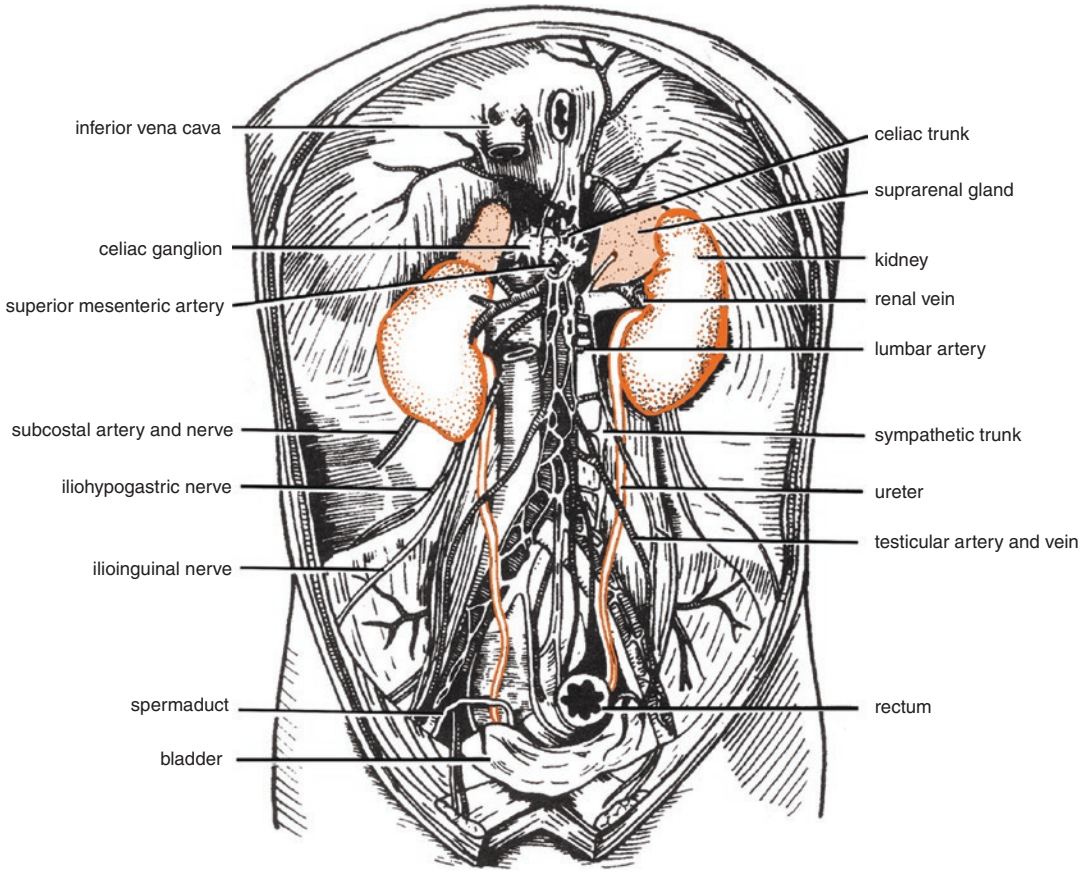

Fig. 1.1 Front view of the organs and the urinary system in the retroperitoneal space

renal artery, renal vein, and renal pelvis. All structures that pass through the renal hilus are enclosed in connective tissues, forming the renal pedicle.

1.2.2 Anatomic Relationships

The upper one third of the anterior left kidney is related to the stomach, the middle one third is adjacent to jejunum, the upper lateral half is in contact with the spleen, and the lower lateral half is adjacent to colic flexure. The upper two thirds of the anterior right kidney is close to the right lobe of the liver, and the lower one third part is in relation to the hepatic flexure of the colon. A narrow area along the curved medial border is in contact with the descending part of the duodenum. The upper pole is separated from suprarenal gland by adipose tissue. Posteriorly, the parts of kidneys above the 12th rib are close to the diaphragm, whereas below the 12th rib they are close to the psoas major, quadratus lumborum, and transversus abdominis, as well as subcostal, iliohypogastric, and ilioinguinal nerves that run downward.

1.2.3 Capsules of the Kidneys

The coverings of the kidneys from outer inward consist of three layers, renal fascia, adipose capsule, and fibrous capsule. The renal fascia is comprised of peritoneal connective tissue and divided into an anterior and a posterior layer, which enclose the kidney and the suprarenal gland along with the anterior of their vessels and adipose capsule. Medially the anterior layer of the fascia is continuous with the contralateral renal fascia across the abdominal aorta and the inferior vena cava. The posterior renal fascia is firmly attached to posterior kidney and the link between the psoas major and quadratus lumborum and medially attached to the side of lumbar vertebrae and intervertebral disks. The anterior and posterior layers of the renal fascia fuse and unite with the fascia of diaphragm above the suprarenal gland but remain separate below it. The posterior renal fascia extends to the lumbar fascia, and the anterior layer encloses the ureter and continues to the pelvis. Perirenal adipose capsule is comprised of adipose tissue, which envelopes both the kidney and suprarenal gland. Especially for the obese, a huge amount of adipose capsule develops, acting as a protective buffer against pressure. There is a very tiny amount or no fatty tissue in front of the kidney, while the renal margin is relatively thicker and enters into the renal sinus. The adipose capsule allows X-ray to pass through, which is in sharp contrast to the renal parenchyma, making it ideally suitable for imaging. The fibrous capsule is an intrinsic renal capsule, enclosing the surface of the renal parenchyma. It is thin, firm, and tenacious, consisting of dense connective tissue and a few elastic fibers. When the fibrous capsule is invaded by retroperitoneal tumors, resection of the renal parenchyma is highly recommended. After partial kidney removal, this layer should be sutured.

1.2.4 Renal Vasculature (Artery and Vein), Lymphatic Vessel, and Nerve

Each kidney weighs about 120–150 g, with a relatively thick and large renal artery and vein. The renal arteries normally arise off the side of the abdominal aorta. The most common location for the origin of renal artery was the L_1-L_2 intervertebral disk level. The right renal artery is normally longer than the left one. An average diameter of renal arteries is 0.77 cm. The renal artery extends exteriorly and ramifies in the renal hilus into the anterior and posterior branches. Most of people have one renal artery originally for each kidney (86%); a minority gives off two branches, occasionally up to three or four branches.

Accessory renal arteries are common; variate is present in 41.8% of Chinese. They enter into the kidneys through the upper or lower pole instead of passing through the renal hilum. The most common types of origins of the accessory renal arteries in Chinese patients are (A) from the renal artery, (B) from a renal artery segment, (C) from the abdominal aorta, and (D) sharing a branch with adrenal artery. Types A and B are most common, followed by type C. When a resection of kidney is required due to invasion of a retroperitoneal tumor, close attention should be paid to the above anatomical variations.

Renal veins are located inside of the renal hilum and typically merge into one large trunk by

2–3 branches running gradually inward. Renal veins run in front of their corresponding arteries and finally join the inferior vena cava at an approximate right angle. The left renal vein is normally 2 or even more than 3 times longer than the right vein. Besides collecting the left renal vein blood, the left renal vein also houses blood from the left suprarenal gland and testicles (ovaries). Therefore, after being invaded by retroperitoneal tumors, left renal vein can reversely drain through testicular (ovarian) vein. Our team previously established one case of renal vein—left ovarian vein anastomosis to preserve the left kidney function in our hospital. Branches of the left renal vein occasionally anastomose with veins of posterior abdominal wall, and more than half of left renal veins have a large branch which coincides with the ascending lumbar vein. During surgery, it should be noted that in this case, the vertebral venous plexus can be connected to the left renal vein through special communications.

Four to five large lymphatic vessels are formed by confluence of renal lymphatic vessels around the renal pedicle, entering into lumbar lymph nodes and lumbar trunk. The constriction of left renal vein by enlarged retroperitoneal lymph nodes may result in testicular varicose veins. Similarly, lymphatic vessels around renal pedicle can become thickened, distorted, or even destroyed due to the compression and obstruction of cisterna chyli or thoracic duct, leading to chyluria.

The kidney plexus is formed by branches from the celiac plexus around the renal artery. Abdominal aortic plexus and branches of lumbar sympathetic trunk are also distributed along the branches of the renal artery. Tumors of neurogenic origin can occur in these areas.

1.3 Suprarenal Gland

The suprarenal gland is one of the most important endocrine organs in the human body. They are connected with the upper poles and anteromedial sides of both kidneys and enclosed by renal fascia and adipose capsule. The right adrenal gland is pyramidal in shape, attaching to the anteromedial side of the upper pole of the right kidney on the recessed bottom surface. The anterior part of adrenal gland is divided by the longitudinal ridge into an inner region which is not covered by peritoneum at the inner side and directly attached to the back of the inferior vena cava and an outer region which is adjacent to the right lobe of liver and the superior part of duodenum. If the suprarenal gland that is posteriorly attached to the diaphragm is at a higher location, visceral nerves pass through between them and join the celiac plexus. The medial margin is convex, adjacent to right celiac ganglion and right inferior phrenic artery. The left suprarenal gland is shaped like a half moon, closely attached to the superior medial side of the left kidney on the recessed bottom surface, connecting to the renal vessels. The anterior aspect of suprarenal gland is adjacent to the posterior wall of stomach superiorly and connected to the splenic artery and vein as well as the pancreas inferiorly. Also, the left splanchnic nerve passes between the posterior aspect of the suprarenal gland and the diaphragm.

The normal size of the suprarenal gland is about 5 cm in length, 3 cm in width, 0.5–1 cm in thickness, and 5–7 g in weight. Suprarenal glands do not move with nephroptosis and have rich blood supply. There are upper, middle, and lower arteries on each side of the suprarenal gland, stemming from the inferior phrenic artery, abdominal artery, and renal arteries, respectively. The origins of these arteries have also been reported as accessory renal artery, gonadal artery, abdominal artery, ureter artery, superior mesenteric artery, renal adipose capsule artery, and common hepatic artery. Each suprarenal gland lack one of the three arteries. Most often each suprarenal vein has only one branch. The left suprarenal vein receives blood from the left inferior phrenic vein on the medial side of the suprarenal glands, descends inwardly, and passes at an acute angle into the upper margin of the left renal vein. The right adrenal vein descends inwardly and mostly flows into the right posterior wall of the inferior vena cava. Otherwise it can enter into the right accessory hepatic vein, etc. Retroperitoneal tumors may displace suprarenal glands, resulting in physical changes in the above blood vessels. For patients with tumors infiltrating the suprarenal gland(s),

the resection should be performed by experienced surgeons who are very familiar with retroperitoneal vascular anatomy in order to avoid intraoperative bleeding or accidental damage to inferior vena cava and other important structures.

Neural tumors, pheochromocytomas, may occur in suprarenal gland medulla that is composed of sympathetic ganglion cells (pheochromocytes). Although beyond the scope of retroperitoneal tumors, they are similar in pathogenesis to extra-adrenal pheochromocytomas (also called paragangliomas) which may be derived from peritoneal sympathetic postganglionic neurons with the same functions as medulla cells.

1.4 Ureter

Ureters are a pair of elongated muscular tubes located in the retroperitoneal space, arising from the pelvis of each kidney superiorly and opening into the bladder inferiorly. In adults, the ureter is 25–30 cm in length and 4–7 mm in diameter. The ureter consists of an abdominal part, a pelvic part, and an intramural part. The abdominal part of ureter descends along the anterior of the psoas major, gradually deviates toward the midline, and goes downwardly to the superior aperture of the small pelvis where the left ureter passes in front of the left common iliac artery; the right ureter passes through in front of the right external iliac artery into the pelvic extraperitoneum. The ureter crosses over the testicular blood vessels in men (ovarian blood vessels in women) slightly below the midpoint of the psoas major, where blood vessels descend in front of the ureter. The anterior of the abdominal part of the left ureter is adjacent to duodenojejunal flexure, the left colonic vessels, and sigmoid colon from up to down. The abdominal part of the right ureter is next to the descending part of duodenum, the root of the small bowel mesentery, and appendix. Clinically, retroperitoneal tumors frequently compress, distort, and even invade ureter(s), eventually leading to obstruction.

The ureteral blood supply is derived from multiple sources. The abdominal origins of arterial blood supply to the ureter include small branches of the abdominal aorta, renal artery, testicular (or ovarian) arteries, and iliac arteries. After reaching the surface of the ureter, the arteries bifurcate into ascending and descending branches, which travel along the ureteral walls upward and downward, respectively, anastomose with each other, and further bifurcate into subbranches to supply the ureteral walls. Ureteral veins travel in parallel to the arteries. During surgery, the ureter should not be dissected excessively from retroperitoneal tumors in order to avoid postoperative ureteral ischemia and necrosis.

The ureteral nerves are derived from the renal plexus, abdominal aortic plexus, and hypogastric plexus, which are distributed in the wall of the ureter and constitute ureteric plexus.

When retroperitoneal tumors invade into the ureter, ureteral resection and anastomosis are often performed. Since the ureter is an elongated fibromuscular tube, the anastomosis should be undertaken at a certain inclination angle to maximize the anastomosis surface of the ureter margin and extend the luminal constriction ring, thereby facilitating ureteral patency. Otherwise, patients are prone to develop scars and consequent stenosis, even obstruction.

1.5 Abdominal Aorta

The abdominal aorta is the segment between the left and right common iliac arteries that are derived from thoracic aorta passing through the aortic hiatus of the diaphragm (equivalent to the inferior margin plane of 12th thoracic vertebrae to the 4th lumbar plane). It is located in left-front of the spine, which on average is 13.4 cm in length.

The abdominal aorta runs parallel to inferior vena cava on its right-hand side and parallel to the left sympathetic trunk on its left-hand side. The splenic vein, pancreas, left renal vein, horizontal part of the duodenum, and root of the small bowel mesentery lie from top to bottom in front of the abdominal aorta. Additionally, the lower end of the thoracic duct is situated on the right side or the rear of the initial segment of the abdominal aorta, while the celiac plexus and

celiac ganglia are located anterior to this segment. The abdominal aorta is surrounded by the aortic plexus inferiorly. Lumbar lymph nodes lie posterior and lateral to the abdominal aorta.

The abdominal aorta can be divided into four branches: (a) unpaired visceral, (b) paired visceral, (c) parietal, and (d) terminal (Fig. 1.2).

Unpaired visceral branches include the celiac and superior and inferior mesenteric arteries. The celiac trunk is also known as celiac artery, which arises from the anterior aortic wall, just below the aortic hiatus of the diaphragm. It consists of three large branches, the left gastric, the hepatic, and the splenic. Symptoms may appear at the early stage of retroperitoneal tumors involving the celiac artery due to the vital roles of the organs to which celiac arteries provide blood supply. If the tumor does not grow very large at the time of surgery, it is not hard to remove. The superior mesenteric arteries originate from the anterior wall of the abdominal aorta on the first lumbar vertebra plane, traveling into the small mesenteric root in front of the horizontal part of duodenum through the posterior pancreas and obliquely descending to the vicinity of the right iliac fossa. Tumors originating from this arterial trunk (strictly speaking, they belong to retroperitoneal tumors) usually involve blood vessels as they are located in the mesenteric roots. The author's team has treated many cases of this type of retroperitoneal tumors

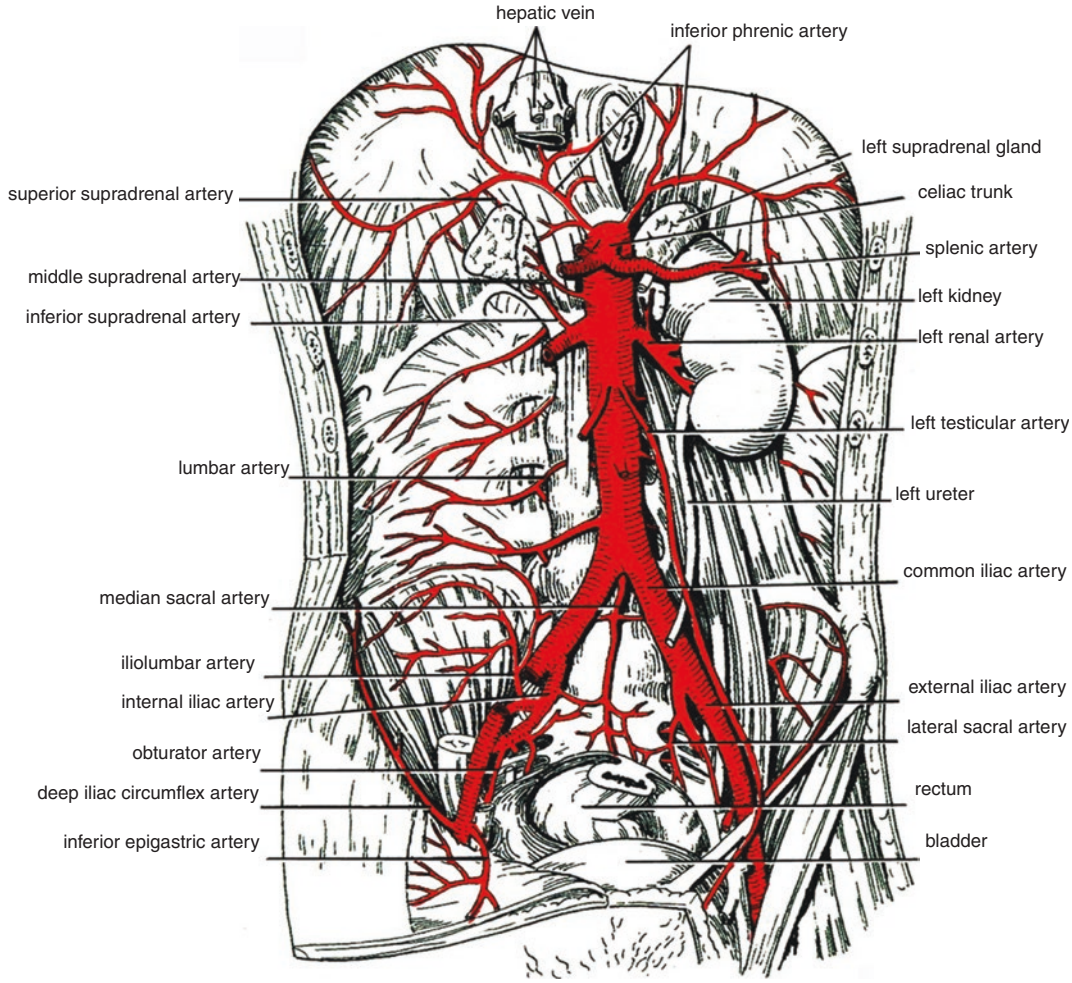

Fig. 1.2 Abdominal aorta and its branches

with end-to-end anastomoses after resection of these arteries, as well as the distal end of the superior mesenteric artery with inferior mesenteric artery, abdominal aorta, or other vasculature anastomoses to reconstruct the blood supply for the digestive tract and successfully resect the tumor. The inferior mesenteric artery arises from the anterior wall of abdominal aorta at the level of the third lumbar vertebra, descending via the left retroperitoneum to the root of the sigmoid mesocolon and extending to the superior rectal artery in the pelvic cavity. If the inferior mesenteric artery is infiltrated by retroperitoneal tumors, its trunk may be resected, and the intestinal blood flow can be maintained through the plexus that communicates between the mesenteric vessels.

Paired visceral branches include the middle suprarenal, renal, and testicular arteries. The middle suprarenal artery originates from the abdominal aortic sidewall on the first lumbar vertebra plane. The anatomy of renal artery was described above. The testicular artery (ovarian artery in women) arises from the anterior wall of the abdominal aorta immediately below the renal artery, obliquely running outward along the anterior psoas major, descending across the anterior ureter, and giving off branches to the ureter. Outwardly passing through the inner ring into the spermatic cord, it is called the internal spermatic artery. The ovarian artery passes across the bifurcation of common iliac artery or initial segment of external iliac artery into the pelvic cavity where it is distributed to the ovaries and ampulla of the fallopian tube. The testicular artery (ovarian artery) may be resected unilaterally when it is invaded by retroperitoneal tumors.

Parietal branches of abdominal aorta include inferior phrenic artery and lumbar artery. The inferior phrenic arteries most often originate from the abdominal aorta and are located on the side of abdominal aorta on T_{12}–L_1 plane. Arteries are 2–2.1 mm in diameter. Additionally, the inferior phrenic artery may also arise from celiac artery, renal artery or accessory renal artery, hepatic artery or accessory hepatic artery, left gastric artery, suprarenal artery, internal spermatic artery, etc. During the resection of retroperitoneal tumors combined with multiple organs, care should be taken to avoid accidental injury to these arteries. If ligation of renal artery or left gastric artery is required, the surgeons should carefully check for the presence of an inferior phrenic artery and perform the ligation and resection as close to the organs as possible in order to ensure a plentiful blood supply to the diaphragm afterward.

The lumbar artery is a major source of blood supply to the posterior abdominal wall and peritoneum. It is mostly composed of four pairs of branches, arising from the posterior and lateral wall of abdominal aorta on the plane between L_1 and $L_{1\sim2}$, between L_2 and $L_{2\sim3}$, and between L_3 and L_4, respectively. Sometimes, a fifth pair of lumbar arteries is derived from the lateral wall of the median sacral artery. The above four pairs of lumbar arteries travel through the deep surface of lumbar sympathetic trunk, cross the tendinous arch over the psoas major to the area between psoas major and spine, and thus are located behind psoas major and lumbar plexus. The first and second pairs of lumbar arteries also pass through the diaphragmatic crura or its posterior surface. The first, second, and third pairs of lumbar arteries cross over the posterior of quadratus lumborum. The right lumbar artery passes posterior of the inferior vena cava to the area between the psoas major and spine. The first and second pairs of the right lumbar arteries also cross over the posterior of cisterna chyli. As the prominent feeding vessels for retroperitoneal tumors mostly arise from lumbar arteries, angiography usually reveals that lumbar arteries have become thickened, stretched, twisted, or ruptured, etc. and given off branches to feed the tumors. Lumbar artery embolization may be performed in such cases. Lumbar arteries should be carefully identified during ligation to avoid uncontrollable bleeding.

Terminal branches of the abdominal aorta include median sacral artery, common iliac artery, and its branches. The median sacral artery is a small terminal branch of the abdominal aorta. It is relegated to the posterior and anterior surface 5 mm above the bifurcation of the aorta after gradually giving way to the iliac artery during human evolution. The median sacral artery descends anterior to

the $L_{4\text{-}5}$ vertebrae, sacrum, and coccyx and eventually terminates at coccygeal body. Special care should be taken to avoid any damage to these vessels during presacral (or retrorectal) tumor resection because the superior hypogastric plexus of the left common iliac vein and the sympathetic nerve passes through in front of the median sacral artery. The lowest lumbar artery arises from the lateral wall of median sacral artery; it gives off branches through the posterolateral common iliac artery to the lateral sacrum on both sides, which eventually terminates in the iliac muscle and coincides with the branches of iliolumbar artery. The median sacral artery also gives off four pairs of branches (lateral sacral, rectal, etc.), which should be carefully identified during surgery.

The common iliac artery and its branches are critical for surgical oncology of retroperitoneal tumors. The left and right common iliac arteries originate from the plane of the middle portion of L_4 vertebral body and the superior portion of L_5 vertebral body. These arteries travel separately to the margin of small pelvis and bifurcate into the internal iliac artery and external iliac artery on the plane between the middle one third of L_4 and the superior one third of S_1. The internal iliac artery descends into the pelvis and gives off the anterior branch and posterior branch on the plane between the inferior L_5 and superior S_4. The external iliac artery runs along the margin of the pelvis to the deep surface of inguinal ligament, extending into the femoral artery. The iliac artery is 10.3–10.4 mm in diameter and 4.3–4.6 cm in length. The vessel wall is thinner at the bifurcation of terminal common iliac artery where it divides into internal and external iliac artery, so special care should be taken to avoid any damage when separating from retroperitoneal tumors.

The superior hypogastric plexus passes inward near the front of the right common iliac artery, while the right ureter crosses over the terminal portion of the lateral right common iliac artery or external iliac artery. In addition, the terminal ileum is located anterior, while L4 and L5 lumbar vertebrae body and intervertebral disk are immediately adjacent to the posterior of right common iliac artery. The superior posterior portion of the right common iliac artery is located near the terminus of the left and right common iliac veins at the origin of inferior vena cava and the right sympathetic trunk. Laterally, right common iliac artery is connected to the origin of inferior vena cava and the right common iliac vein superiorly and to psoas major inferiorly. The right common iliac artery is surrounded by iliac lymph node groups outwardly, inwardly, and posteriorly. The anatomical relations of the left common iliac artery are similar to those of the right common iliac artery, except that the sigmoid colon, mesangial root of sigmoid colon, and superior rectal vessel cross over anterior to the left common iliac artery.

The external iliac artery is a direct extension of common iliac artery and is 10.4–11.8 cm in length and 5.9–6 mm in diameter. It passes along the medial margin of the psoas major and descends laterally to the deep surface of inguinal ligament. When the artery crosses the ligament, it becomes the femoral artery. Retroperitoneal tumors sometimes cause displacement of iliac artery; this anatomical variation should be identified carefully during surgery.

Acute abdominal aortic occlusion at or above the renal artery plane may be fatal, whereas below the plane it frequently leads to lower limb gangrene. Compression of retroperitoneal tumors may contribute to chronic abdominal aortic occlusion, which is not life-threatening. Lumbar sympathectomy performed to dilate small blood vessels of limbs is helpful to prevent and reduce the damage caused by the blockade.

1.6 Inferior Vena Cava

Inferior vena cava is formed by the merger of the left and right common iliac veins on the plane between L4 and L5 lumbar vertebrae. It ascends along the right side of the abdominal aorta behind the liver, is enclosed by the vena cava tube, and eventually passes through the central tendon of diaphragm on the right side into the thoracic cavity. The total length of the inferior vena cava is 25.7–27.1 cm, and its diameter is 2.6–3.4 cm. From top to bottom, the right lobe of the liver, the medial margin of the right kidney, and the descending part of duodenum are located on the right side,

while the caudate lobe, right crus of diaphragm, and abdominal aorta are located on the left side; the right crus of the diaphragm, right kidney and right suprarenal gland, vertebrae and anterior longitudinal ligament, right psoas major, and right sympathetic trunk are located posteriorly; and common iliac arteries, mesenteric root, right internal spermatic vessels, and sometimes right colonic blood vessels are located anteriorly.

Branches of the inferior vena cava include the renal vein, common iliac vein, internal iliac vein, external iliac vein, etc., which travel parallel to their corresponding arteries (Fig. 1.3). The veins are located on or above the plane of renal vein and cannot adapt to sudden complete occlusion of inferior vena cava, so ligation cannot be performed in this area. In contrast, when the ligation of inferior vena cava is performed below the plane of renal vein, collateral circulation can be established as follows: (a) through the femoral vein, inferior epigastric vein, and superior epigastric vein to the subclavian vein; (b) through the deep circumflex iliac vein, ascending lumbar vein, azygos vein, or semi-azygos vein to the superior vena cava; (c) through the internal iliac vein and inferior mesenteric vein to the portal vein; (d) through the common iliac vein, internal iliac vein, and ascending lumbar vein to the internal and external vertebral venous plexus, which is the major collateral circulation after occlusion of the inferior vena cava; and (e) superficial branches, mainly from the femoral vein through superficial epigastric vein, the thoracoepigastric vein, and the lateral thoracic vein to the superior vena cava system. The presence of these collateral circulations lays a theoretical foundation for treatment of inferior vena cava occlusion caused by invasion of retroperitoneal tumors.

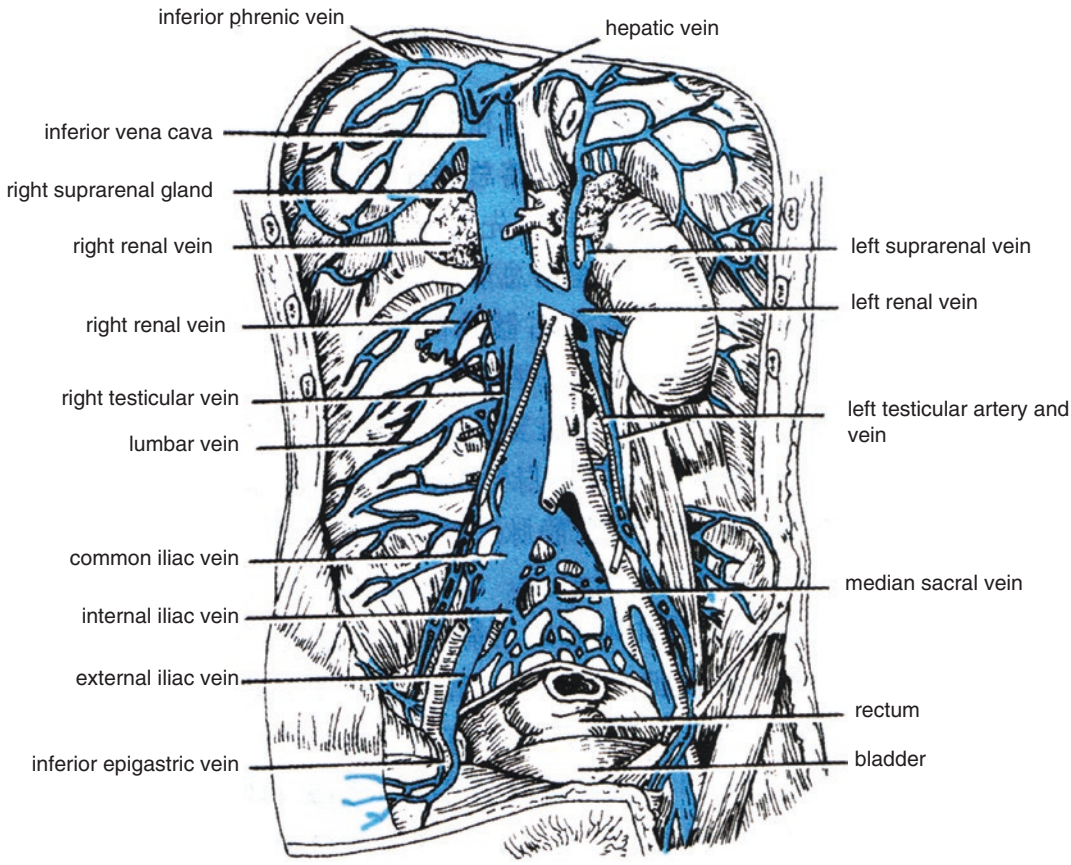

Fig. 1.3 Inferior vena cava and its branches

1.7 Retroperitoneal Lymph Nodes and Lymphatic Vessels

Lymph nodes and lymphatic vessels in retroperitoneal space (Fig. 1.4) are located around the major retroperitoneal blood vessels. They mainly collect the lymph from the lower extremity, pelvis, abdomen, and retroperitoneal organs and drain into the abdominal segment of thoracic duct. They consist of the external iliac, common iliac, and lumbar lymph nodes. External iliac lymph nodes are located medial, lateral, anterior, and posterior to the external iliac vessels, extending upward to the common iliac lymph nodes arranged along the common iliac vessels. Lumbar lymph nodes are distributed around the abdominal aorta and inferior vena cava. Nodular masses formed by confluence of the nodules around

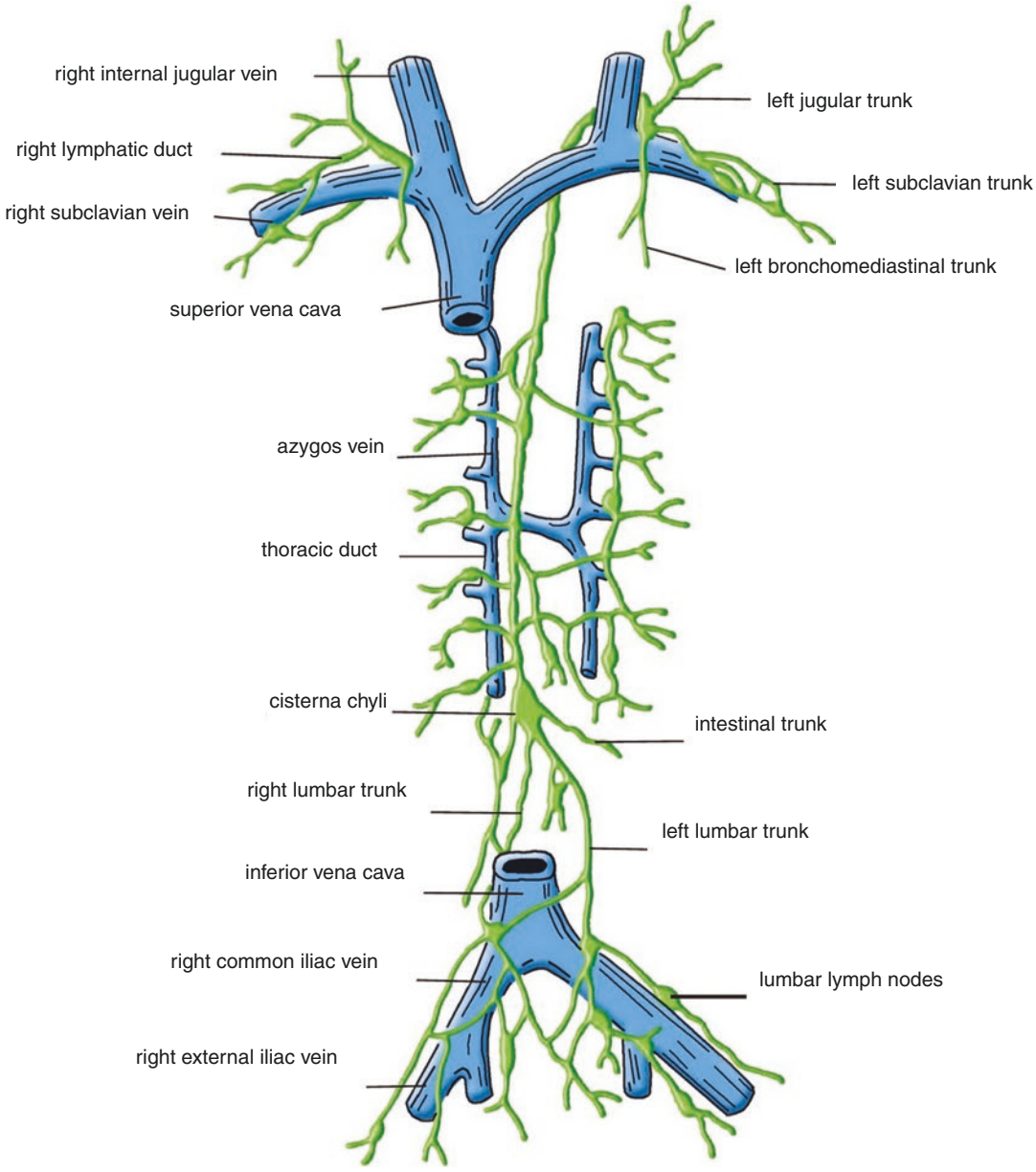

Fig. 1.4 Retroperitoneal lymph nodes and lymphatic vessels (*green*)

these vessels often result from retroperitoneal lymphomas.

The cisterna chyli usually lies in front of the first and second lumbar vertebrae, between right phrenic angle and abdominal aorta, sometimes up to the level of the eleventh thoracic vertebra. It looks like a triangular or spindle-shaped capsule and is 3–4 cm long. It collects the lymph from the left and right lumbar trunks and intestinal trunks (formed by confluence of abdominal lymph nodes, superior mesenteric lymph nodes, and inferior mesenteric lymph nodes). The cisterna chyli ascends through the aortic hiatus into chest, extending to the thoracic duct (Harisinghani et al. 1999).

1.8 Lumbar Sympathetic Trunk and Celiac Plexus

1.8.1 Lumbar Sympathetic Trunk

The lumbar sympathetic trunk (Fig. 1.5) consists of 4–5 lumbar sympathetic ganglia and communicating branches between them. Bilaterally, it is located in front of the lumbar spine and the medial margin of the psoas major. The lumbar sympathetic trunk is covered by the inferior vena cava on the right side and descends along the abdominal aorta on the left side. The lumbar sympathetic trunks on both sides are connected via transverse fibers posterior to abdominal aorta and inferior vena cava. Upwardly,

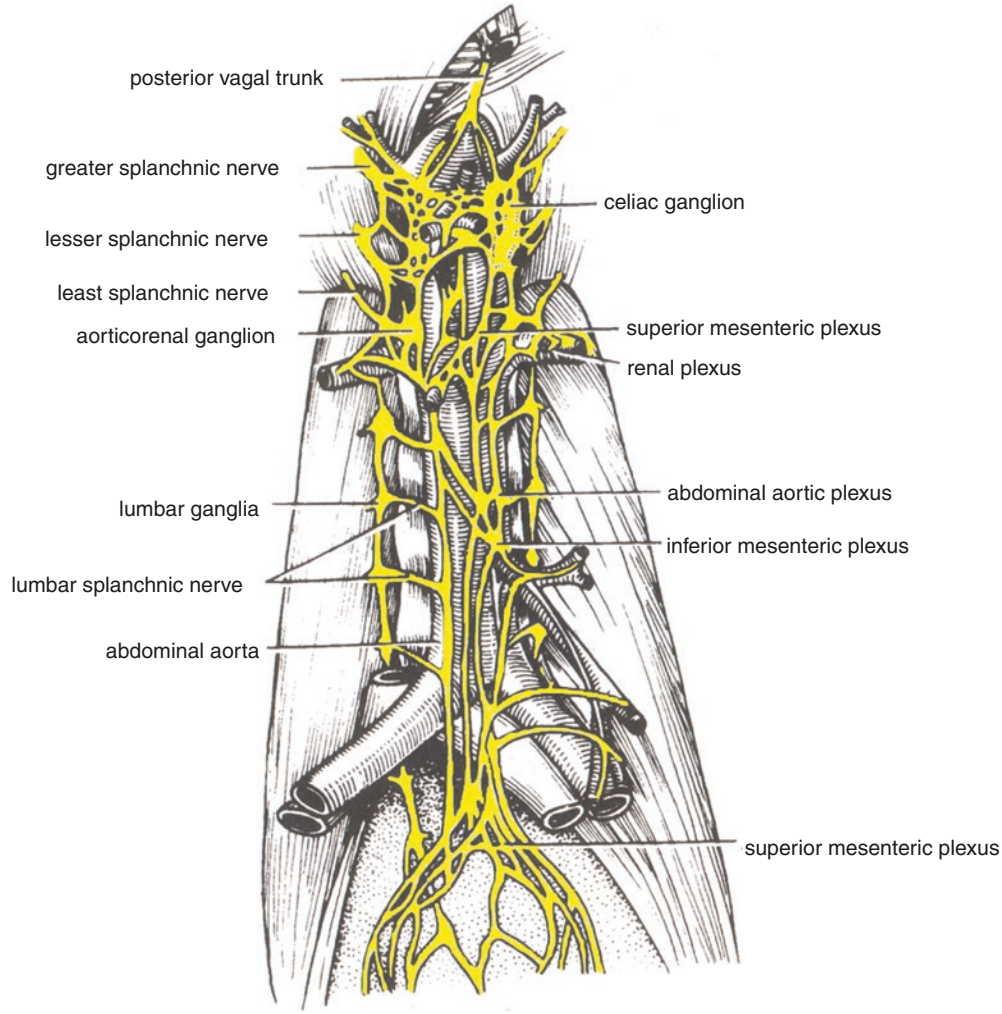

Fig. 1.5 Retroperitoneal autonomic ganglia and nerve plexuses

they are connected to the thoracic portion of sympathetic trunk via interganglionic branches. Downwardly, they are connected to the sacral sympathetic trunk via interganglionic branches along the posterior common iliac vessel. Branches of the lumbar sympathetic trunk include:

a. Gray ramus communicans, which rejoins five pairs of anterior branches of lumbar nerves. Its fibers are distributed not only in sweat glands, small blood vessels, and arrector pili of the skin along with lumbar nerves but also in the lower limbs along with blood vessels.
b. The lumbar splanchnic nerve, which contains preganglionic fibers passing through the lumbar sympathetic ganglia, while postganglionic fibers are distributed in the digestive tract and pelvic organs below the left colic flexure.

1.8.2 Autonomic Nerve Plexuses

Autonomic nerve plexuses including the celiac plexus are located around the celiac trunk and the root of superior mesenteric artery and between the two kidneys. The greater or lesser splanchnic nerve, upper ganglia of lumbar sympathetic trunk, bilateral vagus nerves, and bilateral branches of phrenic nerve are included in the celiac plexus, which gives off many branches joining the phrenic plexus, liver plexus, stomach plexus, spleen plexus, renal plexus, superior mesenteric plexus, inferior mesenteric plexus, suprarenal plexus, and spermatic plexus. These plexuses travel parallel to corresponding arteries and are distributed to various organs.

2 Anatomy of Pelvis

2.1 Pelvis

The bony pelvis (Fig.1.6), a skeletal ring, is formed by sacrum and coccyx connecting to bilateral hip bones, as a protective barrier for pelvic organs. The arcuate line of sacral

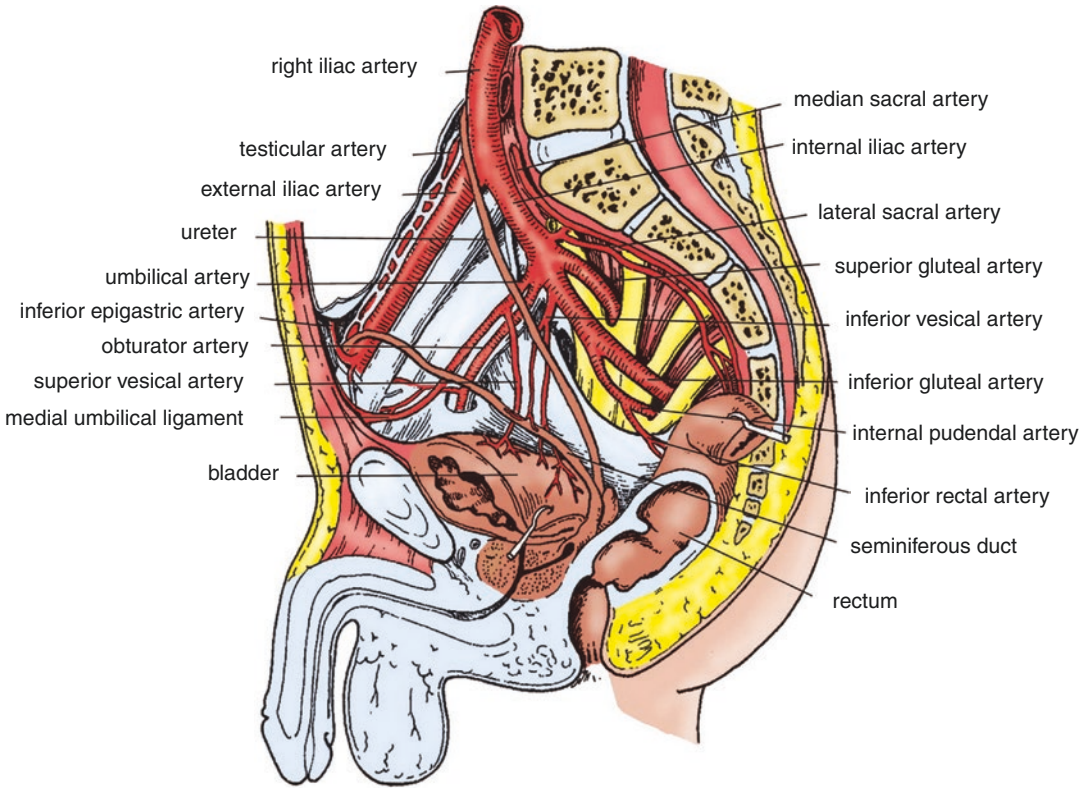

Fig. 1.6 Anatomy of male pelvic extraperitoneum

promontory and ilium, iliopubic eminence, pecten pubis, pubic tubercle, pubic crest, and superior margin of pubic symphysis make up a ring line by which the pelvis is divided into a small inferior portion called the true (minor) pelvis and a large superior one called the false (major) pelvis. The anterior wall of the pelvic cavity consists of bilateral pubic portions of the pubic symphysis. The posterior wall is constituted by sacrum and coccyx, and the lateral wall is composed of the ilium, ischium, sacral spine ligament, and sacrotuberous ligament. The greater sciatic foramen is formed by the sacrospinous ligament and sacrotuberous ligament, anterolaterally bounded by the greater sciatic notch. The lesser sciatic foramen is formed by the sacrospinous ligament and sacrotuberous ligament, defined by the boundaries of lesser sciatic notch and the two ligaments. The greater sciatic foramen is a communication between pelvis and hip, while the lesser sciatic foramen is a communication between the hip and perineum. Blood vessels and nerves pass through these foramina. The obturator canal is located in the obturator foramen at the junction of ilium, pubis, and ischium in the front of sciatic foramen, acting as a communication bridge between the pelvis and the medial portion of femora, where the obturator nerve and vessels pass through. As extraperitoneal tumors that occur in pelvis sometimes pass through sciatic foramen, obturator, etc., familiarity with the anatomy is very important for accurate interpretation of the clinical presentation and for the development of efficient therapeutic strategies.

2.2 Muscles of Pelvic Wall and Pelvic Diaphragm

2.2.1 Internal Obturator Muscle

Internal obturator muscle is a pelvic wall muscle arising from the basal surface of the obturator membrane and the surrounding bone surface, posteriorly crossing the lesser sciatic foramen to the hip and terminating in the trochanteric fossa of the femur outwardly between piriformis and quadratus femoris. The obturator on the upper margin of the muscle is not completely closed; instead, it forms an obturator canal through which tumors in the pelvis may penetrate.

2.2.2 The Piriformis Muscle

The piriformis muscle is a pelvic wall muscle arising from the basal surface of sacrum, laterally crossing through the greater sciatic foramen to the hip, terminating at the tip of the greater trochanter. The piriformis laterally rotates the femur with hip extension and abducts the femur with hip flexion.

2.2.3 The Levator Ani Muscle

The levator ani muscle is a muscle of the pelvic diaphragm which can be divided into four parts according their attachment sites:

a. The pubic vaginal muscle (puboprostatic muscle), originating from the basal surface of the pubis and the anterior part of tendinous arch of the levator ani muscle, traveling posteriorly bilaterally along the urethra and vagina, attaching to the muscular layer in the urethral and vaginal wall (it bypasses the prostate and terminates in the perineal central tendon in men).
b. Puborectalis, which commences in the anterior part of tendinous arch of levator ani muscle and the basal surface of medial part of pubis and posteriorly terminates on the lateral and posterior walls of anal canal as well as the central tendon of perineum. It constitutes a "U"-shaped half a circle with their contralateral counterparts.
c. The pubococcygeus has the same origin as the puborectalis and terminates at the tip of the coccyx and its lateral margin and anococcygeal ligament.
d. The musculus iliococcygeus which originates from the posterior part of tendinous arch of the levator ani muscle and the basal surface of ischial spine and terminates posteromedially at the lateral margin of coccyx and anococcygeal ligament.

2.2.4 The Coccygeal Muscle

The coccygeal muscle is a muscle of the pelvic diaphragm located in the posterolateral musculus iliococcygeus, mostly originating from the ischial

spine posteromedially and terminating in the flank of sacrum and coccyx.

It is not uncommon that extraperitoneal tumors invade the muscles of the pelvic wall and pelvic diaphragm. During surgical resection the involved muscles should be dissected carefully, otherwise residual tumor tissues may develop local recurrence and distant metastases.

2.3 Rectum and Anal Canal

The rectum and anal canal are the terminal parts of digestive tract, posteriorly adjacent to fascia in front of sacrum and coccyx, through which the sacral plexus, pelvic splanchnic nerves, pelvic sympathetic trunk, and superior rectal veins and arteries pass. This is a common area for presacral tumors (e.g., teratoma, etc.) to occur. Bilaterally the rectum is attached to the lateral wall of pelvis through the rectal lateral ligament that encloses the inferior rectal vessels and pelvic splanchnic nerves. The pelvic plexuses and branches of the internal iliac artery are located anteriorly to the ligament. The rectovesical pouch or rectouterine pouch is located anterior to the rectum and superiorly below the peritoneum reflex. The rectum is adjacent to the seminal vesicles, ampulla ductus deferentis, prostate, and ureter in men (adjacent to cervix and vagina in women).

2.4 Bladder

The bladder lies in the extraperitoneum anterior to pelvis, closely attached to the basal surface of pubis. It is filled with loose connective tissue and is where pudendal venous plexus passes through. The bladder is adjacent to the rectum, seminal vesicles, and ampulla ductus deferentis posteriorly in men (to the anterior wall of the vagina and cervix in women). Paravesical tissues are located on both sides of the bladder, through which the arteries and nerves insert into bladder.

The prostate is located posteroinferiorly to the symphysis pubis immediately below the bladder, surrounding the beginning of urethra in the male. The author's team has conducted total pelvic exenteration for eight cases of pelvic extraperitoneal tumors. Detailed knowledge of the pelvic anatomy plays a vital role in this surgery.

2.5 Blood Vessels, Lymph Nodes, and Nerves in Pelvis

In the previous sections, the trunks of common iliac arteries, external iliac arteries, and internal iliac arteries were described in detail. The pelvic vascular anatomy is shown in Fig. 1.6. The internal iliac artery runs along the posterolateral wall of the pelvis within the pelvic fascia. It is posterior and medial to the ureter, anterior to the lumbosacral trunk, and medial to obturator nerve. While running downward to the upper margin of the piriformis, it divides into two large trunks, anterior and posterior. Branches of anterior trunk include (a) the obturator artery, which travels along the pelvic sidewall forward through the obturator canal to the femoral region and (b) the inferior gluteal artery which exits the pelvis via the infrapiriform foramen to the hip. The anterior trunks also give off the umbilical artery, inferior vesical artery, inferior rectal artery, internal pudendal artery, uterine artery, or deferential artery. After birth, the distal segment of umbilical artery occludes, while the proximal segment remains open and bifurcates into 2–3 superior vesical arteries. The inferior rectal artery enters the lateral ligament, which is posterior to the inferior vesical artery and anterior to the internal pudendal artery. The uterine artery descends forward and medially along the pelvic sidewall to the base of broad ligament of uterus and medially 2 cm from the cervical margin where it intersects with the ureter after crossing over its anterior-superior segment and then wiggles upward along the cervical margin in a tortuous manner. The posterior branches include the iliolumbar artery, lateral sacral artery, and superior gluteal artery: the latter exits the pelvis via the suprapiriform foramen to the hip. Combined resection of the sacrum and retroperitoneal tumors often involves the lateral sacral arteries. The internal iliac vein and its tributaries generally travel in parallel to their corresponding arteries. It should be noted that venous plexuses are always formed when the veins surround the organs in the pelvis, such as

exterior anorectal venous plexus, bladder venous plexus, uterine venous plexus, vaginal venous plexus, and genital venous plexus, all of which communicate with one another and eventually confluence into the veins to rejoin the internal iliac vein.

Apart from the abovementioned vessels, the median sacral arteries, superior rectal arteries, and ovarian arteries are also situated in the pelvis, which should be carefully identified during surgical resection of extraperitoneal tumors.

The pelvic lymph nodes are generally arranged along the blood vessels and consist of the common iliac lymph nodes, external iliac lymph nodes, internal iliac lymph nodes, and sacral lymph nodes; the latter is located in front of the sacrum along the median sacral artery.

The pelvic nerves include:

(a) The sacral plexus, located in front of the sacrum and piriformis. It gives off branches that exit the pelvis via the suprapiriform foramen and the infrapiriform foramen of the piriformis. Presacral tumors may compress these nerves leading to pain of lower limbs.

(b) The pelvic sympathetic trunk which extends downwardly from the lumbar sympathetic trunk. The left and the right trunk separately descend along the medial side of the anterior sacral foramen to the anterior surface of coccyx, where they merge. After confluence, the sympathetic trunks give off postganglionic fibers to constitute the pelvic plexuses.

(c) The pelvic splanchnic nerve, also known as pelvic nerve or erectile nerve, belongs to the parasympathetic nerves and is formed by 2–4 fibers from the anterior rami of sacral nerve. It subsequently joins the pelvic plexus.

(d) The superior hypogastric plexus and inferior hypogastric plexus. The superior hypogastric plexus (also known as the anterior sacral nerve) is located anterior to the 5th lumbar spine, between the bilateral common iliac arteries, as a descending extension from abdominal aortic plexus. It gives off the left and the right hypogastric nerves which connect to the left and the right inferior hypogastric plexus (pelvic plexus), respectively. The inferior hypogastric plexus that runs on both sides of the rectum lateral ligament is formed by the intertwining of the hypogastric nerve, pelvic splanchnic nerve, and postganglionic fibers arising from pelvic sympathetic ganglia, etc.

(e) The obturator nerve which arises from the lumbar plexus through the medial border of the psoas major and posterior aspect of the common iliac artery into the pelvic cavity. It travels along the pelvic sidewall lateral to the ureter, superior to its corresponding vessels, and forward through the obturator canal to the femoral region. Tumors on the sidewall of the pelvis that grow into the obturator foramen can compress the obturator nerve and cause pain in hip and lower limbs (Harisinghani et al. 1999).

3 Sectional Anatomy of Abdomen and Pelvis

CT and MRI imaging is a vital tool for diagnosis and therapy of retroperitoneal tumors. Surgeons in the department of retroperitoneal surgical oncology should have a firm grasp on the sectional anatomy and thus be able to interpret the imaging accurately before surgery.

3.1 Cross Section of Retroperitoneal Space

When viewing from the cross section of the first lumbar vertebra (Fig.1.7), the psoas major lies on both sides of the lumbar spine within the intraperitoneal space, medial to renal cross section and

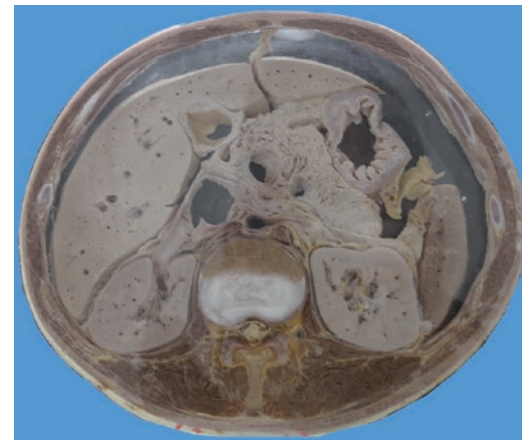

Fig. 1.7 Cross section of abdomen (L_1 level)

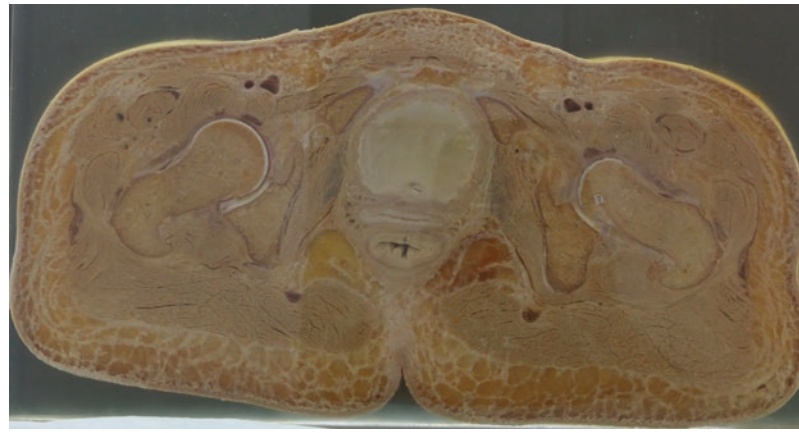

Fig. 1.8 Cross section of pelvis (vaginal and urethral sphincter level)

posterior to the ureter. Ascending and descending colons are located lateral and anterior to the kidneys.

On this plane, the abdominal great vessels are situated anterior to lumbar vertebrae. Cross section of the inferior portion of the duodenum can be seen in front of the abdominal aorta (left) and the inferior vena cava (right).

3.2 Cross Section of Extraperitoneal Pelvis

Viewing from the horizontal cross section of urethral sphincter and vagina (Fig. 1.8), sacrum, rectum, and other extraperitoneal organs can be found.

The normal retroperitoneal and pelvic extraperitoneal spaces are not very distinct on cross section making it difficult to determine their boundaries using CT and MRI images. However, it is necessary to identify whether tumors, especially large tumors present in these spaces, are located in the retroperitoneum (extraperitoneum) or intraperitoneum. In addition, a huge retroperitoneal tumor that expands far beyond the retroperitoneal space can occupy the normal position of the abdominal cavity and abdominal organs. Therefore, comprehensive understanding of the retroperitoneal or extraperitoneal space must be based on the structural anatomy of the abdominal and pelvic cavities, as well as the organs in the abdomen and pelvis.

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2 Characteristics and Clinical Manifestations of Retroperitoneal Tumor

Cheng-Hua Luo and Chengli Miao

1 Introduction

Primary retroperitoneal tumors (PRPTs) are a group of neoplasms that originate from the retroperitoneal space excluding those arising in the major retroperitoneal organs, such as the liver, duodenum, pancreas, spleen, kidney, suprarenal gland, ureters, and bone. Also excluded are metastatic malignancies from distant sites. Theoretically the tumors originating from the above retroperitoneal organs, e.g., duodenum, pancreas, and suprarenal gland, belong within the scope of "retroperitoneal tumors"; however, they are considered "visceral tumors" in academics. Many scholars still use the term "retroperitoneal tumor" instead of PRPTs. For convenience, in this book, PRPTs are hereinafter referred to as "retroperitoneal tumors."

Tumors located in pelvic retroperitoneum (including retroperitoneal, bilateral peritoneum, inferior and anterior of peritoneum) are also categorized within the scope of retroperitoneal tumors due to the fact they share common biological characteristics and therapeutic strategies with retroperitoneal tumors. The exception is tumors arising from the bladder and prostate.

The origin of retroperitoneal tumors is generally from soft tissue which is defined as non-epithelial extra-skeletal tissues exclusive of the reticuloendothelial system, glia, and supporting tissue of various parenchymal organs. Soft tissue is represented by the skeletal (voluntary) muscles, fat, and fibrous tissue, along with the feeding vessels. It also includes the peripheral nervous system because tumors arising from nerves present as soft tissue masses and are similar in both differential diagnosis and therapy. Embryologically, soft tissue is derived principally from mesoderm with contributions from the neuroectoderm.

Soft tissue tumors are a highly heterogeneous group of neoplasms that are classified based on histology; many of them resemble adult tissue. For example, lipomas and liposarcomas are tumors that recapitulate the normal fatty tissue to various degrees, while hemangiomas and angiosarcomas contain cells with characteristics of vascular endothelium. Within the various histopathological categories, soft tissue tumors are usually divided into benign and malignant types.

Benign tumors more closely resemble normal tissue and have a limited capacity for autonomous growth. These tumors exhibit little tendency to invade locally and have a low incidence of local recurrence following complete excision. To the contrary, malignant tumors or sarcoma is locally aggressive and capable of invasive or destructive growth, recurrence, and distant metastases. Radical surgery is required to ensure relatively complete removal of such tumors. However, the term "sarcoma" does not necessarily indicate the likelihood or rapidity of metastasis. Some types of sarcomas, e.g., malignant fibrous histiocytomas,

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frequently metastasize, whereas others rarely do. For these reasons, it is essential to qualify the term "sarcoma" by describing the degree of differentiation or the histological grade. "Well differentiated" and "poorly differentiated" are qualitative and subjective terms indicating the relative maturity of the tumor with respect to normal adult tissue. Histologic grade is quantitative and measures the degree of differentiation by employing a set of histologic and cytological criteria. It is well accepted that well-differentiated sarcomas are low-grade lesions, whereas poorly differentiated sarcomas are high-grade neoplasms. There are also intermediate or borderline lesions, whose malignant potential is difficult to be determined. Occasionally, benign tumors or non-tumorous lesions are present with malignant histological features but clinically behave like benign diseases; a canonical example would be pseudosarcomas.

2 Pathogenesis of Retroperitoneal Tumors

As with other malignancies, the pathogenesis and etiology of retroperitoneal tumor remain unclear. Recognized risk factors include physical and chemical factors, exposure to ionizing radiation, and genetic/inherited and acquired immunodeficiency. Due to the long latency period after exposure to hazardous factors and the interaction of multiple environmental and genetic factors, it is difficult to determine the exact cause of such tumors. Retroperitoneal sarcoma that arises from of benign tumors is extremely rare. We have treated several rare cases of benign teratoma that underwent malignant transformation. Malignant peripheral nerve sheath tumors mostly arise from benign type I neurofibromas (von Recklinghausen disease).

2.1 Environmental Factors

Environmental carcinogens have been implicated in the pathogenesis of retroperitoneal sarcoma; however, molecular mechanism has not been explored thoroughly (Newhouse and Thompson 1993). Asbestos is one of the most important environmental carcinogens. A person who inhales asbestos may develop mesothelioma afterward. Phenoxy acid herbicides, chlorophenols, and their contaminants, 2, 3, 7, 8- tetrachlorodibenzo-para-dioxin (TCDD) are involved in retroperitoneal sarcomagenesis. A causal effect of vinyl chloride on hepatic angiosarcoma has been established; this agent may also contribute to the development of retroperitoneal sarcomas.

Radiation exposure is associated with sarcomagenesis (Sindelar et al. 1993). Due to limited population who has undergone abdominal radiotherapy, radiation-induced retroperitoneal sarcoma is extremely rare, and the risk is very low compared to therapeutic benefit from radiotherapy. The incidence of radiotherapy-induced sarcoma has been reported between 0.03% and 0.8% in the literature (Argiris et al. 1995). The diagnostic criteria for radiotherapy-induced sarcoma include sarcoma development within the irradiated field of previous radiotherapy, histologic confirmation of the diagnosis, latency of at least 3 years between irradiation and the presence of a sarcoma, and the region bearing a sarcoma being normal prior to irradiation (Sheppard and Libshitz 2001). The most common postradiation sarcoma is malignant fibrous histiocytoma, which accounts for almost 70% of cases, followed by fibrosarcoma, malignant peripheral nerve sheath tumor, and angiosarcoma. Unfortunately, most postradiation sarcomas are high-grade lesions and diagnosed at a relatively late stage than their sporadic counterparts. Thus, the prognosis of these tumors is dismal, with a 5-year survival rate of less than 5%.

2.2 Oncogenic Viruses

Despite evidence that herpes virus 8 (HHV8) is the causative factor of Kaposi sarcoma, the role of oncogenic viruses in the evolution of retroperitoneal sarcomas is still poorly understood. Accumulating evidence supports the involvement of Epstein-Barr virus in the pathogenesis of smooth muscle tumors in patients with immunodeficiency syndrome or following therapeutic immunosuppression in organ transplantation settings (Lujan and Hoang 2003).

2.3 Immunologic Factors

As mentioned above, immunodeficiency and therapeutic immunosuppression plays a role in the development of retroperitoneal soft tissue sarcomas, particularly smooth muscle tumors and Kaposi sarcoma. Additionally, acquired immunodeficiency or loss of regional immune surveillance may also participate in the pathogenesis of the relatively rare angiosarcomas that arise in the setting of chronic lymphedema, either congenital or secondary to radical mastectomy, or infectious diseases (Naresh et al. 2007).

2.4 Genetic Factors

Numerous genetic diseases have been linked to retroperitoneal tumors (Legius et al. 1994). Classic examples are neurofibromatosis type 1 and type 2, which are previously referred to as peripheral and central neurofibromatosis, respectively. The causal gene for neurofibromatosis type 1 and type 2 is located in the pericentromeric region of chromosome 17 and chromosome 22, respectively. Some cases of retroperitoneal tumors combined with subcutaneous neurofibromatosis have been diagnosed and treated in our hospital. All of these patients had a family history of neurofibromatosis.

Familial adenomatous polyposis (FAP) and the variant Gardner syndrome are caused by adenomatous polyposis coli (APC) gene mutations, often accompanied by mesenteric fibromatosis. Retroperitoneal sarcoma is a type of tumor associated with hereditary familial cancer syndromes (Scott et al. 1996).

3 Epidemiological Characteristics of Retroperitoneal Tumors

Retroperitoneal tumors account for less than 0.5% of all neoplasms. Retroperitoneal tumors are mostly soft tissue tumors and account for 10–20% of the total soft tissue tumors. Of malignant retroperitoneal tumors, 55% are sarcomas. Primary retroperitoneal tumors can occur at any age, but most occur in the 50–60-year-old group as reported in the literature. However, 15% of retroperitoneal tumors occur in children younger than 10 years old. Men account for 50–67% of retroperitoneal tumors. It has been reported that 82% of primary retroperitoneal tumors are malignant, and 5–18% are benign. Many patients with retroperitoneal tumors are never diagnosed. The population incidence has yet to be reported in China. In the United States, soft tissue sarcomas account for less than 1% of all malignant tumors. Nevertheless, the incidence of such tumors has tended to increase worldwide. It is unclear whether this can be ascribed to a true increase in incidence, an improvement in diagnostic techniques, or more public attention paid to such tumors. Up to now, our team has reported 687 cases of retroperitoneal tumors (in China, 2014). Clinicopathological characteristics of our patient population are male 59%, female 41%, benign 25.2%, borderline 6.4%, and malignant 68.4%. The age of onset ranges between 0.3 and 80 years with the median age of 40 years.

4 Oncobiological Characteristics of Retroperitoneal Tumors

Successful therapy of any tumor should be based on understanding of its oncogenic and biological features. Regardless of histologic subtype, primary retroperitoneal tumors generally share the following four common biological phenotypes.

4.1 Expansive Growth Most of the Time

The most important feature is expansive growth while being rarely invasive. Primary retroperitoneal tumors, either benign or malignant, grow by expansion and seldom infiltrate the surrounding tissues or organs, which distinguishes them from other cancers. This unique feature of tumor growth usually causes compression or displacement of adjacent tissue or organs. There are often no symptoms until the tumors become quite large. Due to non-invasiveness, intact capsules

can be identified even for large tumors. A pseudocapsule formed by the tumor pushing against surrounding tissues may be completely resected.

4.2 Tumors Generally Have Intact Capsules

The vast majority of retroperitoneal tumors, either benign or malignant, have complete capsules. This structure can be clearly identified from preoperative imaging, allowing surgeons to perform tumor resection. The key step is to localize accurately the tumor capsule during surgery, sharply dissect the tumor along that line, and thus achieve complete dissection of the tumor while simultaneously minimizing bleeding.

4.3 Tumors Seldom Develop Distant Metastases

In most cases, malignant retroperitoneal tumors, even of very long duration and quite a large size, rarely metastasize through the blood vessels to various distant organs and surrounding lymph nodes, instead, it primarily grows locally. Most patients with retroperitoneal tumors die of organ dysfunction (or failure) resulting from local malignant growth rather than from metastases to distant organs. Even in a late stage, these tumors mainly metastasize through blood vessels and very rarely through lymph nodes. This feature provides the principle for thorough surgical resection of retroperitoneal tumors or combined resection of involved organs/tissues without the corresponding lymph nodes dissection.

4.4 Malignant Retroperitoneal Tumors Are Prone to Local Recurrence

According to the literature and our experience, about 60% of retroperitoneal tumors relapse after surgical resection (DeMatteo et al. 2000). Local recurrence at primary sites or local planting is very common. Satellite lesions are prevalent surrounding retroperitoneal sarcomas, serving as the origin of local recurrence. For recurrent tumors, surgical resection should be strongly considered. Another common cause of recurrence is that the surgeon fails to eradicate the residual tumor tissues adjacent to blood vessels and vital organs, often due to lack of experience. Surgeons familiar with biological features of retroperitoneal tumors should seize every opportunity to surgically remove a large retroperitoneal tumor and perform a complete radical resection. For patient with recurrent tumors, multiple resections are still feasible and are highly recommended.

4.5 Criteria for Total Retroperitoneal Fat Lipectomy in the Treatment of Retroperitoneal Liposarcoma

Retroperitoneal liposarcoma is the most common (41%) primary retroperitoneal soft tissue sarcoma (Nagy et al. 2013). It is difficult to diagnose in its early stage as generally patients do not consult the doctor until the mass has grown to a very large size. Thus, retroperitoneal liposarcoma has a low resection rate and a high recurrence rate. The 5-year local recurrence rate was reported to be 40–60%, accounting for death in 75% of cases.

Surgical resection is the primary therapy of retroperitoneal liposarcoma; however, the diverse biological characteristics and complicated anatomical structures of retroperitoneal liposarcoma have contributed to the high recurrence rate, which seriously affects the clinical outcome (long-term survival rate) of these patients and is the reason why surgical resection has become a great challenge.

The experience of surgery for retroperitoneal liposarcoma has mainly been reported in retrospective studies which limits the strength for recommendation in evidence-based medicine. Nevertheless, it is excited to see some relatively widely accepted results. Multivariate analysis has indicated two important prognostic factors influencing the specific survival rate of retroperitoneal

liposarcoma, i.e., tumor pathological subtypes and gross resection margins. The Memorial Sloan-Kettering Cancer Center has reported the 5-year survival rate of low-grade malignant mucinous liposarcoma as approximately 90% for the well-differentiated subtype with ≤5% round cell area, whereas 30–50%, 60%, and 75%, respectively, for high-grade malignancies, i.e., pleomorphic, round cell (>5% round cell area), and dedifferentiated subtypes (Dotan et al. 2006).

Additionally, the scope of resection is an important predictor for recurrence of retroperitoneal liposarcomas. Complete removal of the tumor to achieve R0 resection (absence of residual tumor cells at the margin under microscope) is an ideal result. However, this goal is almost impossible to be achieved in most retroperitoneal liposarcomas. Firstly, at the time of surgery, retroperitoneal liposarcoma is usually very large and adhere to the surrounding organs. Thus, it is extremely difficult to separate the outer margin of tumor from normal tissue to achieve the entire R0 resection. For this reason, it is well accepted that gross complete resection (R1) of retroperitoneal liposarcoma can significantly reduce its recurrence, which has become a major goal that surgeons in the treatment of retroperitoneal liposarcomas.

In order to achieve gross total resection (R1) of retroperitoneal liposarcomas, some centers strongly recommend regional resection including co-resection of the tumor-infiltrated organs (Strauss 2014). Twenty years ago, many scholars advocated the removal of retroperitoneal liposarcoma combined with the ipsilateral kidney. However, nowadays accumulating evidence has supported that removal of the kidney does not affect the disease-specific survival rate of retroperitoneal liposarcomas. Biological characteristics of renal parapharyngeal sarcomas have shown involvement of renal peritoneal fat capsule in 15%, involvement of renal parenchyma in 9%, and involvement of renal vein in 3% of patients with no involvement of renal tissue in >73% of patients. This observation indicates that retroperitoneal liposarcomas rarely invade renal parenchyma compared with other sarcomas. We now believe that resection of the kidney should be avoided unless the renal hilus circumference is invaded, while the perirenal fat capsule must be removed during surgery for retroperitoneal liposarcomas. Extended surgery, including combined multiple organ resection and perirenal fat capsule excision, namely, regional resection has been widely recognized. European scholars who firstly explored this area have reported that the 5-year recurrence-free and overall survival rate after regional resection of retroperitoneal liposarcoma could approach 55% and 75%, respectively.

Can surgical procedures reduce the recurrence rate of retroperitoneal liposarcoma? This is a vital scientific challenge faced by retroperitoneal tumor surgeons worldwide.

Further investigations have shown that retroperitoneal liposarcoma is often multifocal with satellite foci in normal fat far away from the main tumor body. Many recurrent retroperitoneal liposarcomas are not in situ, but grow at multiple distant sites from the primary location. The retroperitoneal fat invaded by liposarcoma is no longer normal but is "regionally altered (transformed)." It is very difficult to identify these microsatellite lesions in fat tissue during surgery. Based on the above findings, we propose a new surgical procedure for retroperitoneal liposarcoma: total ipsilateral retroperitoneal lipectomy.

The range of total ipsilateral retroperitoneal lipectomy is delineated by the upper border (diaphragm surface), inferior border (iliac vascular surface), lateral border (abdominal wall), medial border (inferior vena cava [to the right] or abdominal aortic [to the left] surface), posterior border (psoas muscle and iliopsoas muscle surface), and anterior border (colon and mesocolon). The contents of surgical excision include the liposarcoma, adipose tissue, perirenal fat capsule, and other organs, which are invaded by the tumor in the above-mentioned range and cannot be separated.

Autopsy findings (unpublished data) have suggested that the ipsilateral retroperitoneal fat is anatomically a contiguous "organ," both from front aspect of view (Fig. 2.1) and from back aspect of view (Fig. 2.2), and it can be treated as an "organ" with no important functions. Total retroperitoneal lipectomy is equivalent to total

Fig. 2.1 Anterior view of autopsy findings in left-sided retroperitoneal fat

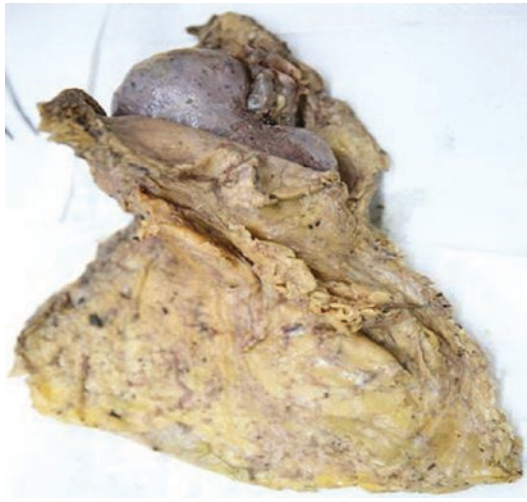

Fig. 2.2 Posterior view of autopsy findings in left-sided retroperitoneal fat

resection of the ipsilateral retroperitoneal fat tissue. It is a safe operation without causing significant physiological or pathological complications. The author is currently conducting a prospective RCT study on total retroperitoneal lipectomy vs. extended regional resection of retroperitoneal liposarcoma in order to assess the clinical value of this procedure.

5 Clinical Presentations of Retroperitoneal Tumor

Retroperitoneal tumor growth in the loose retroperitoneal connective tissue space is limited to the surrounding region (but rarely grows posteriorly and penetrating through the back). Small tumors are usually asymptomatic and can only be possibly detected by physical examination. When the tumor grows much bigger, it causes symptoms as a result of compression and displacement or invasion of adjacent organs. Clinical symptoms of retroperitoneal tumors are determined by specific properties of their primary sites. Tumor compression or infiltration of blood vessels, nerves, or other vital organs or structures can lead to corresponding symptoms and syndromes (Felix et al. 1981).

The most common symptom caused by retroperitoneal tumors is pain, including abdominal pain, low back pain, and leg pain and so on. Abdominal pain or back pain occurs in 44–75% of patients. The nature of pain may be dull, sharp, excruciating, or colicky. Pain mainly localizes at the site of the tumor, however sometimes it is difficult to determine the accurate location of the pain. Direct compression by tumor is the most common cause of abdominal pain, while hydronephrosis as a result of ureteral compression can indirectly induce low back pain. Fortunately, abdominal pain and low back pain usually do not lead to loss of activity.

Gastrointestinal symptoms such as nausea, vomiting, change in bowel habits, and constipation are frequently seen in these patients. Bloating may occur in 4–35% of patients, and some cases even develop intestinal obstruction. Anorexia, weight loss, weakness, and fatigue are observed in 40–50% of patients with advanced-stage retroperitoneal malignant tumors, compared to only 3% of those with early stage disease.

Patients sometimes develop urinary and reproductive symptoms since retroperitoneal tumors are located in the pelvis, adjacent to the kidney or ureters. Urinary tract symptoms such as hematuria, frequent urination, urgent urination, urodynia, and dysuria are common, whereas oliguria

or anuria is rare. These symptoms are caused by urinary tract compression, with or without direct involvement of the kidneys and ureters. Patients with retroperitoneal tumors may develop azotemia (e.g., skin itching) caused by bilateral ureteral obstruction.

Retroperitoneal tumors arising from pelvic peritoneum or spreading to the pelvis may compress or invade sacral or lumbar plexus root, resulting in low back pain that radiates toward unilaterally to both lower extremities. Spinal cord compression caused by tumor infiltration of intervertebral foramen may lead to incontinence and lower limb paralysis. Perineal and lower extremity edema and varicose veins result from obstruction of pelvic veins and lymphatic flux when tumors spread to the pelvis. In this respect, patients present with unilateral and even bilateral lower extremity edema. Tumor-induced acute obstruction of the inferior vena cava leads to lower extremity edema; however, this is not the case in chronic obstruction due to the abundant collateral circulation within the retroperitoneum.

Fever has been reported in 10% of patients with retroperitoneal tumors. It is common in patients with large retroperitoneal liposarcomas, especially in relapsed cases. This may be attributed to dramatic necrosis (or necroptosis) within the tumor, and fever can abate immediately after resection of the tumor. Cancer fever classically is related to retroperitoneal lymphomas.

If retroperitoneal tumors compress the portal or hepatic veins, ascites and abdominal varicose veins may occur; a few cases may experience hematemesis. Occasionally, hypoglycemia may be observed, attributable to insulin-like factors secreted by poorly differentiated retroperitoneal sarcomas, or accelerated utilization of fatty acids pool by large tumors with high rate of metabolism. If tumors infiltrate through the hollow organs within the abdominal cavity, patients may develop acute or chronic gastrointestinal bleeding.

The first visit to clinic for a patient with retroperitoneal tumor usually takes place at 3–6 months after the appearance of symptoms. Sometimes retroperitoneal tumors are detected in patients who receive physical examination only because of abdominal bloating, satiety, and heaviness. About 30% of patients with retroperitoneal tumors initially present with an asymptomatic abdominal mass. As the first presentation of retroperitoneal tumors, such mass is mostly palpated by adult patients themselves or detected by their parents or pediatricians of pediatric patients. Due to lack of specific manifestations, patients with retroperitoneal tumors have generally developed advanced disease when they present with palpable masses, abdominal pain, and gastrointestinal symptoms.

Although the patients' medical history may be suggestive of intra-abdominal diseases, physical examination is the key step in diagnosing retroperitoneal tumors. Abdominal mass can be detected by physical examination in more than 90% of patients vs. only 5% of pelvic masses. Masses with different sizes located in the pelvis may be palpated by digital rectal or vaginal examination, 80% of which result in no tenderness. Retroperitoneal tumors generally do not move with respiratory movements. Tumor movability and hardness are quite important indicators in determining whether the tumor has become fixed to the abdominal wall, pelvic wall, or bone structures. A hard and fixed mass is more suggestive of a malignant nature, teratoma, or hamartoma, etc., while a soft and flexible mass is more indicative of lipoma or liposarcoma. Malignant aggressiveness and resectability of retroperitoneal tumors are not always conferred by the sizes of the lesions.

Metastases of retroperitoneal tumors can cause hepatomegaly, compression, and displacement of the liver. Venous reflux disorders resulting from portal vein obstruction leads to ascites in about 15% of patients with retroperitoneal tumors. Varicose veins of the testicles are clinical manifestations of spermatic vein obstruction, indicating left renal vein obstruction if it occurs on the left side. Hypertension is common in patients with extra-suprarenal paragangliomas. Bleeding tendency is observed in patients with vascular sarcomas.

Other clinical manifestations of retroperitoneal tumors include abdominal and flank tension, abdominal distension, splenomegaly, lymph nodes enlargement, pale face, coughing, shortness of breath, and venous thrombosis, as well as intra-abdominal bleeding, jaundice, cachexia, etc.

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CT in Diagnosis of Retroperitoneal Tumors

3

Yuanchun Feng

Images of retroperitoneal tumors lack specificity as different tumors resemble one another to and often remain undetectable until they have grown quite large, making diagnosis difficult. Major challenges in diagnosis include how to accurately locate the tumor, how to evaluate the extent of tumor invasion, how to identify the tumor qualitatively, and how to determine the cellular origin of the tumor.

It is therefore very important to understand the normal anatomy of retroperitoneal space. The retroperitoneal space is a potential space posterior to the peritoneum and anterior to the posterior abdominal wall, located between the parietal peritoneum and transverse abdominal muscle, originating downward from the diaphragm, descending to sacral promontory and iliac crest, and communicating with the pelvic extraperitoneal space inferiorly. The retroperitoneal space contains a large amount of loose connective tissue, and it can be divided into three compartments:

1. The anterior pararenal space between posterior peritoneum and prerenal fascia, containing the pancreas, descending horizontal parts of the duodenum, ascending colon, mesenteric vessels, lymph nodes, as well as the vessels of the liver, pancreas, and spleen but very small amounts of adipose tissue
2. The perirenal space between prerenal fascia and post-renal fascia, containing the kidney, adrenal gland, renal artery and vein, and perirenal fat
3. The posterior pararenal space between the post-renal fascia and transverse fascia, which is filled with fat, blood vessels, and lymphatics, but no major organs in there. In addition, the pelvic retroperitoneal space consists of the pre-bladder space, para-bladder space, and perirectal space

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1 Implication and Limitations of CT Scanning

1.1 Implication of CT Scanning in the Diagnosis of Retroperitoneal Tumors

Plain and enhanced CT scanning of the abdomen is able to provide significant information about the retroperitoneal anatomy. Based on an in-depth analysis of CT images, lesions can be accurately localized. The specific nature (cystic, solid, or cystic-solid), appearance (round, oval, irregular, or lobulated), size, relation to adjacent organs and tissue structure, and boundaries

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(clear or ill-defined, namely, halo sign) (Pilavaki et al. 2004)—a retroperitoneal tumor—may be assessed according to the image intensity. CT scanning can rule out most tumors derived from the retroperitoneum rather than from the abdominal viscera and, more importantly, identify the specific growth pattern and invasion behavior of tumors. Differential CT attenuation cannot determine specific components of tumors (e.g., fat, muscle, soft tissue, mucus, and fibrous septa). The diagnosis of a retroperitoneal tumor can only be confirmed by a combination of clinical information and imaging features, which enables surgeons to make a tentative diagnosis, select an optimal surgical approach, as well as evaluate efficacy and recurrence in postoperative follow-up. Therefore, CT is a preferred major choice for detecting retroperitoneal tumors.

1.1.1 CT Determines the Exact Location of Retroperitoneal Tumor

In most cases, primary retroperitoneal tumors will have grown quite large before they are detected. These tumors result in compression, displacement, deformation, or even invasion and destruction of adjacent organs. The fatty spaces may become blurred and narrowed if the tumors involve posterior abdominal wall and pelvic wall muscles. Axial thin-section CT scan in combination with coronal and sagittal multi-planar CT reconstruction can multi-directionally display the morphology, structure, and location of tumors as well as the relationship between tumors and the posterior peritoneum (Mizuki et al. 2003, Cohan et al. 1998, Lane et al. 1989).

1.1.2 CT Assesses the Invasion Range of Retroperitoneal Tumor

CT scans have a high resolution for density and spatial distribution. Multi-slice spiral CT scanning can achieve extremely thin section reconstructions. Based on the original thin-slice axial CT scanning, images in sagittal and coronal planes can be reconstructed using CT post-processing workstation. This post process plays a vital role in displaying the growth pattern and invasion scope of retroperitoneal tumors, by visually localizing the exact involvement range of tumors and demonstrating subtle changes in the relationship of the larger tumor with surrounding organs or tissues. (a) Among retroperitoneal organs, retroperitoneal tumors most frequently invade the kidney(s), which may involve the perirenal fat capsule contour resulting in deformation by compressing the renal parenchyma and even hydronephrosis of the renal pelvis and calices. Retroperitoneal tumors in the middle and lower abdomen often invade unilateral ureters, leading to hydronephrosis secondary to ureteral stenosis or invasion-induced obstruction. (b) When the tumor grows adjacent to a unilateral psoas major, it may compress, deform, or even invade the muscle. (c) The abdominal aorta, inferior vena cava, and renal vein may also be displaced as a result of compression. When a tumor grows quite large and occupies the entire space of abdominal cavity, the tumor often invades the hepatic hilus, resulting in a series of secondary pathologic changes. In this setting, it is very difficult to reveal anatomical structure even with CT scans.

1.1.3 CT Distinguishes Benign from Malignant Retroperitoneal Tumors

Retroperitoneal tumor accounts for 0.07%–0.2% of all types of neoplasms, of which approximately 60–85% are malignant (Oldendorf and Zeitler 1996). Tumor size, boundary, necrosis, calcification, and other factors indicate its nature (Nzkashima et al. 1997). Benign retroperitoneal tumors are relatively rare, including lipomas, paragangliomas, hemangiomas, lymphangioma, benign teratoma, leiomyoma, and benign neurogenic tumors. Malignant retroperitoneal tumors include iposarcoma, leimyosarcoma, malignant neurogenic tumors, lymphoma, malignant fibrous histiocytoma (MFH), vascular sarcoma and malignant teratoma.

It is challenging to qualitatively determine the nature of a retroperitoneal tumor before surgery. Malignant retroperitoneal tumor without a capsule can invade surrounding structures (Hughes et al. 2005). For this reason, CT scan findings often indicate malignant lesions under the following

circumstances: (a) tissue and blood vessels adjacent to the tumor are invaded, with metastases to lymph nodes and distal organs; (b) the tumor has irregular margins with ill-defined boundaries with surrounding organs; the fatty space around the organs disappears and instead displays abnormal density; (c) the tumor directly invades the organs or bones, leading to distant metastases or bone destruction; and (d) enhanced CT scans show significant inhomogeneity and abnormal enhancement, suggesting the ample blood supply to the tumor. Malignant retroperitoneal lesions should be considered after ruling out benign hemangioma.

1.1.4 CT Identifies the Cellular Origin of Retroperitoneal Tumor

Familiarity with the growth pattern, characteristic features, enhancement features, regional distribution, as well as clinical manifestations of retroperitoneal a tumor is essential to determine its histological type on the basis of CT scans (Hughes et al. 2005; Lane et al. 1989; Sung et al. 2003).

Growth Pattern of Tumors and Distribution of Lesions

Some tumors have special growth patterns, for example, deep cystic lymphangioma originating from the retroperitoneal space creeps along the mesentery, fascia or muscle, large blood vessels, and nerves. By contrast, retroperitoneal neurofibromas and schwannomas are mostly located in the middle area of abdomen or presacral and retroperitoneal space and often cause unilateral foraminal expansion. CT can clearly display the lesion and reveal its progression and traveling direction. For example, paragangliomas grow and extend along the aortic sympathetic chain with homogeneous soft tissue density accompanied by central necrosis.

Characteristic Components of Retroperitoneal Tumors

1. Fat: fat is a common component of lipomas, liposarcomas, and teratoma; CT displays fat-containing lesion as obviously a lower density than water.
2. Mucus: mucus has a lower density than muscle within lesions but a higher density than water. After injection of contrast media, mucus-containing tumor exhibits mild enhancement or gradually delayed enhancement, which is observed in neurogenic tumors, mucinous liposarcoma, and mucinous malignant fibrous histiocytoma. The underlying pathological mechanism is the enhancement of mucus matrix constituent of the tumor seen in delayed enhanced CT scans.
3. Cyst: a cystic retroperitoneal tumor may be considered as a lymphangioma, cystic teratoma, and neurogenic tumors.
4. Soft tissue: a substantive tumor with the density of soft tissue occurs in a variety of sarcomas, lymphomas, as well as benign fibromas. If cystic degeneration or necrosis is observed in solid tumors, ectopic pheochromocytoma and schwannoma should be considered; however, cystic degeneration is rarely seen in neurofibroma.
5. Calcification: calcification is suggestive of malignant fibrous histiocytoma, neuroblastoma, and teratoma.

Lesion's Hallmarks of Enhancement

The solid elements of hypervascular tumors (pheochromocytoma, paragangliomas, etc.) or vascular-origin tumors will be significantly enhanced. Tumors with moderate blood supply (e.g., malignant mucous fibrous histiocytoma and leiomyosarcoma) show significant heterogeneous enhancement. Tumors that lack a rich blood supply, including low-grade malignant liposarcoma, lymphangioma, and the majority of benign tumors, exhibit no significant enhancement. Dynamic enhanced CT helps to distinguish specific tumors, for example, ganglion cell tumor (contain abundant mucus matrix) characterized by delayed enhancement (Ota et al. 2001). Hypervascular tumors refer to them as originated from vessels, tumors with moderate blood supply including mucinous malignant fibrous histiocytoma and leiomyosarcoma. Tumors with poor blood supply are represented by low-grade liposarcomas, lymphomas, and the majority of benign tumors. Abnormal blood supply may suggest the nature of a tumor, benign vs. malignant. When tumors grow to a certain extent, malignant tumors

steal blood supply from the surrounding adipose tissue and fascia vascular network or seize parasitic blood supply by invading adjacent organs.

1.2 Multi-slice Spiral CT: Great Post-processing Functional Capabilities

Multi-slice spiral CT has great post-processing capabilities: a multiphase enhanced scanning and post-processing technology can provide complete information on anatomy, localization, and invasion of lesions. As a noninvasive examined method, it can simultaneously assist in solving practical clinical problems and improve diagnostic accuracy. Multi-planar reconstruction (MPR) displays any cross section of a tumor, the anatomical morphology of adjacent organs as well as their relationship at any one or multiple sections, and filters out overlapping structures. By reconstructing the image with the maximum density that encodes the volume data of the projection trajectory, MIP (maximum density projection) technique truly reflects the blood supply of the lesion, and generates a sharp contrast between the tumor and its surrounding structures. Shaded surface display (SSD) can decipher three-dimensional relationships and surface morphology of mutually overlapped or distorted structures and is suitable for identifying complex anatomical features. SSD can directly display the morphology of lesions, spatial relationship between organs and tumors within the abdomen, and involvement of the outer wall of organs, thus providing valuable clues for the development and implementation of a surgical strategy. However, SSD has limited capacity to elucidate subtle structure of the lesion. Combining with shadow depth, shaded surface display, multi-angle rotation, and proper cutting-edge density, SSD encodes different structures with different colors and displays simultaneously the images of either superficial or deep structures, thus creating a stronger three-dimensional impression. It can demonstrate three-dimensional spatial relationships among organs, lesions, and the surrounding structures. For example, with multi-slice spiral CT urography, the ureteral involvement and consequent stricture can be reconstructed (Chow and Sommer 2001; Ohnesorge et al. 1999).

1.3 Limitations of CT in Retroperitoneal Tumors

For example, vivid visibility of color, texture, subtle adhesions, and the tumor capsule on CT is inferior to visual inspection by human eyes. Lesions with complicated presentations may be misdiagnosed. Radiologist may incorrectly locate large retroperitoneal tumors that have changed their anatomical relationships with surrounding organs and vessels. CT scan is also not suitable for identification of special pathological features.

2 CT Manifestations of Various Retroperitoneal Tumors and Tumor-Like Lesions

2.1 Benign Retroperitoneal Tumor

2.1.1 Retroperitoneal Lipoma

Retroperitoneal lipoma is a common benign retroperitoneal tumor, which commonly occurs in patient age 40–60 years with a ratio of 2:1 between male and female. It is most often found in the paraspinal and pararenal areas, with the same density as normal adipose tissue on CT. Adipose tissue has CT attenuation ranging from −80 to −130 Hu, with uniform density as well as clear smooth boundaries. A capsule may envelope the lesion. Structure within the tumor is uniform occasionally with tiny septum or stripe-like fibrous tissue, which is essential to distinguish lipomas from well-differentiated liposarcomas.

2.1.2 Teratoma

Each component of a benign teratoma is distinctive on CT images. Adipose presents negative CT attenuation with low density, muscle and soft tissue have density similar to that of solid organs, fluid displays cystic density shade, and dental or the bone shows intensive calcification shade.

Lesions may tightly adhere to with surrounding tissues (Figs. 3.1, 3.2, 3.3, 3.4, and 3.5).

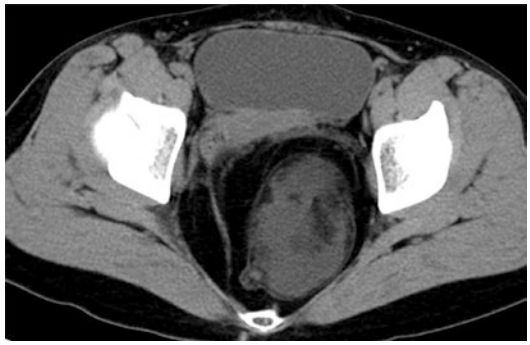


Fig. 3.1 CT axial plain image identifies a large lesion containing fat and soft tissue density anterior to coccyx, with punctate calcification, well-defined boundary, and uterine compression

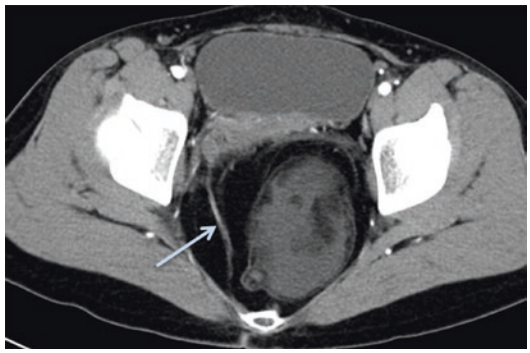


Fig. 3.2 Contrast-enhanced CT axial image in arterial phase displays no enhancement of the solid portion or the fat content but marked enhancement of the fibrous septa in the lesion (↗)

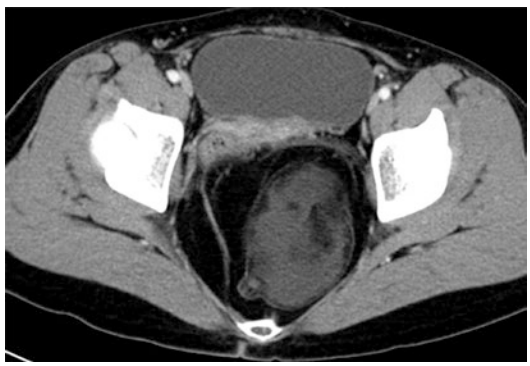


Fig. 3.3 Contrast-enhanced axial image in venous phase displays no marked enhancement of solid components within the lesion but enhancement of the partition

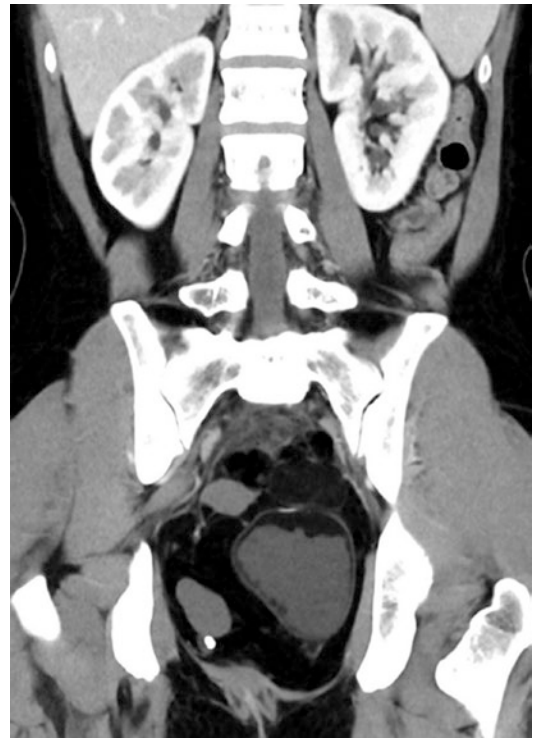


Fig. 3.4 Contrast-enhanced coronal image in venous phase shows multiple solid components within the lesion. Large solid lesion is well-encapsulated with a little calcification, and bone shape of the pelvis is intact

2.1.3 Schwannomas and Neurofibromas

It is difficult to distinguish schwannomas from neurofibromas as they present similar CT manifestations. CT images frequently display round or oval tumors with lower density than muscle and soft tissue, confined by clear smooth boundaries. If cystic degeneration is observed within schwannoma and neurofibroma, malignant transformation should be suspected. Neurofibromatosis can be multiple, and other benign neurogenic tumors are solitary (Schwannomas as shown in Figs. 3.6, 3.7, 3.8, 3.9, and neurofibroma as shown in Figs. 3.10, 3.11, 3.12, and 3.13).

2.1.4 Paraganglioma

Paraganglioma, also known as extra-adrenal pheochromocytoma, develops at extra-adrenal sites, among which the retroperitoneal space is the most common location. CT shows a solid mass in the retroperitoneum (para-aorta and

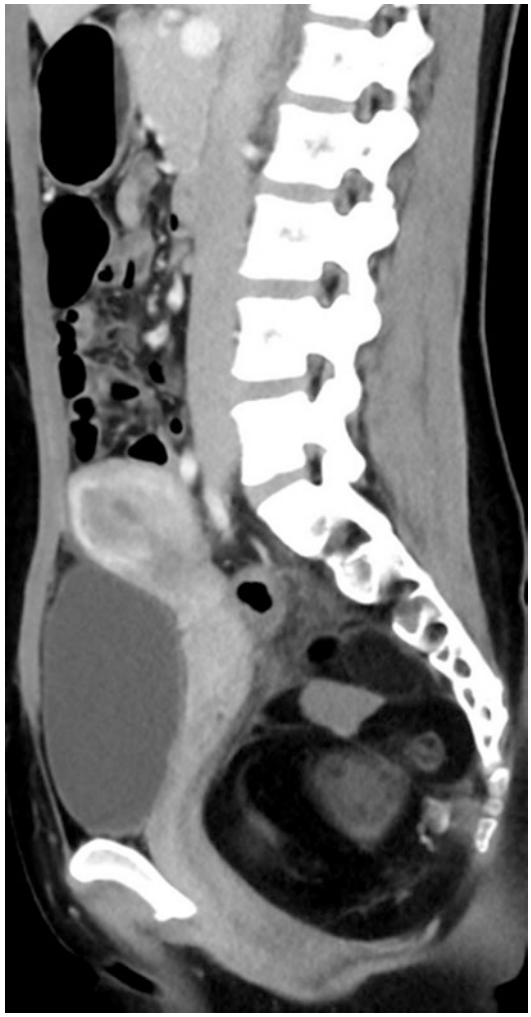


Fig. 3.5 Contrast-enhanced sagittal image in venous phase demonstrates the lesion occupying the entire small pelvis and pushing the uterus, resulting in elongation of uterine cervix, but maintaining clear demarcation. Rectum that is invisible within the midline structure is pushed toward the right. The boundary between the sacrum and coccyx is clear and smooth

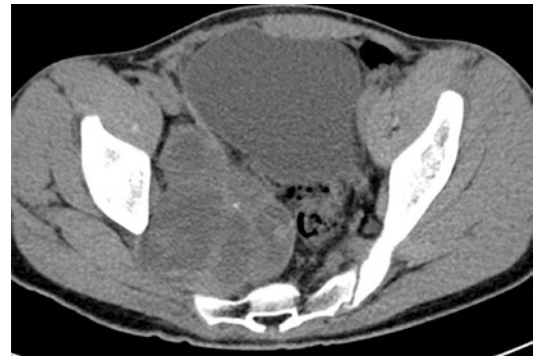


Fig. 3.6 CT axial plain image identifies a lobulated mass anterior to the right sacroiliac joint with an inhomogeneous internal density. The main lesion area has lower density than muscle tissue, with fibrous partitions and punctate calcification internally and smooth margin. Intestinal structure is pushed toward the left side

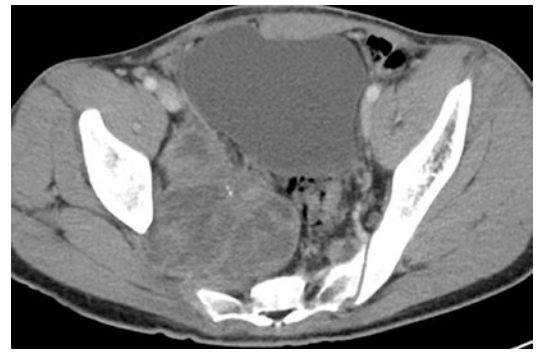


Fig. 3.7 Contrast-enhanced CT axial image displays enhancement of the partition within the lesion but no significant enhancement of the contents, with a more clearly boundary. The adjacent bone is intact

pararenal hilum), regularly or irregularly shaped, with internally heterogeneous density, adequate blood supply, visible intra-tumor necrosis and calcification, and a clear smooth boundary. After injection of contrast media, the lesion is remarkably inhomogeneous enhanced. Spiral CT and CT angiography reveal clear relationships of a representative tumor with the abdominal aorta/renal artery or liver/kidney, with a visible tissue space. The abdominal aorta and/or IVC are often displaced as a result of compression.

2.1.5 Retroperitoneal Cysts

Retroperitoneal cysts can be divided into simple, lymphocytic, and vasogenic types. CT shows smooth margins, thin-walled water-like density shade, and round or oval in shape. Lymphatic cyst can be solitary or multiple with mildly enhanced cystic walls. It frequently penetrates into the existing structures and vascular space, or encircles adjacent vessels, characterized by the floating aorta sign (Mizuki et al. 2003).

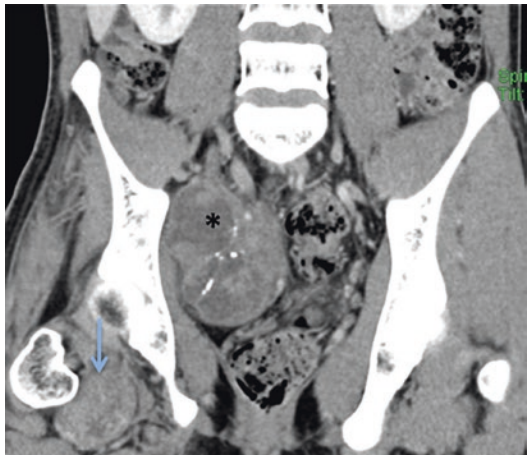


Fig. 3.8 Contrast-enhanced CT coronal image identifies a lobulated lesion, presenting with more calcification foci and unenhanced necrotic areas within the lesion (*). Another smaller lesion (↓) is visible within the soft tissue inferior to the right femoral head

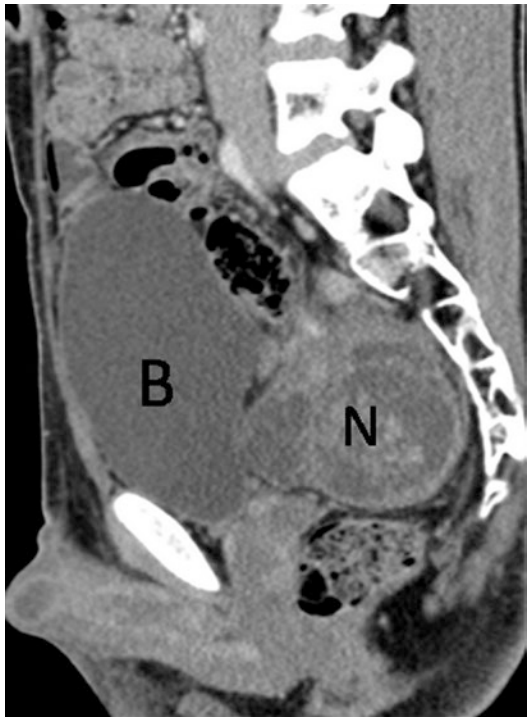


Fig. 3.9 Contrast-enhanced CT sagittal image identifies that the lesion (**N**) is pushing slightly forward to the posterior-inferior portion of the bladder (**B**). The rectum and sigmoid colon are pushed to the left side of the midline. There is a well-defined boundary between the sacrococcygeal bone and the lesion

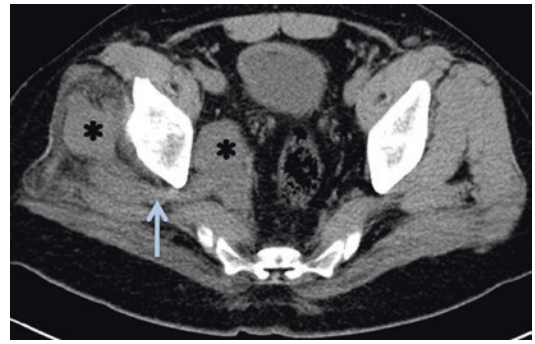


Fig. 3.10 CT axial plain image identifies multiple nodules (*) and lumpy soft tissue (↑) which are interconnected medially and laterally to the right iliac bone. The lesion is of homogeneous density with a well-defined boundary

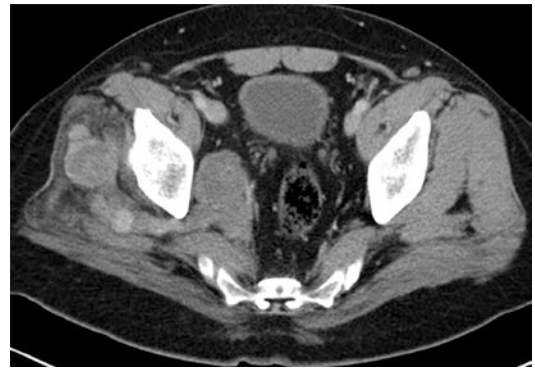


Fig. 3.11 Contrast-enhanced CT axial image displays inhomogeneous enhancement of the lesion and inhomogeneous enhancement of foci lateral to the iliac bone, with a well-defined boundary

2.1.6 Retroperitoneal Fibrosis

Idiopathic retroperitoneal fibrosis or inflammatory retroperitoneal fibrosis and other benign lesions are discussed herein except for fibrosis secondary to malignancies. The pathogenesis of idiopathic retroperitoneal fibrosis remains unclear. CT images demonstrate lesions located in the central retroperitoneum, plaque-like, and 2–5 cm in diameter thick. Lesions are significantly enhanced after contrast media injection, while it is difficult to distinguish such lesions from enlarged retroperitoneal lymph nodes. Widely spread lesions often encapsulate the majority of blood vessels and ureters in retroperitoneum, leading to stenosis.

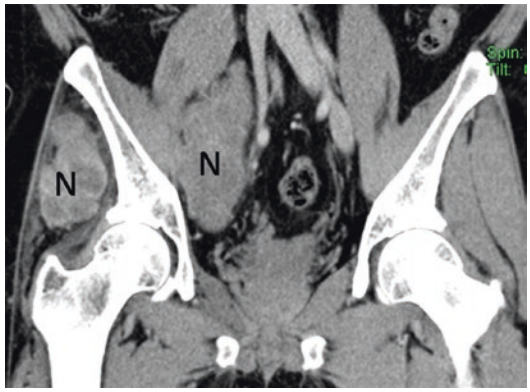


Fig. 3.12 Contrast-enhanced CT coronal image demonstrates that the lesion (N) is divided into two portions by the pelvis, internal and external, at the coronal level, which are in slightly different patterns of enhancement. Irregular necrosis is obvious within the lesion medial to the iliac bone (an area of low density). There is a well-defined boundary between the lesion medial to the iliac bone and the right psoas major and iliacus. The right external iliac vein is migrated toward the left under the compression

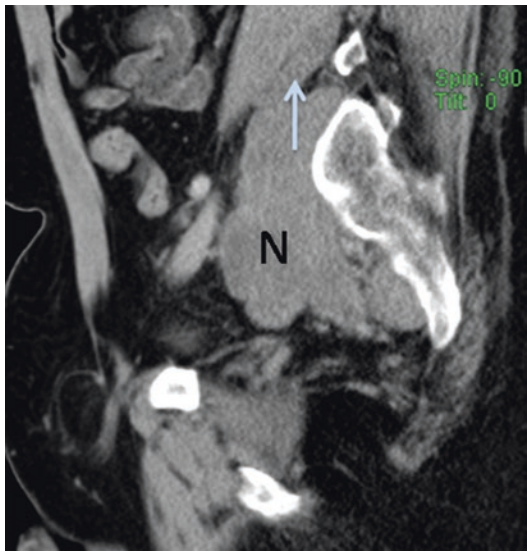


Fig. 3.13 Contrast-enhanced CT sagittal image identifies lobulated growth of lesions (N) medial to the right iliac bone, with a clear demarcation, and slightly heterogeneous enhancement. The strip-like shadow at the inferior margin of the lesion is thickened nerve root within the right foramen between the L5-S1 vertebra (↑). The inferior portion of the nerve root merges into the lesions medial to the right iliac bone. The posterior portion of the lesion closely attaches to the sacral vertebrae but does not infringe the sacrum

2.2 Malignant Retroperitoneal Tumors

2.2.1 Retroperitoneal Liposarcoma

Liposarcoma is the most common type, of retroperitoneal tumors, which grows quite large as they are hidden in the deep retroperitoneal region and difficult to find at an early stage. The tumor is irregular shaped, with an ill-defined border and heterogeneous density, containing fatty components. Malignant retroperitoneal tumor can be divided into five histological subtypes: well differentiated, dedifferentiated, myxoid, round cell and pleomorphic. The tumor exists rarely in single subtype but frequently in multiple subtypes (mixture):

1. The well-differentiated subtype is mainly composed of adipose tissue and also containing a small amount of fibrous component. Strip- or sheet-like blurred fibrous septum is seen in the background of fat density. The fatty element is not enhanced after contrast media injection, whereas the septum is enhanced mildly or moderately. Well-differentiated liposarcoma is the most common subtype of retroperitoneal liposarcomas.
2. Dedifferentiated liposarcoma is generally a large lesion with multiple nodular fields of fat density as well as scattered solid fields of non-fat density. Notably, the solid areas are often necrotic, without distinct boundaries to the fat areas. Enhanced CT often shows significantly enhanced solid elements.
3. Pleomorphic liposarcoma is less common. Well-differentiated liposarcoma is often mixed with various amounts of pleomorphic, multivacuolated, bubble-like patterns of lipoblastoma cells. Therefore, CT mainly suggests a soft tissue mass, with the signal intensity similar to that of skeletal muscle on both plain and enhanced scans.
4. Myxoid liposarcoma is mostly metastatic derived from distant sites rather than primary (which is very rare). Myxoid tissue is the major constituent with unenhanced CT attenuation of 16–30Hu. The cystic wall is enhanced after contrast injection, wherein mesh- or island-like enhancement is visible.

A delayed scan shows progressive enhancement, to a lesser extent than skeletal muscle.

5. Round cell liposarcoma is seen as a soft tissue mass, almost without any fatty element. After contrast injection, the lesion is significantly enhanced, homogeneous in nature, almost without necrosis. Such lesion is often metastatic from other sites and extremely rare from the primary site (Figs. 3.14, 3.15, 3.16, 3.17, and 3.18).

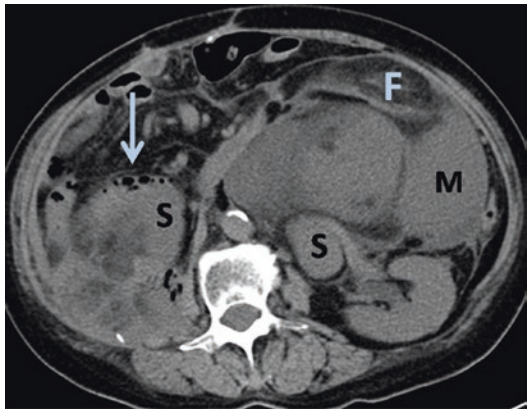


Fig. 3.14 CT axial plain image identifies a patient with recurrent differentiated liposarcoma post-operatively. Multiple irregular lumpy shadows of mixed density can be visible within the left retroperitoneal space. The lesion foci contain fat (F), mucus (M), soft tissue (S) and fiber elements. No obvious encapsulation is observed. A larger lesion is closely related to the retroperitoneum and pushing forward the small intestine (↓)

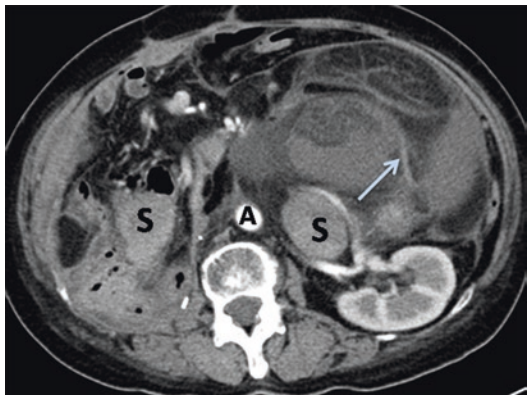


Fig. 3.15 Contrast-enhanced CT axial image in arterial phase identifies abnormally homogeneous enhancement of the solid component (S), no enhancement of the fat component, but enhancement of the partition within the abnormal adipose tissue (↗). No lesion has been revealed surrounding the abdominal aorta (A)

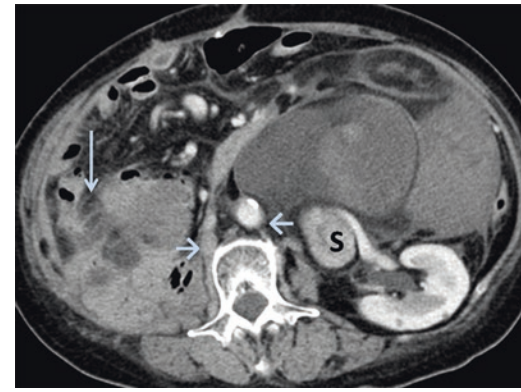


Fig. 3.16 Contrast-enhanced axial image in venous phase displays further enhancement of the solid component of the lesion (S) with an ill-defined boundary (↓). The abdominal aorta (←) and inferior vena cava (→) are homogeneously enhanced and well demarcated

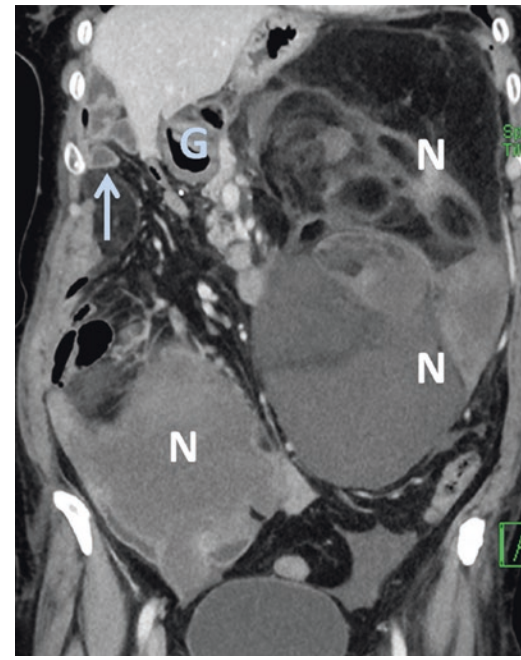


Fig. 3.17 Contrast-enhanced CT coronal image in venous phase displays significant enhancement of the solid component with a clear and smooth boundary from the adjacent structure. Multiple abnormal mass-like lesions (N) occupy the entire left abdominal cavity and the right lower quadrant area, while the gastric body, small intestine and mesentery (↖↗) are seen only in the right upper quadrant. There is a small amount of ascites in the left-inferior abdominal cavity

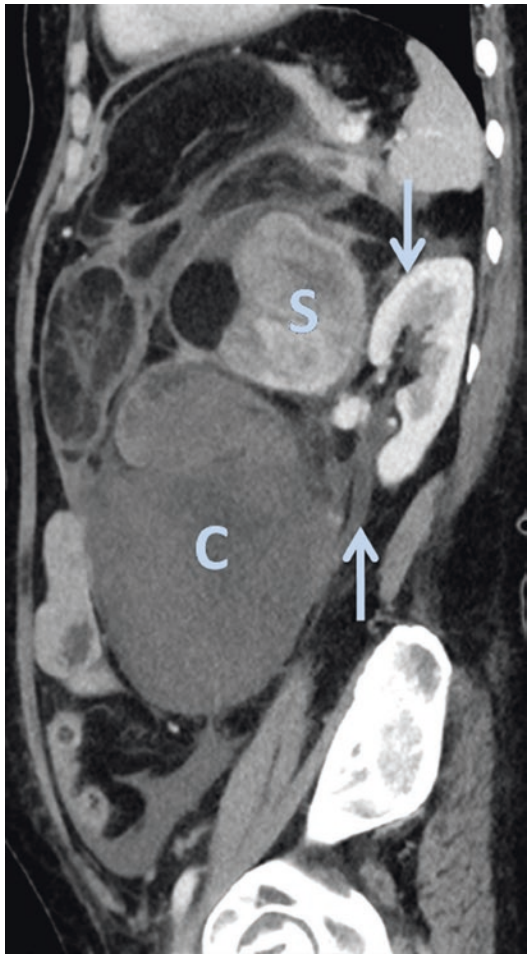


Fig. 3.18 Contrast-enhanced CT sagittal image in venous phase displays complex and diverse components of the lesion, significant enhancement of the solid component (S) and mildly homogeneous enhancement of cystic degeneration (C), but no enhancement of adipose tissue. The anatomical structure from the sagittal view demonstrates that the lesion is located anterior to the left kidney (↓), inferior to the spleen, and superior-posterior to small intestine that is pushed to the inferior space of the anterior abdominal wall. The upper segment of the left ureter (↑) is slightly dilated. No abdominal visceral organs are visible in the mass

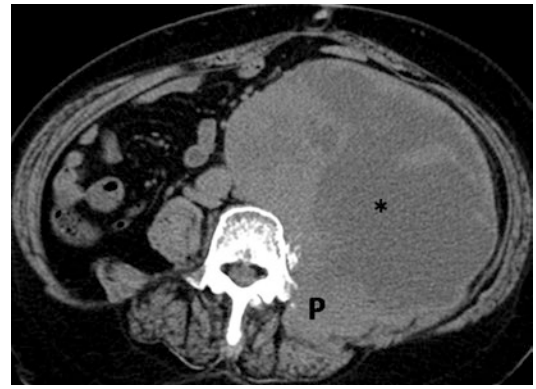


Fig. 3.19 CT axial plain image identifies a huge lump-like mass travelling through the left psoas major (P), with heterogeneously internal density and a large necrotic area (*) of low density. The left psoas major is ill-defined. Adjacent vertebral bone is rough and destroyed

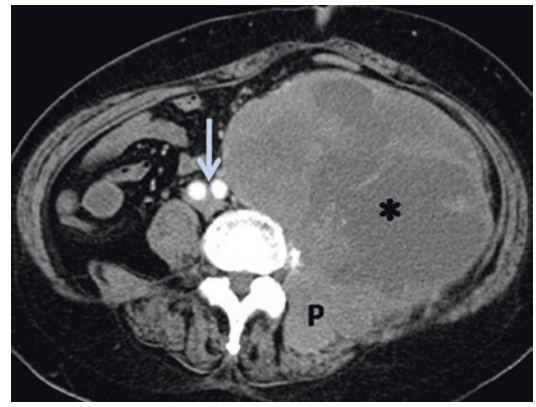


Fig. 3.20 Contrast-enhanced CT axial image in arterial phase displays mildly heterogeneous enhancement within the lesion invading psoas major (P), and no enhancement of the necrotic area within the lesion (*). The left and right iliac arteries (↓) are migrated towards the right under compression

2.2.2 Retroperitoneal Leiomyosarcoma

Leiomyosarcoma contains prominent necrosis; CT shows low density, without calcification. Such a tumor has an extremely rich blood supply. Primary retroperitoneal leiomyosarcoma is more common in women and usually presents as a large soft tissue mass, with a rich blood supply, accompanied by irregular necrosis and cystic degeneration. The CT scan shows significant enhancement after contrast injection, rarely with calcification. Leiomyosarcomas tend to metastasize to the liver, lungs, and mesentery (Figs. 3.19, 3.20, 3.21, 3.22, 3.23, 3.24, and 3.25).

2.2.3 Retroperitoneal Malignant Fibrous Histiocytoma (MFH)

MFH occurs in muscle and connective tissue. The most common locations are the lower limbs, followed by the retroperitoneum. The elderly is prone to develop MFH. Such tumors are mainly

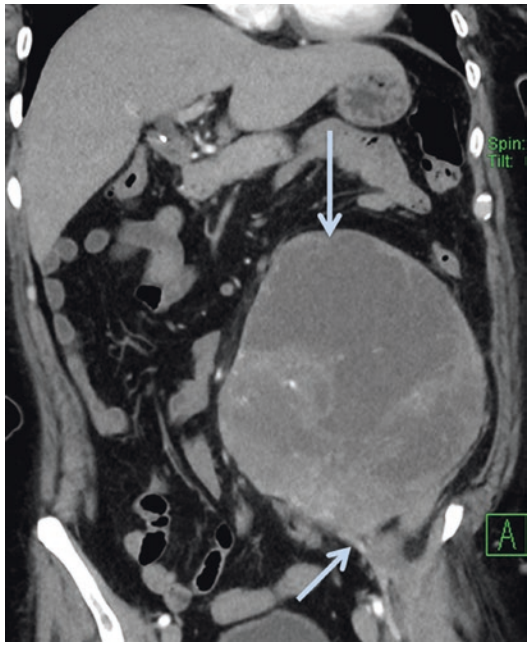


Fig. 3.21 Contrast-enhanced CT coronal image in arterial phase elucidates heterogeneous enhancement and tiny abnormal vascular shadows within the lesion. The tumor mostly has a clear and smooth boundary(↓). This reconstructed plane displays fibrous adhesion between the inferior margin of the tumor and the left iliac muscle(↗)

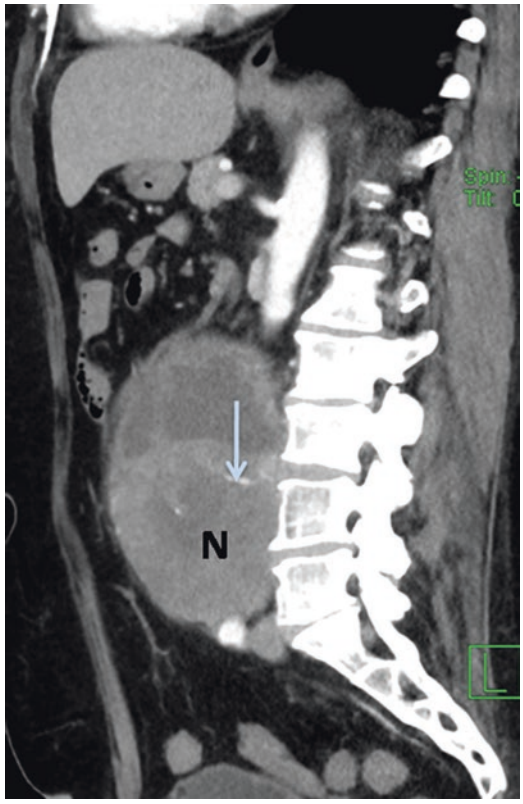


Fig. 3.22 Contrast-enhanced CT sagittal image in arterial phase identifies heterogeneous enhancement within a mass(N) that is located anterior to the spine. The mass is well-defined, wherein tiny abnormal blood vessels(↓) are visible

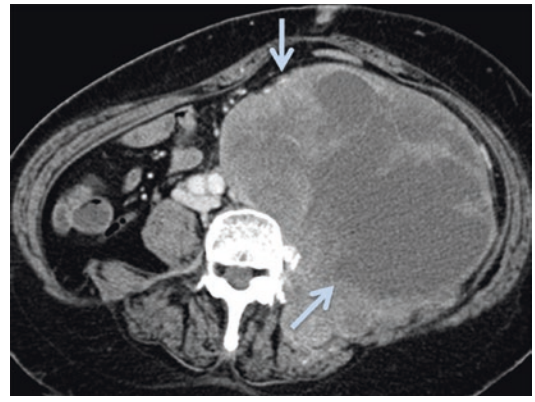


Fig. 3.23 Contrast-enhanced CT axial image in venous phase displays further enhancement of the solid component within the mass, with abnormal tiny feeding vessels anteriorly(↓). The left psoas major has been infiltrated,lost normal contour(↗), and shown significantly abnormal enhancement

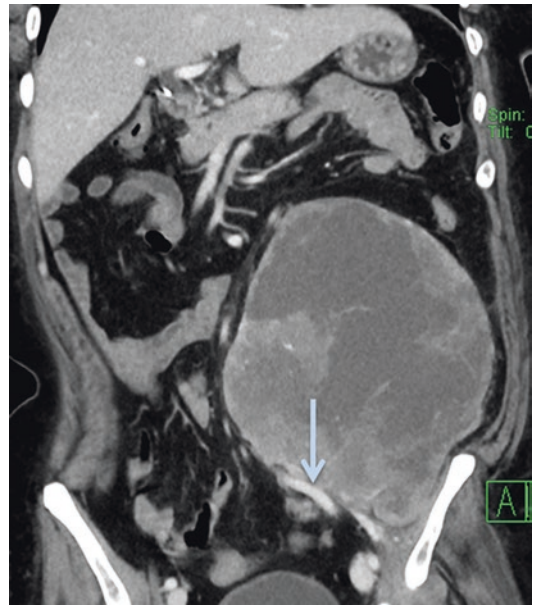


Fig. 3.24 Contrast-enhanced CT coronal image in venous phase displays further enhancement of the solid component within the mass, with a clear and smooth boundary. The left iliac vessel (↓) is migrated towards the right under compression

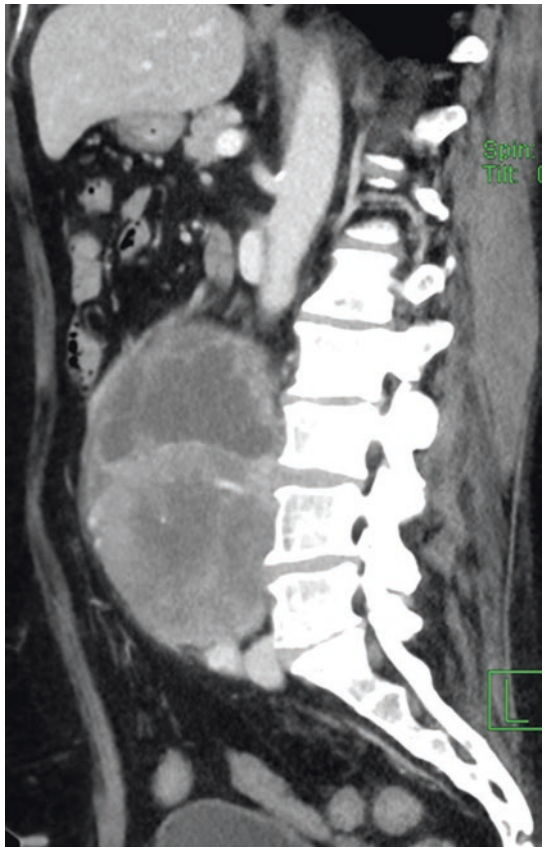


Fig. 3.25 Contrast-enhanced CT sagittal image in venous phase displays further heterogeneous enhancement within a well-defined mass (N) that is located anterior to the spine

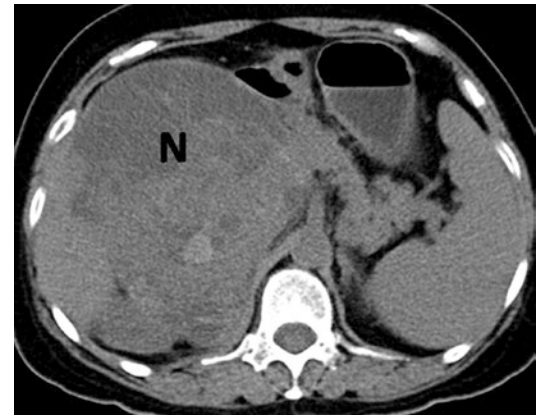


Fig. 3.26 CT axial plain image identifies a large soft tissue mass(N) located in pancreatic head and anterior to the right kidney, with heterogeneouslyinternal density and multiple focal necrosis of low-density

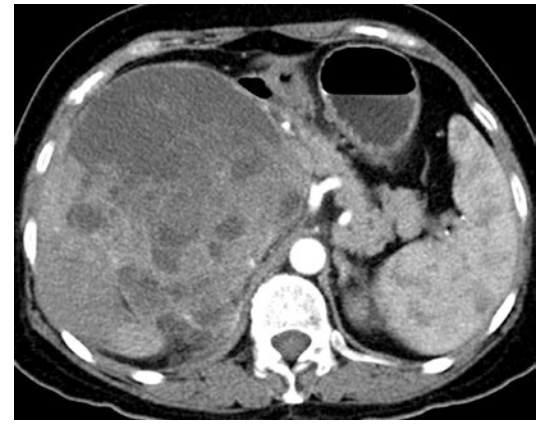


Fig. 3.27 Contrast-enhanced CT axial image in arterial phase displays significantly heterogeneous enhancement of a mass. The pancreatic head under compression cannot be clearly displayed, and the celiac trunk is compressed. The liver presents with an irregular and ill-defined boundary and abnormal enhancement, suggesting the involvement of liver margins (*). The right kidney (K) is migrated under compression(↓). The right diaphragm is slightly thickened

composed of fibroblast- and histiocyte-like cells. CT scan shows a soft tissue mass with a distinct boundary when the tumor is small. Necrosis or even liquefaction can be visible when the tumor has grown larger, occasionally with calcification. MFH has rich blood supply and exhibits significant enhancement after contrast injection. MFH is highly invasive and frequently relapses postoperatively (Figs. 3.26, 3.27, 3.28, 3.29, and 3.30).

2.2.4 Retroperitoneal Malignant Schwannoma

Retroperitoneal malignant schwannoma is located within the midline area of the body. When cystic degeneration occurs in a soft tissue mass with homogeneous density, malignant lesions should be considered (Figs. 3.31, 3.32, 3.33, 3.34, 3.35, and 3.36).

2.2.5 Retroperitoneal Lymphoma

When the size of retroperitoneal lymph nodular shadow is greater than 2.0 cm in diameter, abnormally enlarged lymph nodes should be considered. When multiple lymph nodes with various sizes are clustered together, or a num-

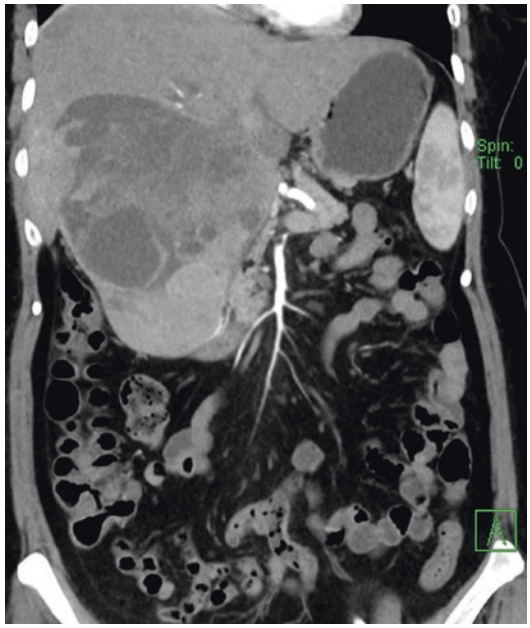
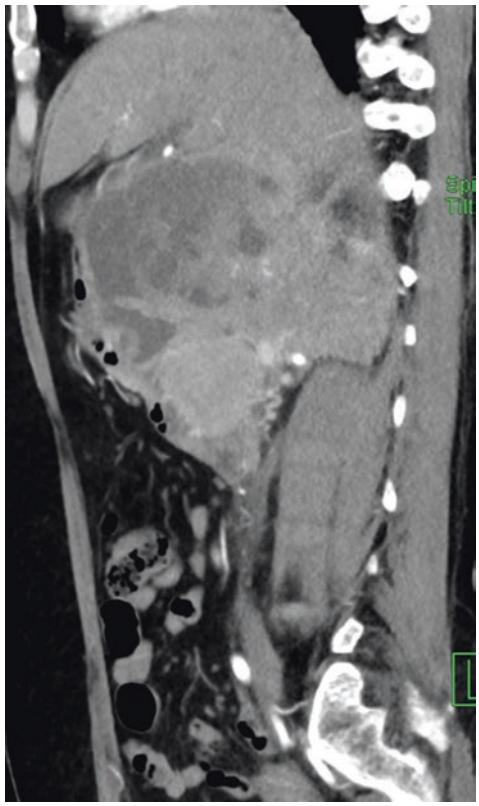


Fig. 3.28 Contrast-enhanced CT coronal image in arterial phase displays a mass (→) with obviously heterogeneous internal density, marked enhancement of the lower part, more necrotic foci in the upper part, and a well-defined boundary. The large mass spreads to the inferior margin of the right lobe, compresses the hepatic hilus and pushes the pancreas and duodenum towards the left



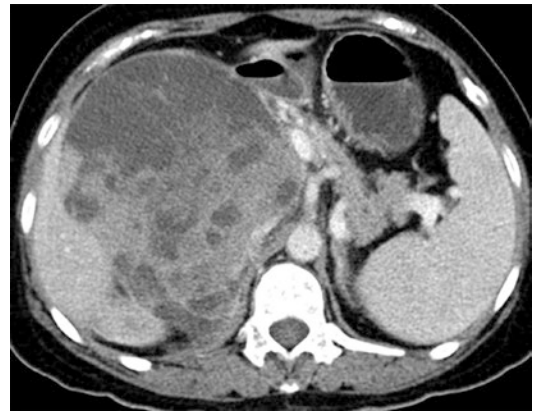


Fig. 3.30 Contrast-enhanced CTaxial image in venous phase displays further development of abnormal enhancement and necrosis within the lesion. The pancreatic neck and splenic vein(↓) are compressed. The inferior vena cava becomes flat under compression with heterogeneous density, but no significant filling defect. The celiac trunk is compressed and the peripheral area of the abdominal aorta is clearly demarcated. The right diaphragm is slightly thickened

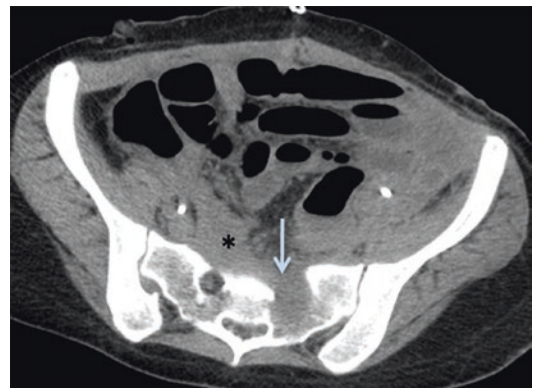


Fig. 3.31 CT axial plain image demonstrates that one week after surgery, the left sacral foramina in the surgical field is excavated with resection of partial bone (↓), and encapsulated fluid (*)is visible anterior to the right sacral foramina

Fig. 3.29 Contrast-enhanced CT sagittal image in arterial phase displays obviously abnormal enhancement and necrosis (*) within the lesion, with slim and abnormal vascular shadows inferiorly. The anterior portion of the mass adheres to small intestine, and its posterior portion involves the posterior space between the liver and kidney, with an ill-defined boundary

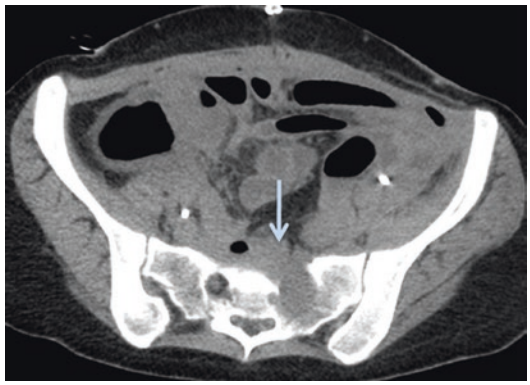


Fig. 3.32 CT axial plain image displays that two weeks after surgery,the left sacral foramina in the surgical field is excavated with resection of partial bone and tiny abnormally thickenedshadowof soft tissue intensity (↓). The presacral encapsulated fluid is slightly reduced after treatment, wherein small bubble-like shadowsare visible

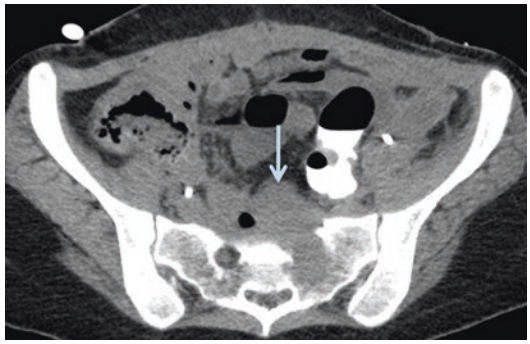


Fig. 3.33 CT axial plain image displays that 3 weeks after surgery,nodular soft tissue shadows (↓) appear in the surgical field located in the left sacral foramen

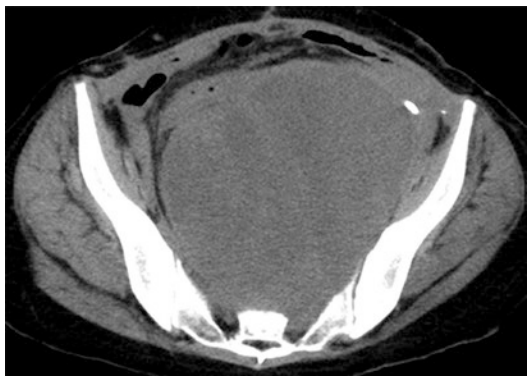


Fig. 3.34 CT axial plain image displays that the tumor(N) has grown rapidly and almost occupied the pelvis two months after surgery. Internal density of the tumor is substantially homogeneous, and a streak-like shadow of higher density is barely visible

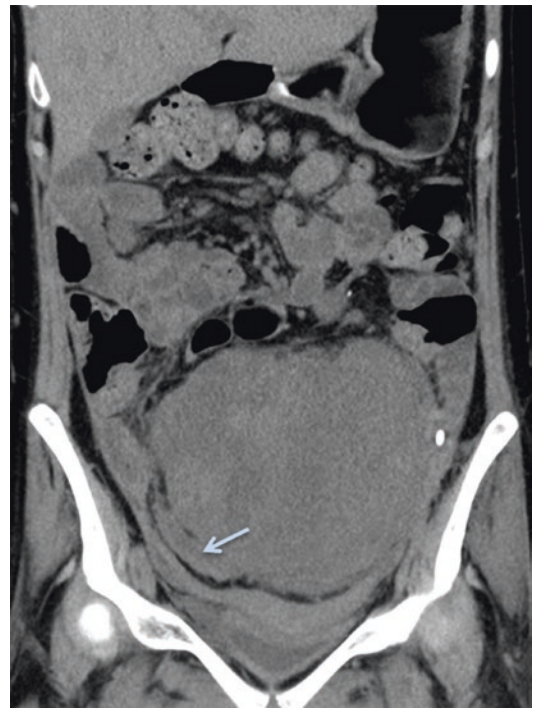


Fig. 3.35 Reconstructed image in coronal plane of CT scan identifies ahuge tumor has occupiedthe entire pelvic cavity two months after surgery. Thetumor displays substantially homogeneous density with a clear and smooth boundary. The sigmoid is migrated to the lower right area of the pelvis under compression (↙)

ber of enlarged lymph nodes are fused into an irregular lump-like soft tissue mass, lymphoma should be considered after ruling out other diseases which cause lymph node enlarged. Necrosis may occur within the enlarged lymph nodes. Non-Hodgkin's lymphoma (NHL) is the most common type of retroperitoneal lymphoma, which invades retroperitoneal organs and presents as enlarged para-aortic lymph nodes at the early stage. CT scanning may help reveal abnormally enlarged lymph nodes, the status of lymph nodes around retroperitoneal organs, as well as abnormally enlarged lymph nodes in distant regions, thus playing a critical role in determining clinical stages. In addition, CT may be used in the follow-up of non-Hodgkin's lymphoma after radiotherapy and chemotherapy.

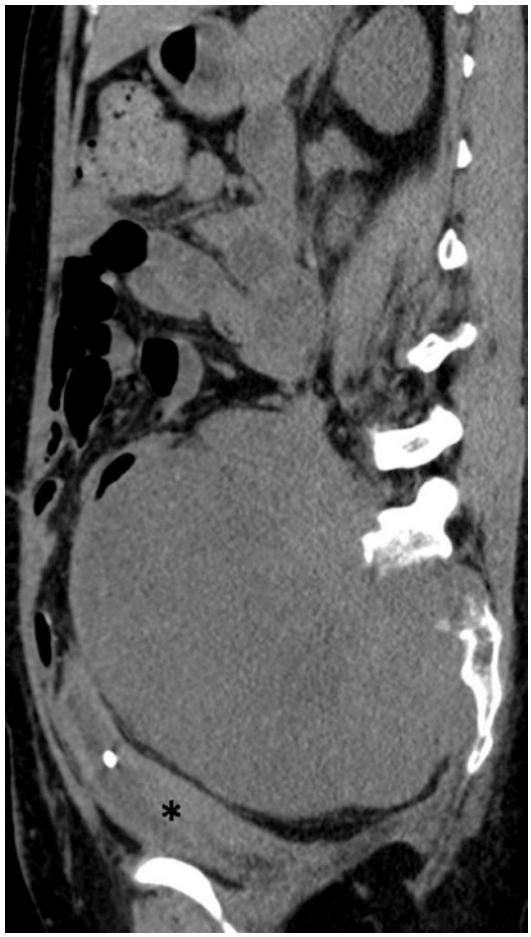


Fig. 3.36 Reconstructed image in sagittal plane of CT scanidentifies a huge tumor with a clear and smooth boundary has occupies the entire pelvic cavity two months after surgery. The tumor displays substantially homogeneous density. The intestine within the pelvis is migrated towards the middle abdomen. Bladder (*) and uterine become flat under compression

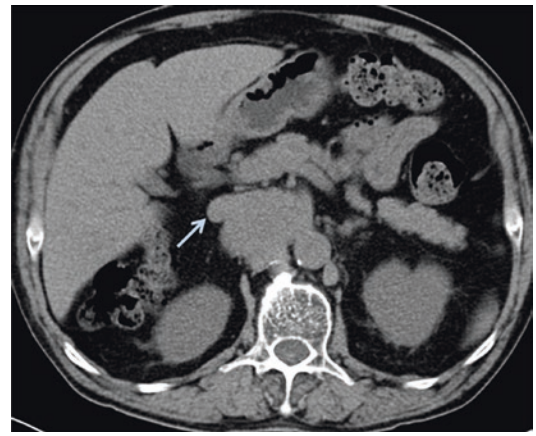


Fig. 3.37 CT axial plain image identifies irregular and homogeneous soft tissue density posterior to the inferior vena cava, on the right side of the abdominal aorta and anterior to the diaphragm angle, with a well-defined boundary.The inferior vena cava (↗)is migrated onward under compression

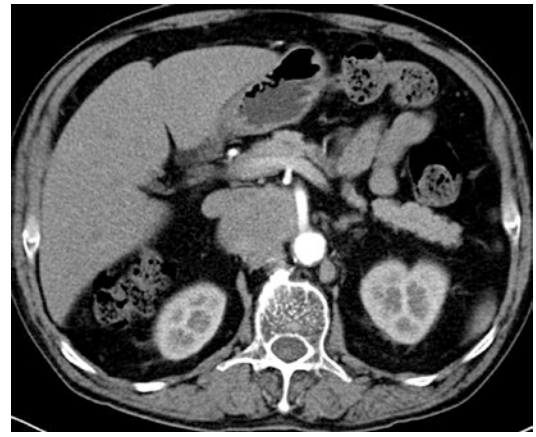


Fig. 3.38 Contrast-enhanced CT axial image in arterial phase identifies a mass with mildly homogeneous enhancement. The celiac trunk is travelling through the left side of the mass, and a clear boundary exists between them. The head of the pancreas and splenic vein are relatively far apart from the mass

2.2.6 Retroperitoneal Malignant Paraganglioma

Ten percent of paragangliomas are malignant as reported previously (Shulkin et al. 1999). It is difficult to differentiate malignant from benign tumors, which can only be distinguished by size. On CT imaging, a malignant paraganglioma is larger than a benign one, with an irregular shape, an incomplete capsule, and locally enlarged lymph nodes. Spiral CT three-dimensional reconstruction and CT angiography demonstrate that the tumor is closely related to the abdominal aorta, renal artery, liver, and kidney; in addition, the gap between the organs is infiltrated or disappears (Figs. 3.37, 3.38, 3.39, 3.40, and 3.41).

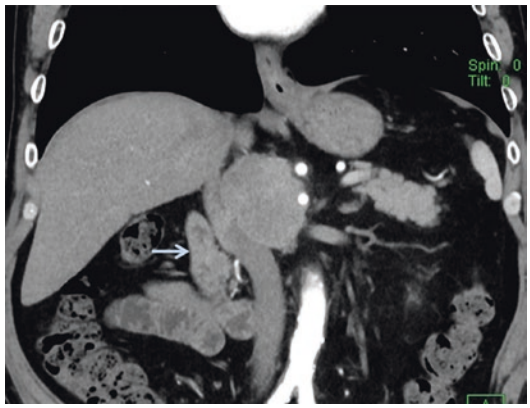


Fig. 3.39 Contrast-enhanced CT coronal image in arterial phase demonstrates the inferior vena cava is compressed by the mass, but a well-defined boundary exists between them. The celiac trunk is travelling next to the tumor. The duodenum (→)is located in the lower right side of the mass

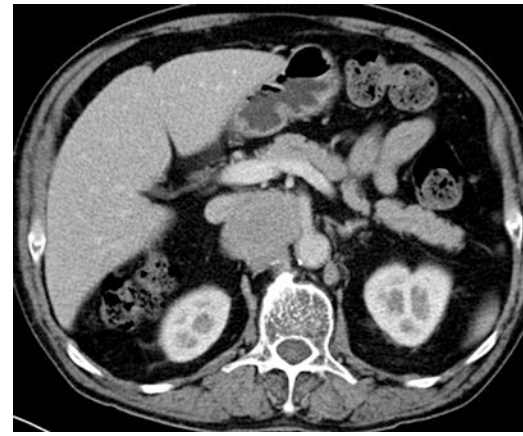


Fig. 3.41 Contrast-enhanced CT axial image in venous phase displays further homogeneous enhancement of the mass. The inferior vena cava is compressed forwardly, however, the inferior vena cava has homogeneous density without any filling defects

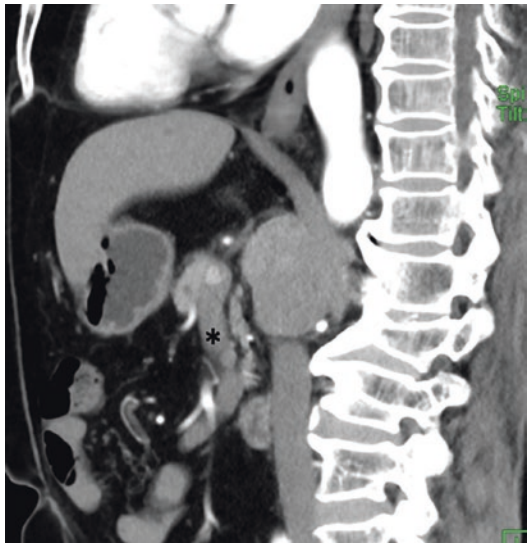


Fig. 3.40 Contrast-enhanced CT sagittal image displays the mass originates anterior and inferior to the diaphragm angle, while partial pancreas and superior mesenteric vein (*) are located anterior and slightly inferior to the lesion

2.2.7 Retroperitoneal Malignant Teratoma

Retroperitoneal malignant teratoma frequently occurs in the upper part of retroperitoneal space and anterior-superior part around the kidney, more common at the left side than the right. Malignant teratoma grows rapidly and invades surrounding tissue, which is mostly solid and ill defined. It compresses ureters, leading to hydronephrosis because the ureter is obstructed.

2.2.8 Retroperitoneal Rhabdomyosarcoma

Retroperitoneal rhabdomyosarcoma belongs to malignant tumors of soft tissue with characteristics of skeletal muscle, which is common in childhood. The incidence of retroperitoneal rhabdomyosarcoma is extremely low. CT shows a soft tissue mass with clear boundary. Since necrosis caused by liquefaction of tissue often occurs in the mass, CT scan presents heterogeneous density with water-like change in density. After injection of a contrast agent, the tumor exhibits heterogeneous enhancement, which is more prominent in the peripheral region compared with the central region. Invasion of surrounding structures or enlargement of lymph nodes is visible (Figs. 3.42, 3.43, 3.44, 3.45, and 3.46).

2.2.9 Retroperitoneal GIST

Retroperitoneal gastrointestinal stromal tumor (GIST): A GIST is usually a solitary soft tissue mass which is greater than 5 cm in diameter, quasi-circular or lobulated in shape. Therefore, CT shows heterogeneous density, with rich but heterogeneous blood supply. GISTs are susceptible to develop

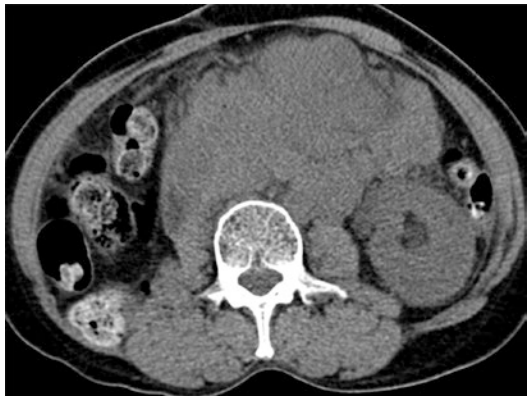


Fig. 3.42 CT axial plain image displays lumpy soft tissue density (N)at the inferior pole of the left kidney and anterior to the abdominal aorta. The mass is lobulated with irregular margins.The abdominal aorta and inferior vena cava are wrapped, and the adipose space anterior to the left kidney is ill-defined

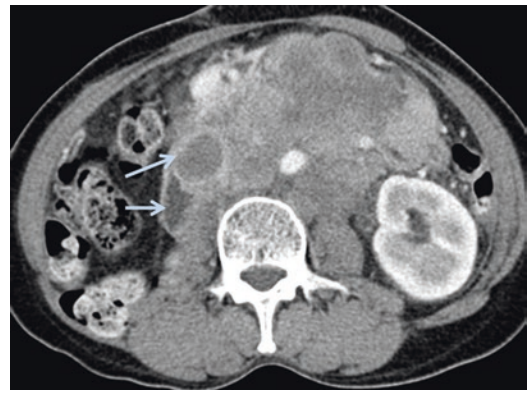


Fig. 3.44 Contrast-enhanced CT axial image in venous phase displays further heterogeneous enhancement of the lesion, homogeneous enhancement of the abdominal aorta, and no significant enhancement of the inferior vena cava (↗). The lesion has an ill-defined border, with suspected adhesion and involvement of duodenal wall (→). The anterior margins of bilateral psoas muscle are adhered to the tumor

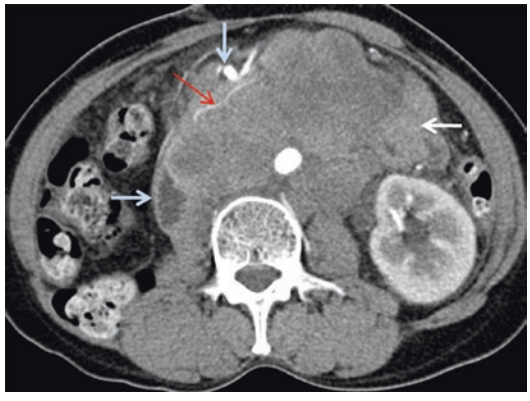


Fig. 3.43 Contrast-enhanced CT axial image in arterial phase displays heterogeneous enhancement of the lesion with abnormal vascular shadow (↘)in the peripheral area. Abdominal aortic is completely wrapped bythe tumor body. The duodenum (→) and the left side of the lesion adhere to a part of the small intestine (←). The vessel that lies anterior to the lesion is the superior mesenteric artery (↓)

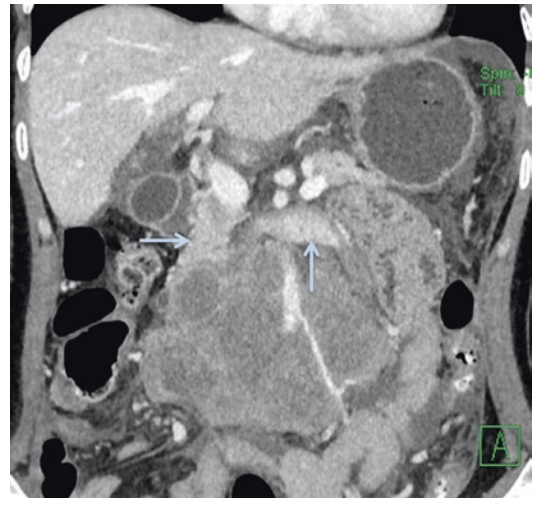


Fig. 3.45 Contrast-enhanced CT coronal image in venousphase displays the superior mesenteric artery is travelling through the lesion, and the transverse strip-like shadow of high density at the superior margin of the lesion is the thickened left renal vein (↑). The pancreatic head (→) and portal vein lie slightly towards the right at the superior margin of the lesion

necrosis and cystic degeneration. Solid elements of the tumor show moderately heterogeneous enhancement after contrast injection. This phenomenon is most prominent in venous phase, presenting as strip-like enhancement extending from the peripheral to the central region of the tumor, or in a criss-crossing pattern, or as septum-like enhancement in the cystic degeneration. GISTs can compress the surrounding organs, leading to deformation and displacement, even exhibit invasive growth into retroperitoneal space and adhesion with the surrounding structures, or enclose the abdominal aorta, inferior

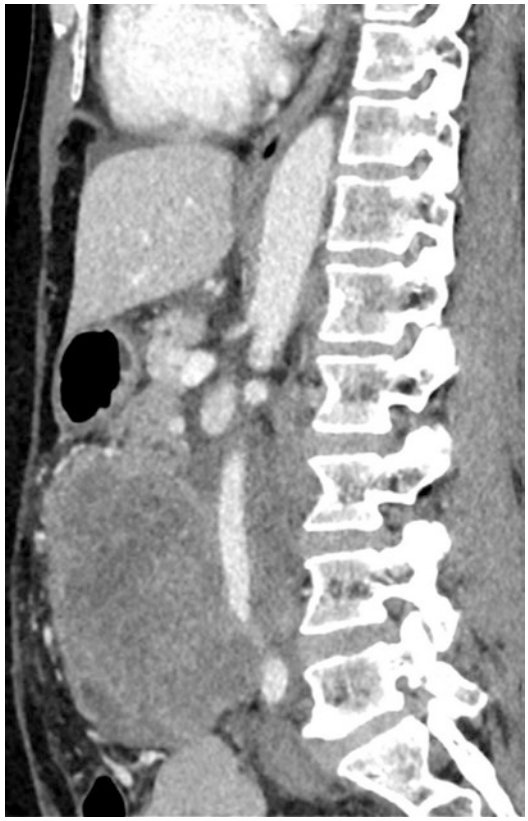


Fig. 3.46 Contrast-enhanced CT sagittal image in venous phase displays a space-occupying lesion (N) that is located anterior and posterior to the abdominal aorta, with gastric antrum (→) containing air superiorly

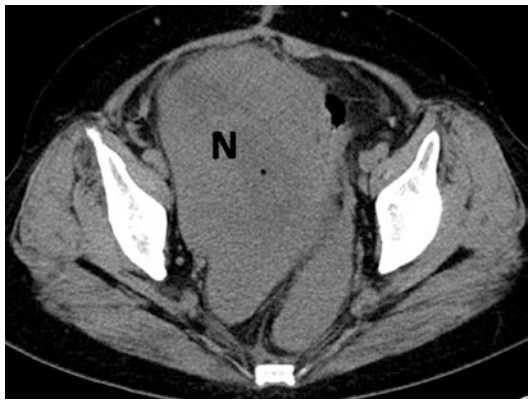


Fig. 3.47 CT axial plain image displays a huge mass (N) of uneven density in the lower abdomen pelvic cavity. Patchy low-density area is seen in the central area of the mass. The lesion's margin is clear;however, the rectum is migrated to left side under compression

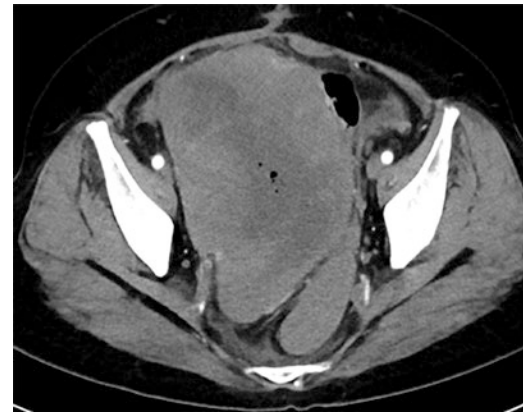


Fig. 3.48 Contrast-enhanced CT axial image in arterial phase identifiesheterogeneous enhancement of the lesion-withpatchy low density in the centralarea.The little gas bubble in the central area is suspected from the bowel after intestinal wall is involved. The distal rectum wall located on the left side of lesion is well recognized. The right internal and external iliac arteries are not involved

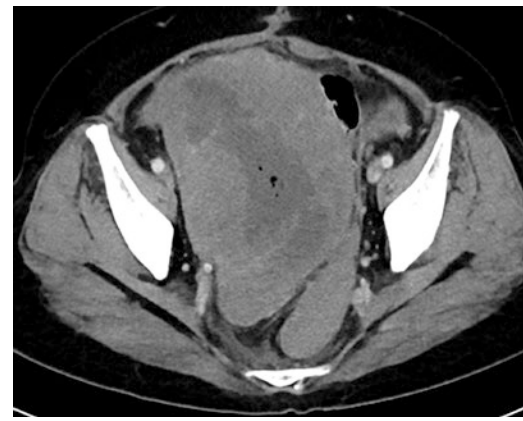


Fig. 3.49 Contrast-enhanced CT axial image in venous phase displays the surrounding area of the lesion is further enhanced, but part of lesion density in the central area is not improved. Therefore, the difference in density within the lesion becomes more evident

vena cava, and other abdominal blood vessels. GISTs can metastasize hematogenously to the liver, lungs, or other distant sites; however, lymphatic metastasis is very rare. GISTs occur more frequently in the pelvic extraperitoneal space than in retroperitoneal space and are more likely to relapse (Figs. 3.47, 3.48, 3.49, 3.50, and 3.51).

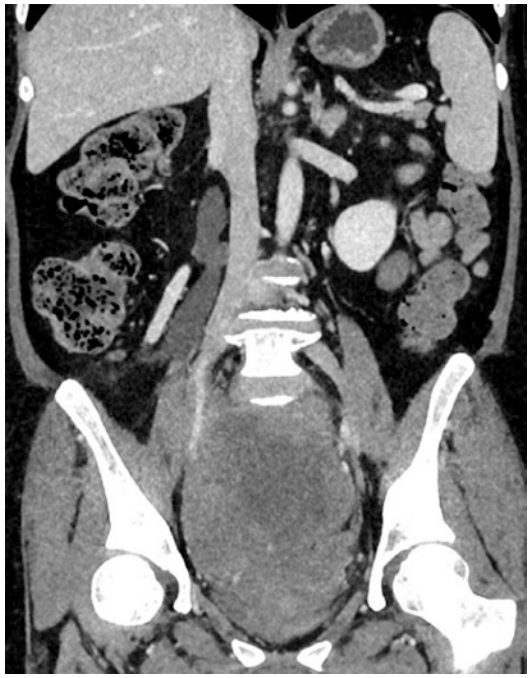


Fig. 3.50 Contrast-enhanced coronal image in venous phase displays relatively low density in the central area of the lesion, which represents failed enhancement. Uterine is shifted downward under compression

2.2.10 Retroperitoneal Seminoma

Seminoma most frequently occurs in upper and middle parts of retroperitoneum, close to the pancreas or kidneys. CT scan displays a solitary mass, which has compressed the surrounding organs and tissues. The large mass, which has compressed the surrounding organs and tissues (Figs. 3.52, 3.53, and 3.54).

2.2.11 Peripheral Primitive Neuroectodermal Tumors (pPNETs)/Ewing's Sarcoma

Retroperitoneal primitive neuroectodermal tumor (PNET) and Ewing's sarcoma are very rare and highly invasive and aggressive. They are susceptible to relapse and early metastasis. Those tumors most likely metastasize to the lung, liver, bone, or local lymph nodes. Primary retroperitoneal PNETs often present as large perivascular soft tissue masses with ill-defined boundaries, causing compression and displacement of adjacent organs. CT shows an equal- or low-density

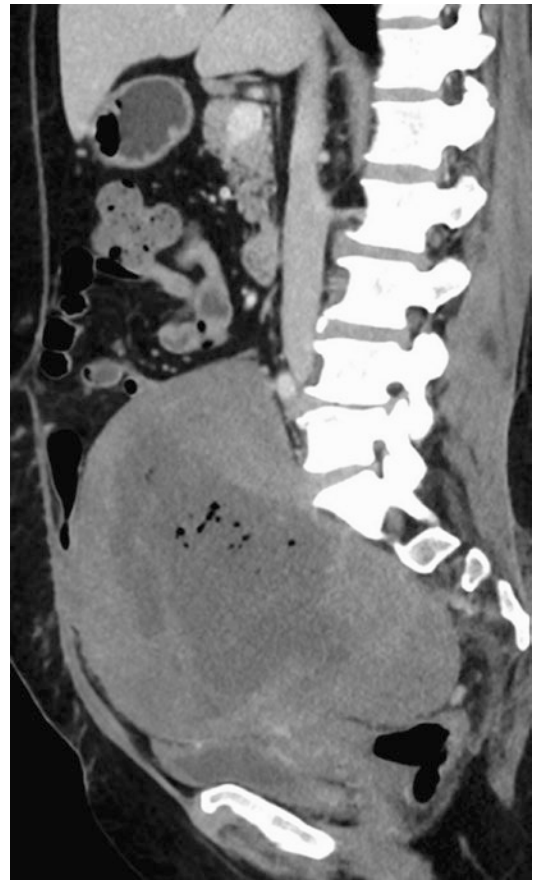


Fig. 3.51 Contrast-enhanced CT sagittal image in venous phase shows a huge lesion located in the lower abdomen and pelvic cavity. Bladder and uterus are compressed. Rectum offsets the central line under lesion's pressure

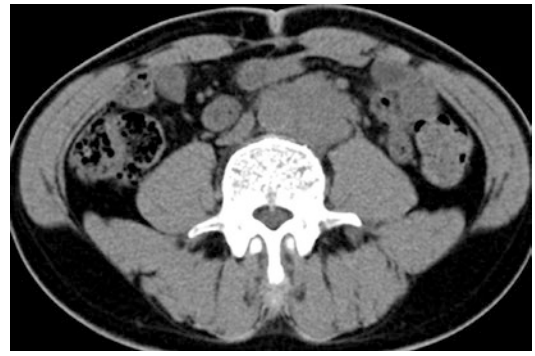


Fig. 3.52 CT axial plain image displays nodular soft tissue lesion (N) on the left side of the abdominal aortic in the middle abdomen (belly button level). The lesion boundary is clear but is not smooth, but the aortic border is not clear near the mass in CT non-enhanced scanning. The left psoas major boundary is clear

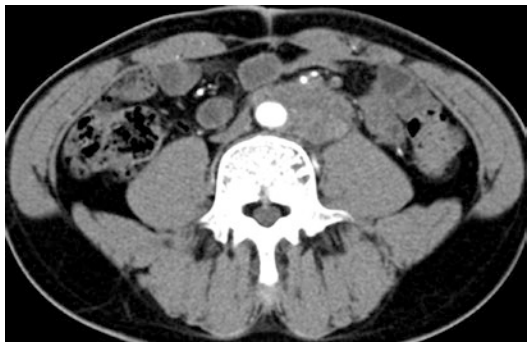


Fig. 3.53 Contrast-enhanced CT axial image in arterial phase displays anenhanced lesion (N) that is heterogeneous with clear boundary. Abdominal aorta wall (A) is wrapped around more than one-half. Mesenteric artery (↓) located to the left of lesion. Left psoas major and local lumbar vertebral are not involved

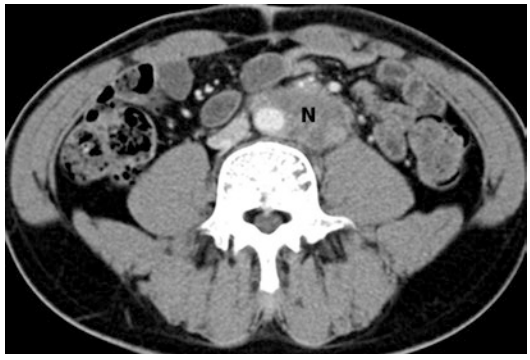


Fig. 3.54 Contrast-enhanced CT axial image in venous phase displays heterogeneous enhancement within the lesion (N) more obviously. Abdominal aorta is wrapped in lesion. Inferior vena cava is seen enhanced on the right side of mass and no involved

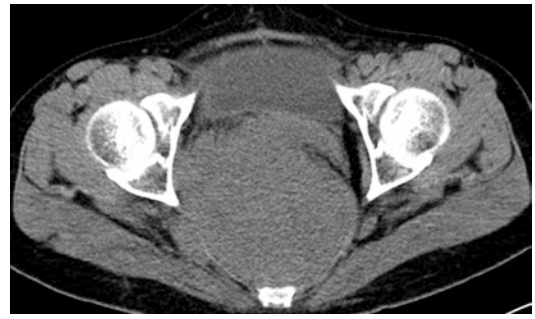


Fig. 3.55 CT axial plain image displays circular mass lesion (N) on the right side of pelvic retroperitoneal space in front of coccyx. Uterus neck and rectum are push to left-front space, and boundary between them is fuzzy. Coccyx is wrapped in lesion

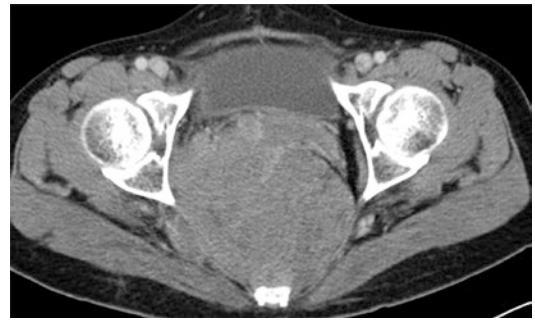


Fig. 3.56 Contrast-enhanced CT axial image in venous phase shows obviously heterogeneous enhancement in the lesion with a clear border on the left side and a fuzzy border (↓) on the right side. Part of lesion protrudes into right obturator clearance. The right internal iliac artery is not clearly presented

mass in which necrosis of lower density is visible, with rare calcification. The lesion is heterogeneously enhanced after contrast injection (Khong et al. 2002). The CT imaging manifestation is determined by microscopic structures and pathological components of the tumor, which indirectly reflects its gross pathology, thus providing information on the overall subtle structure and major elements of the lesion. For an adolescent patient with a short clinical course, if CT displays an ill-defined mass without calcification, PNETs should be considered. CT/MRI can demonstrate the location of the tumor, absence or presence of bleeding within the lesion, gross pathological constituents, as well as involvement, compression, and invasion of multiple surrounding tissue structures, which are essential for evaluation of resectability and surgical efficacy, as well as for development of a novel therapeutic strategy (Figs. 3.55, 3.56, 3.57, and 3.58).

In one word, primary retroperitoneal neoplasms can arise from any tissue in the retroperitoneum and represent diverse pathologic

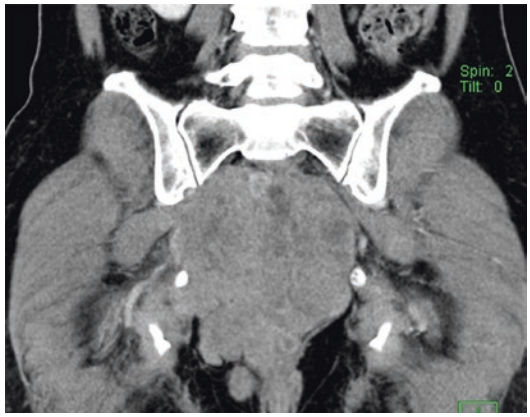


Fig. 3.57 Contrast-enhanced CT coronal image in venous phase displays a heterogeneously enhanced lesion (N) that occupies the whole pelvic retroperitoneal space. Its right boundary shows irregular nodular protrusions

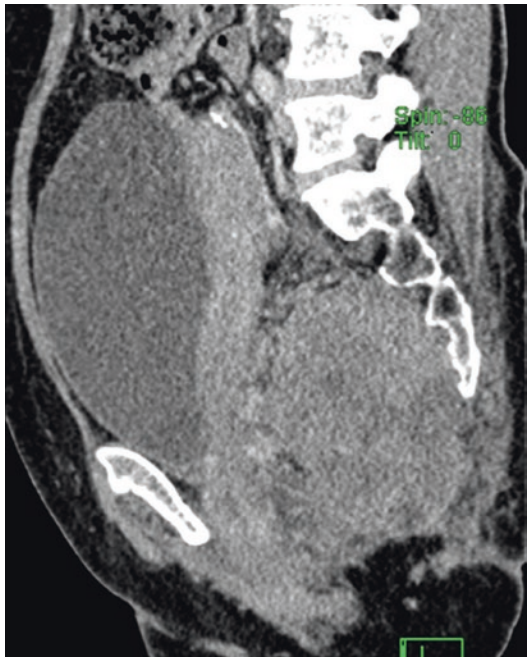


Fig. 3.58 Contrast-enhanced CT sagittal image in venous phase displays a lesion (N) located in front of sacral vertebrae, and heterogeneously enhanced with a blurry border. Mass compresses uterus neck (U), which has been shifted forward. The bottom of the lesion is close to pelvic floor structures

types of tumors. CT is the preferred tool to display characteristics of these tumors, thus providing supporting evidence for accurate diagnosis.

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MRI in Diagnosis of Retroperitoneal Tumors

4

Dianjiang Zhao

1 MRI Technique to Image Abdominal (Pelvic) Retroperitoneum

1.1 Basic Working Principle of MRI

Magnetic resonance imaging (MRI) is an imaging technique by which image reconstruction is generated using nuclear resonance signal in strong magnetic fields. MRI scanners also use radio waves and field gradients to form images of the body. In the natural state, ^{1}H spins randomly. However, in the presence of a strong external magnetic field, ^{1}H aligns with or opposite to the direction of applied field at a specific frequency (the frequency of spin precession is determined by the external magnetic field), known as the equilibrium state of ^{1}H. At this point, if pulsed radiofrequency (PRF) stimulation with the same frequency is applied to the human body, ^{1}H in the body will absorb the energy of RF pulse. This process is called magnetic resonance. When the applied PRF suddenly disappears, the in vivo ^{1}H will release the absorbed energy and recovers to the equilibrium state. After comprehensively processing the released energy, a precise MRI image will be constructed. An MRI sequence is an ordered combination of RF and gradient pulses designed to acquire the data to form the image.

1.2 Relaxation Time

Relaxation is the process in which ^{1}H goes from a higher energy state back to the lower energy state after the applied RF pulse has disappeared, and relaxation time is the duration required for this whole process. It consists of two simultaneous events: (1) longitudinal relaxation time, which is required for ^{1}H to rise from zero to the maximum amount of magnetization along the *Y*-axis, i.e., T_1 relaxation time. The image that demonstrates the differences in T_1 relaxation times among tissues is called T_1-weighted image (T_1WI); (2) horizontal relaxation time, which is required for ^{1}H, reduces from the maximum amount of magnetization to zero along the *X*-axis, i.e., T_2 relaxation time. The image that reflects the differences in T_2 relaxation times among tissues is called T_2WI. Each tissue has relatively stable relaxation time.

1.3 MRI Signal

On T_1WI, signal intensity (SI) is inversely related to T_1 relaxation time: the longer T_1, the lower SI, and vice versa. For example, water, muscle, and adipose show low-, moderate-, and high-intensity signal on T_1WI, respectively. On T_2WI, SI is positively related to T_2 relaxation time: the longer

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the T_2, the higher SI, and vice versa. Here, water, muscle, and adipose show high-, moderate-, and moderate- to slightly high-intensity signal on T_2WI, respectively. Air and compact bone show low-intensity signal on both T_1WI and T_2WI due to less absorption of ^{1}H. Intravascular blood flow generally shows low signal (flow void effect).

1.4 Scanning Protocol

Spin-echo T_1WI and fast spin-echo T_2WI are conventional MRI sequences for detecting retroperitoneal lesions. On such basis, additional fat-suppressed T_1WI or T_2WI scan is performed when appropriate. Spin-echo or fast spin-echo sequence can be employed to conventional or dynamic Gd-DTPA-enhanced scanning, respectively. To show the relationship between the retroperitoneal tumor and adjacent important blood vessels or ureters, MR angiography (MRA) or MR urography (MRU) are performed to evaluate the ureteral or vascular invasion. Cross-sectional, sagittal and coronal planes are routine.

2 MRI Interpretation Skills for Retroperitoneal Tumors

Diagnostic MRI plays a vital role in localization and quantification of retroperitoneal tumors.

For retroperitoneal tumors, MRI is used to precisely localize the lesion, not only suggestive for qualitative diagnosis and is helpful in narrowing the differentiation range but also pivotal for the development of therapeutic strategies and the evaluation of clinical response. The first step is to determine whether the lesion is located in the retroperitoneal space. If yes, the second step is to narrow down to a specific space. For example, pancreatic cancer (in the tail of the pancreas) and liposarcoma are common in the left anterior extrarenal space; pancreatic cancer (in the head of the pancreas), liver cancer, liposarcoma, and gastrointestinal stromal tumors occur frequently in the right anterior extrarenal space; liposarcoma, leiomyosarcoma, renal cancer, suprarenal gland tumor, and pedunculated hepatocellular carcinoma (P-HCC) (or extrahepatic growth of HCC) are often located in the perirenal space; malignant peripheral nerve sheath tumor (MPNST), malignant fibrous histiocytoma, leiomyosarcoma, paraganglioma, fibrosarcoma, teratoma, and lymphoma are usually located in the posterior renal space.

Retroperitoneal tumors are characterized by low incidence, numerous pathological types, and complex origins; in addition, MRI findings are varied and overlap each other and lack specificity (Goenka et al. 2012). Thus, it is not easy to quantitatively diagnose some retroperitoneal tumors with MRI images. A comprehensive analysis should be conducted based on the location, number, size, shape, margin, signal enhancement pattern of the lesion, as well as its relationship with surrounding organs, in combination with age, gender, medical, and clinical information of the patient. First, tumors should be roughly distinguished as benign from malignant; second, the possible cellular origin of the tumor should be considered, such as adipogenic, myogenic, neurogenic, and so on; and finally, the specific tumor may be determined successfully.

2.1 Location Diagnosis

The following signs are helpful in determining whether the tumor is located in the retroperitoneal space.

2.1.1 Retroperitoneal Organ or Vascular Displacement

Retroperitoneal tumors can push and compress retroperitoneal organs (such as the pancreas, suprarenal gland, kidney, ureter, ascending colon, descending colon, rectum, as well as the horizontal and ascending parts of duodenum) and blood vessels (such as abdominal aorta, celiac trunk, inferior vena cava, superior mesenteric artery, and superior mesenteric vein) to make them move forward or up and down. It is called

vascular or organ displacement syndrome. Tracking the direction of displaced organs or blood vessels is helpful in accurately locating the tumors (Nishino et al. 2003; Cohan et al. 1988).

2.1.2 Interface Signs of Retroperitoneal Tumors

When the boundary between the tumor and adjacent organs or structures disappears or becomes blurred, it is called the positive interface sign; vice versa, it is called the negative or absence of interface sign. Positive interface signs are defined when the fat space between the retroperitoneal tumor and posterior abdominal wall, psoas major or pelvic muscles, and retroperitoneal vessels or organs becomes invisible or blurred. Under the circumstance of a negative interface sign, compression and displacement of intraperitoneal viscera may suggest the tumor's location in the retroperitoneal space.

2.1.3 Imaging Signs of Tumors Originating from Retroperitoneal Organs (Nishino et al. 2003)

(a) Beak sign. When the boundary between the tumor and an adjacent organ becomes invisible, the interface is acute-angled, with the edge protruding like a beak. The beak sign indicates that the tumor may be derived from this specific organ. In contrast, if the edge of interface presents slightly arc shaped or obtuse angled, the tumor may arise from another organ. (b) Phantom (invisible) organ sign. The organ may become "undetectable" on MRI when a giant mass arises from it. However, false-positive findings cannot be completely ruled out. (c) Embedded organ sign. A tumor can encapsulate an adjacent organ partially or mostly, and closely relate to the organ, with disappearance of fat layer and ill-defined boundary. Such sign indicates the lesion originated from the specific organs being invaded. (d) Central area of the tumor. When the center or the main body of a tumor is located within an adjacent organ, the tumor may have originated from this organ. On the contrary, when the center or the main body of the tumor is located outside an adjacent organ, the tumor may not arise from it. (e) Prominent feeding artery sign. MRI may display feeding arteries for hypervascular masses, thus providing important clues to identify the origin of the mass.

2.2 Etiologically Qualitative Diagnosis

2.2.1 Characteristic Components of Retroperitoneal Tumors

Specific tumor contents (such as fat, myxoid stroma, muscle fibers, calcification/ossification, hemorrhage, necrosis, and cystic degeneration) can be clearly demonstrated by MR imaging and thus provide vital clues for narrowing the scope of the differential diagnoses.

(a) Fat: The presence of fat is recognized as a high-intensity signal on T_1WI, middle to high-intensity signal on T_2WI, or loss of signal on fat-suppressed images, respectively. Fat-containing retroperitoneal tumors mainly include lipomyoma, lipoblastoma, liposarcoma, teratoma, angiomyolipoma, and myelolipoma.

(b) Myxoid stroma: Myxoid stroma appears hypointense on T_1WI, hyperintense on T_2WI, and progressive delayed enhancement after injection of contrast medium, respectively. Myxoid stroma-containing retroperitoneal tumors include neurogenic tumors, myxoid liposarcomas, and myxoid malignant fibrous histiocytoma (Otal et al. 2001; Kim et al. 1996).

(c) Collagen fiber: Collagen fiber displays as hypointense on both T_1WI and T_2WI and mild or progressive delayed enhancement after injection of contrast medium. Collagen fiber-containing retroperitoneal tumors mainly include neurofibromas, ganglioneuroma, leiomyosarcoma, malignant fibrous histiocytoma and fibrosarcoma.

(d) Calcification/ossification: Calcification/ossification is hypointense on T_2WI. MRI that cannot demonstrate the presence of

calcification/ossification as clearly as CT. Calcification/ossification-containing retroperitoneal benign tumors/tumor-like lesions include teratoma, hemangioma, giant lymph node hyperplasia, and benign lesions (such as cysts, hematoma, and abscess). Calcification/ossification-containing malignant tumors include malignant fibrous histiocytoma, neuroblastoma, angiosarcoma, liposarcoma, fibrosarcoma, ectopic osteosarcoma, synovial sarcoma, and ectopic chondrosarcoma.

(e) Necrosis: Necrotic areas within the tumor present as hypointense on T_1WI and hyperintense on T_2WI, respectively and without contrast enhancement. Necrosis is usually seen in benign tumors (such as paraganglioma, neurilemmoma) as well as in malignant tumors (such as leiomyosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, and synovial sarcoma).

(f) Cystic degeneration: cystic degeneration within the tumor has homogeneously long T_1 and long T_2 signals, similar to cerebrospinal fluid (CSF), without contrast enhancement. Retroperitoneal tumors or tumor-like lesions presenting as completely cystic denegation include lymphangioma, cystic myxoma (cystomyxoma), congenital cysts (epidermoid cyst, bronchogenic cyst, intestinal cyst, mesonephric tubular cyst) or pseudocyst. Solid-cystic masses include neurilemmoma, paragangliomas, and mucinous cystadenoma.

2.2.2 Enhancement Characteristics of Tumors

Enhanced scanning can reflect blood supply and angiogenesis of tumors to some extent (Otal et al. 2001). No enhancement or early enhancement with subsequently rapid clearance is common in benign lesions; however, early enhancement with slow or no clearance is common in malignant tumors (very few benign tumors); and delayed enhancement is frequent in malignant tumors (rarely in neurogenic tumors).

Extremely hypervascular retroperitoneal tumor/tumor-like lesions mainly include pheochromocytoma, paraganglioma, perivascular epithelioid cell tumor, and giant lymph node hyperplasia. Moderately hypervascular tumors include mucinous malignant fibrous histiocytoma, leiomyosarcoma, and the majority of sarcomas. Hypovascular tumors include well-differentiated liposarcoma, lymphoma, and the majority of benign tumors (Nishimura et al. 2001).

2.2.3 Determination of the Benign Versus Malignant Nature of Retroperitoneal Tumors

Benign tumors are generally small in size, with a regular shape, a smooth boundary, and homogeneous signals, which display no enhancement or relatively homogeneous enhancement after contrast media injection. They compress and deform the surrounding structures; however, a fat space between the tumor and the adjacent structure would remain.

Malignant tumors are generally large in size, with an irregular shape and an ill-defined boundary. They usually exhibit lobulated borders and heterogeneous signals. After contrast media injection, such tumors display heterogeneous enhancement. They often invade the surrounding structure and blood vessels, resulting in a blurred boundary between the tumor and normal adjacent organs. Importantly, they can spread to lymph nodes and distant sites (Nishino et al. 2003; Nakashima et al. 1997).

3 MRI Findings of Retroperitoneal Tumors of Different Nature

3.1 Adipose Tissue Tumors

3.1.1 Lipoma

Lipoma presents typical characteristics on MRI, with a clear boundary and homogeneous internal signals. It displays high signal on T_1WI similar to subcutaneous fat, medium, to high signal on T_2WI, and low signals on fat-suppressed T_1WI or T_2WI (when fat signals are significantly inhibited). After injection of contrast media, it exhibits no enhancement and minimum blood vessel

intensity. In the presence of fiber, smooth muscle, or mucus matrix within a lipoma, an abnormal strip and sheet-like, mesh-like, or cloud-like signals can be visible.

3.1.2 Liposarcoma

Manifestations of liposarcomas on MRI are correlated with its pathological subtype. Due to their complicated composition, MRI findings of liposarcomas are complex and diverse (Tateishi et al. 2003; Hekimoglu 2013). Most tumors present as large irregular lumps on MRI, with an ill-defined boundary or invasive growth, and are frequently lobulated. They exhibit heterogeneously mild to high enhancement after injection of contrast media. Fat-containing liposarcomas display characteristic MRI findings, with clearly short T_1 and long T_2 signals of fat intensity, or signals of cord-like or irregular soft tissue intensity. After injection of contrast media, their solid area exhibits mild, moderate, or even marked enhancement. Liposarcoma with minimal fat mostly shows a signal of soft tissue, without specificity due to lack of fat.

3.2 Muscle Tissue Tumors

3.2.1 Leiomyoma

Leiomyomas are most common in women between 20 and 50 years of age, and 40% of the patients have a history of surgery for uterine fibroids. It often presents a globular or an oval mass with equal T_1 and T_2 signals, smooth edges, and clear boundaries. It displays persistent and slow enhancement after injection of contrast media, mostly to a moderate to high degree. When it becomes larger in size, the tumor may present heterogeneous signals due to necrosis or cystic degeneration.

3.2.2 Leiomyosarcoma

Leiomyosarcomas are most common in the elderly, with smooth edges or lobes and clear boundaries. It mainly shows equal T_1 and T_2 signals, mixed with significantly long T_1 and T_2 signals. It mostly exhibits significantly but heterogeneously slow and persistent enhancement after injection of contrast media.

3.2.3 Rhabdomyosarcoma

Rhabdomyosarcoma is a common childhood malignancy, most often in children under the age of 15. It presents irregular edges with visible lobes and an ill-defined boundary. It displays homogeneous signals, with heterogeneously persistent enhancement, and especially peripheral enhancement after injection of contrast media, which gradually extends to the interior.

3.3 Fibrous Tissue Tumors

3.3.1 Fibrosarcoma

They present as a giant soft tissue mass and show unevenly low T_1WI, often accompanied by hemorrhage, necrosis, or calcification. They show unequally high signals on T_2WI, most of which are heterogeneous with significantly enhancement.

3.3.2 Malignant Fibrous Histiocytoma (MFH)

They are generally large in size and lack a clear boundary with the surrounding tissue. Due to necrosis, cystic degeneration, and hemorrhage, it often shows heterogeneous signals. The majority of such tumors have slightly lower or equal signals on T_1WI, while heterogeneously high, mixed, or extremely high signals on T_2WI. Fibrous tissue shows low signals on T_2WI, hemorrhage presents short T_1 and long T_2 signals, and cystic degeneration has long T_1 and T_2 signals, with unequal enhancement after injection of contrast media. Solid areas are slowly but persistently enhanced to a moderate-to-high degree. Areas between significant and no enhancement are visible within the tumor. Crisscross distribution is a prominent feature on the MRI image. Lumpish lesion of calcification is suggestive of MFH; however, for the unobvious calcification, MRI is inferior to CT.

3.4 Vascular Tissue Neoplasms

3.4.1 Hemangioma

It usually presents with a complete envelope and clear boundaries. It shows homogeneously low to

equal signal on T_1WI, or heterogeneous signals due to necrosis, mucinization, organization, or calcification. It has a high signal-based mixed signal on T_2WI. Multiple scattered plaque-like calcifications within the tumor, as well as intratumorally or peritumorally embedded blood vessels, are visible on images. It significantly is either homogeneously or heterogeneously enhanced after injection of contrast media.

3.4.2 Hemangiopericytoma

It often presents as an irregular soft tissue mass in the retroperitoneum, with visible lobes on the edge, and either a clear or ill-defined boundary. Because of significant bleeding and necrosis, it generally shows heterogeneous (mostly equal to high) T_2WI signals. Solid components show flaky-like delayed progressive enhancement to a substantial extent after injection of contrast media, similar to the vessels on the same section.

3.5 Neurogenic Tumors

3.5.1 Schwannoma

It is usually located in the track where the retroperitoneal neural stem is travelling, commonly seen on the paraspinal or on the medial side of kidneys. It is round, oval, dumbbell, or irregular shaped, with clear boundary. It can be cystic, solid, or a combination of both. It shows either homogeneous or heterogeneous signals on MRI images. After injection of contrast media, solid components most often show mild to moderate progressive delayed enhancement.

3.5.2 Neurofibromatosis

MRI findings of neurofibromatosis are similar to schwannoma. Neurofibromatosis can present as small and scattered loculation or cystization. By contrast, large flake-like cystic lesion tends to be considered as schwannoma.

3.5.3 Paraganglioma

It is usually located in the area where the paraganglia around the inferior vena cava, abdominal aorta, renal artery ,and superior mesenteric artery are distributed. It is round or oval shaped, with smooth edges and clear boundaries. It shows a heterogeneous signal, accompanied by the flow void sign (for vessels) within the tumor, with a persistent heterogeneous enhancement after injection of contrast media.

3.6 Reproductive Embryonic Tumors

3.6.1 Seminoma

MRI demonstrates a large mass located in midline with heterogeneous signals, accompanied by bleeding and necrosis. T_1WI shows slightly low to equal signal, whereas T_2WI has slightly high to high signals, mostly moderate and above heterogeneous enhancement.

3.6.2 Teratoma

On MRI, this tumor shows mixed signal intensity on both T_1WI and T_2WI. It may contain calcification, bone, teeth, and fat tissue, which are specific for the diagnosis of teratoma; however, MRI findings must be combined with CT and comprehensively interpreted.

3.7 Retroperitoneal Cystic Lesions

Retroperitoneal cystic lesions include mesonephric tubular cyst, Mullerian cyst, epidermoid cyst, bronchogenic cyst, and enterogenous cyst. They commonly present as round or oval cystic lesions with smooth edges and clear boundaries in the retroperitoneal space. They exhibit homogeneous long T_1 and T_2 signals with no enhancement after injection of contrast media. A fluid-fluid interface is visible in the presence of different components in the cyst. Diffusion-weighted imaging (DWI) shows high-signal intensity for epidermoid cysts.

4 Diagnostic Values of MRI in Surgical Treatment of Retroperitoneal Tumors

Before the surgical removal of retroperitoneal tumors, MRI should be used to address three major questions: tumor localization, tumor characterization, and tumor relationship with its surrounding

organs/large blood vessels, of which the last one is the key in preoperative examination.

MRI has distinct advantages over CT scans, such as identification of soft tissue with high resolution, multi-dimensional and multi-parameters imaging, without radiation injury (Testini et al. 1996). MRI provides more accurate and intuitive images, with higher diagnostic orientation value in defining the tumor. In addition, it is also superior to CT in determining tissue components by providing more detailed information. MRI can identify hematomas, effusion, empyema, tissue necrosis, and edema within tumors, thus playing an important role in determining the benign versus malignant nature of retroperitoneal tumors.

The relationship between retroperitoneal tumors and surrounding parenchymal organs can be clearly presented on T_1WI. T_2WI is suitable for displaying the invasion of retroperitoneal tumors to adjacent muscles, and especially valuable in determining the degree of invasion to the psoas major or quadratus lumborum. Fat-suppressed T_2WI displays small retroperitoneal tumors, whereas fat-suppressed T_1WI clearly presents enlarged retroperitoneal lymph nodes. Enhanced MRI can excellently overview the relationship between the tumor and surrounding large blood vessels and vital organs.

In summary, the exact location, size, shape, and scope of tumors, as well as the relationship between the tumor and adjacent organs, can be accurately determined by MR based on multi-directional scanning and comprehensive analysis, thus providing an important clue for judging resectability and developing a surgical strategy. MRI may assist in defining clinical stages and predicting the prognosis of retroperitoneal tumors. In addition, it is useful for postoperative follow-up.

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Pathological Diagnosis of Retroperitoneal Tumors

5

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1 Approach to the Pathological Diagnosis of Retroperitoneal Tumors

1.1 Clinical Information

To achieve the correct diagnosis, the pathologist should be apprised of clinical information, including the age of the patient, as well as the location and growth features of the tumor (Tambo et al. 2007). The imaging data, particularly magnetic resonance imaging (MRI), can help demonstrate the extent and texture of the lesion and its relationship to peripheral structures.

1.2 Biopsy Diagnosis

Biopsy for soft tissue tumors was decided by the size and location of the lesion. For example, incision biopsy could be considered for a large and deeply situated mass. Its principal disadvantages are spillage of tumor cells into adjacent compartments attributed to poor hemostasis or faulty biopsy placement, wound infection, and the requirement for hospitalization. Excision biopsy is more expedient and can obtain an entire lesion; however, it could only be performed on small and superficial lesions amenable to complete resection. Fine needle aspiration biopsy may be considered when complete surgical resection is impossible and especially suitable for lesions suspected to be sensitive to chemotherapy by clinical data, e.g., malignant lymphoma.

The biopsy paradigm has evolved in the direction of core needle biopsy, a minimally invasive technique to obtain tissue sample, which is convenient for subsequent procedures, including immunohistochemical staining and molecular test, to reach a correct diagnosis. It is essential to understand the limitations and pitfalls of core needle biopsy. Following basic principles should be kept in mind. First, the pathologist should be aware of the clinician's expectation. The goal of a core needle biopsy may be as simple as to discern primary mesenchymal neoplasm as opposed to lymphoma or metastatic lesion; a distinction usually can be easily made in majority of such cases with the help of adjuvant immunohistochemistry. If definitive surgery will be arranged based on the biopsy, the priority is to determine whether or not the lesion is a sarcoma. If the intention is to provide preoperative

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(neoadjuvant) radio- or chemotherapy, the diagnosis of sarcoma is a requisite. Moreover, the lesion should be subclassified and graded as far as possible. Occasionally, it may be impossible to reliably grade a sarcoma on the basis of limited samples obtained by core needle biopsy. If a serial of biopsies has indicated a high grade, the lesion is often diagnosed as a high-grade sarcoma. Meanwhile, if the lesion is insufficiently sampled or imaging examination suggests characteristics of high-grade sarcoma (i.e., necrosis), this lesion to be hastily diagnosed as low grade should be with more cautions.

Anatomical constraints restrict wide surgical resection of retroperitoneal sarcomas (RPS). Preoperative radiotherapy for RPS is resource intensive, requiring joint effort from diagnostic and treatment teams (Alford et al. 2013). An accurate preoperative diagnosis is required before formulating the therapeutic strategy. Correct diagnosis heavily depends on imaging which determines the acquirement of specimens for pathological assessment with limited amounts of sample.

1.3 Frozen Section Diagnosis

Frozen section diagnosis was commonly performed in the past, with the expectation that definitive surgery would be accomplished using the same intraoperative procedure. However, frozen sections are now procured primarily to assure the surgeon that representative tissue has been obtained that is adequate for the diagnosis or to evaluate resection margin. The former may be accomplished by freezing a portion of the sample or performing a touch preparation (as in the case of a needle biopsy). On a touch preparation, the presence of malignant cells in a nonnecrotic background ensures that the specimen is adequate. A background of reactive or necrotic cells suggests either a pseudocapsule or largely necrotic specimen, requiring additional material depending on the clinical impression.

1.4 Evaluation of Resection Specimens

If malignancy is suspected when a tumor is grossly checked, careful assessment of its relationship with surrounding structures is mandatory. This includes its location, size, relation to vital structure, and the status of necrosis (if it can be judged grossly). For a sarcoma, size provides information about T description for the surgeon. Lesions less than 5 cm are classified as T1, whereas those larger than 5 cm are classified as T2 (Tsujimoto et al. 1988; Trojani et al. 1984). Assessment of the degree of necrosis is important for untreated sarcomas, as this parameter is used in grading systems. The extent of necrosis in lesions treated with preoperative irradiation or chemotherapy is also vital, as it helps to assess the efficacy of the treatment, although it does not carry the same implication as it is in an untreated lesion. The gross appearance of the tumor may be deceptive. Sarcomas may appear to be well circumscribed, whereas some benign tumors present infiltrative and invasive growth patterns. Encapsulation is often misleading, leading to inadequate excision by shelling out or enucleation of the tumor.

To some extent, sampling is tailored according to the specific case. For a benign lesion, a few representative blocks are sufficient, and the entire lesion can be handled if it is small. For a sarcoma, different approaches should be taken. It may be less important to submit numerous sections for a high-grade sarcoma than for a low-grade lesion in which the sampling is being driven by the need to rule out the presence of a high-grade lesion. Generally, one section is obtained for each centimeter of tumor diameter, with no more than ten sections if the lesion appears uniform. Representative sections of the margins or sections designed to display impingement on vital structures are required. Blocks are selected for margins judiciously, depending on the gross appearance of the lesion. Lesions several centimeters away from a margin seldom have positive margins microscopically. Therefore, extensive margin sampling in these situations is less critical

than with excisions containing grossly close margins. One exception is epithelioid sarcoma, a lesion that is deceptive in its gross extent. Digital images can provide visual clues as to the orientation of the specimen and sampling sites.

Most specimens would be handled adequately as described above. However, when diagnostic difficulty is anticipated, archiving some frozen tissue for the possible future ancillary molecular studies is important.

1.5 Microscopic Examination

The first and most important step in reaching a correct diagnosis is careful scrutiny of H&E-stained sections with light microscopy under low-power magnification. Specifically, microscopic features include the size and depth of the lesion, its relation to overlying skin and underlying fascia, and the nature of the borders (e.g., pushing, infiltrative, clear, and ill-defined). The key question is whether the lesion is a reactive process or a neoplasm. Once a reactive lesion can be excluded, the pathologist is justified in proceeding with analysis of the neoplasm. At low power, the architectural pattern, the appearance of the cells, and the characteristics of the stroma can contribute to various differential diagnostic categories categories (Weiss and Goldblum 2001).

1.5.1 Fasciculated Spindle Cell Tumors

These lesions comprise a large group of tumors characterized by long fascicles. Most spindle cell tumors arising from retroperitoneal location are malignant, e.g., malignant peripheral nerve sheath tumor (MPNST) and synovial sarcoma. Cellular schwannoma and fibromatosis must be distinguished from the others, because of their non-metastatic behavior. Fibromatosis is typically a lesion with low cellularity and low-grade nucleus. Cellular schwannoma is characterized by diffuse and intense S100 protein immunoreactivity.

1.5.2 Myxoid Lesion

Soft tissue tumors may appear myxoid from time to time; many lesions display myxoid features consistently. In adults, the differential diagnosis of myxoid tumors includes myxoma, myxoid malignant fibrous histiocytoma (myxofibrosarcoma), myxoid liposarcoma, and myxoid chondrosarcoma. The vascular pattern, the degree of nuclear atypia, and occasionally the staining characteristics of the matrix indicate this distinction. An intricate vasculature suggests myxoid liposarcoma and myxoid malignant fibrous histiocytoma, instead of myxoid chondrosarcoma or myxoma.

1.5.3 Epithelioid Tumors

For the differential diagnosis of epithelioid soft tissue tumors, it is essential to rule out metastatic carcinoma, melanoma, and large-cell lymphomas in the first place. Immunohistochemistry plays a decidedly pivotal role in this regard.

1.5.4 Round Cell Tumors

Round cell tumor is not equivalent to round cell sarcoma, as some benign lesions (e.g., glomus tumor, tenosynovial giant cell tumor poor of giant cell) also enter the differential diagnosis. Some non-soft tissue malignancies that mimic round cell sarcomas (e.g., lymphoma, poorly differentiated carcinoma) should be excluded as well. In general, the age of the patient helps to reach the correct diagnosis of round cell sarcomas. In children, the most common sarcomas are neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma/primitive neuroectodermal tumor (Ewing/PNET), and the rare desmoplastic small round cell tumor. Most of these tumors would not be considered first in adults.

1.5.5 Pleomorphic Tumors

The differential diagnosis of pleomorphic sarcomas relies heavily on sufficient tumor sampling, in conjunction with immunohistochemistry, to identify regions of specific differentiation. Most

pleomorphic sarcomas are actually the extreme manifestation of other tumors, most common with carcinoma, melanoma, and lymphoma, which must be excluded. With the advances of immunohistochemistry and molecular approach, pleomorphic undifferentiated sarcoma (malignant fibrous histiocytoma) has been very rarely encountered.

1.5.6 Hemorrhagic and Vascular Lesions

Although sarcomas are generally highly vascularized, soft tissue lesions presenting as a hemorrhagic mass are limited, including nonvascular (non-endothelial) tumors. Conversely, many vascular tumors (e.g., intramuscular hemangiomas) do not appear hemorrhagic. When evaluating vascular lesions, it is necessary to ascertain whether the lesion is predominantly intravascular or extravascular. Intravascular lesions are always benign, including primarily organizing thrombus/hematoma followed by the occasional angiocentric vascular tumors. Extravascular lesions can be either benign or malignant; features that favor benignancy include sharp circumscription, lobular arrangement of vessels, and the presence of both large (thick-walled) and small vessels. On the other hand, angiosarcomas have irregular margins, lack a lobular arrangement of vessels, and are composed of naked endothelial cells that dissect randomly through tissue planes.

H&E-stained sections provide critical information on growth patterns, degree of cellularity, as well as amount and type of matrix. Growth patterns vary considerably among tumors, ranging from fascicular, herringbone, or storiform patterns in fibroblastic, myofibroblastic, and fibrohistiocytic tumors to plexiform or endocrine patterns, palisading, as well as Homer-Wright and Flexner-Wintersteiner rosettes in various benign and malignant neural tumors. Biphasic cellular patterns with epithelial and spindle cell areas are characteristic of synovial sarcoma and mesothelioma. Although growth patterns could not provide a definitive diagnosis, they help to narrow the various differential diagnostic possibilities.

In addition, the amount and type of extracellular matrix can aid in the differential diagnosis. Abundant myxoid material is produced by a variety of benign and malignant soft tissue tumors, for example, myxoma, myxoid neurofibroma, myxoid liposarcoma, and myxoid chondrosarcoma. Abundant myxoid is usually an indication of a relatively slow-growing tumor. The degree of myxoid change in some malignant tumors is inversely related to the metastatic potential (e.g., myxoid malignant fibrous histiocytoma, myxoid liposarcoma). Abundant collagen formation is more frequently observed in slowly growing tumors than in rapidly growing ones. However, this finding is not always significant and may be a prominent feature of some highly malignant fibrous histiocytomas and postirradiation sarcomas. Examination may provide information as to the presence of calcification and metaplastic changes, especially metaplastic cartilage and bone formation.

The degree and type of cellular differentiation can be determined under high-power examination. Lipoblasts are characterized by sharply defined intracellular droplets of lipid and centrally or peripherally placed round or scalloped nuclei. Round- and spindle-shaped rhabdomyoblasts can be identified in conventionally H&E-stained sections, characterized by deeply eosinophilic cytoplasm with whorls of eosinophilic fibrillary near the nucleus and cytoplasmic cross-striations. Caution is indicated because occasionally entrapped normal or atrophic fat or muscle tissue may closely resemble lipoblasts or rhabdomyoblasts, respectively. Differentiated smooth muscle cells are characterized by elongated shape, eosinophilic longitudinal fibrils, as well as long, slender (cigar-shaped) nuclei, with juxtanuclear vacuoles. Other spindle cells are even more difficult to identify. Distinguishing fibroblasts, myofibroblasts, Schwann cells, and the spindle cells of synovial sarcoma and mesothelioma usually relies on the location and growth pattern rather than on cytologic features. Correct identification of these cells usually relies on immunohistochemical staining. Intracellular inclusions are rare in soft tissue pathology; alveolar soft part sarcoma can be identified by intracellular periodic acid-Schiff (PAS)-positive crystalline material; and digital fibromatosis can

be identified by eosinophilic inclusions consisting of actin-like microfilaments.

Examination under high-power field [HPF] is essential for mitotic counts. Atypical mitotic figures are rare in benign soft tissue tumors, almost always indicating malignancy. Mitotic counts are pivotal for differentiating benign from malignant nerve sheath tumor or smooth muscle tumors; however, they are of little use for diagnosing nodular fasciitis, localized and diffuse giant cell tumors, or malignant fibrous histiocytoma. Although nuclear atypia is associated with malignancy, it may occur as a degenerative feature in benign lesions, such as in ancient schwannoma.

1.5.7 Immature Teratoma

Immature teratoma is usually seen in children and adolescents. It is composed of a mixture of embryonal and adult tissues derived from all three germ layers. Its major components are neuroepithelial and mesodermal elements. Some tumors are predominantly composed of endodermal derivatives, including the esophagus, liver, and intestinal structures. The grading systems of teratomas arising from ovary are as follows:

Grade I: Tumors with rare foci of immature neuroepithelial tissue that occupy <1 low-power field in any slide (low grade)

Grade II: Tumors with similar elements, occupying one to three low-power fields in any slide (high grade)

Grade III: Tumors with a large amount of immature neuroepithelial tissue occupying >3 low-power fields in any slide (high grade)

Obviously, thorough tumor sampling is necessary for this grading scheme; the amount of immature neuroepithelial tissue may be expressed as an estimated percentage of all the tissue examined microscopically. It is important to separate from this group the teratomas with yolk sac or embryonal carcinoma patterns.

1.5.8 Mature Solid Teratoma

Mature solid teratoma has a predominantly solid gross appearance, but multiple small cystic areas also are present. Clearly, extensive sampling is required to exclude the grade I immature teratoma.

1.5.9 Mature Cystic Teratoma

The cystic cavities are lined by mature epidermis. Skin appendages and neural (particularly glial) tissue are extremely common, followed by the cartilage, respiratory tissue, and gastrointestinal tract tissue. Other tissues include the thyroid, various types of melanin-containing tissue, anterior pituitary, various types of neuroendocrine cells, prostate, pancreas, and cavernous blood vessels. By definition, all of the components present in mature cystic teratomas should appear histologically mature. However, on occasions, microscopic foci of immature tissue can be visible, but less than one low-power field in any slide. The behavior of these tumors is usually benign.

1.5.10 Yolk Sac Tumor

Yolk sac tumor is generally a neoplasm of children and young adults. Microscopically, the appearance of yolk sac tumors is very variable. There are reticular or microcystic areas formed by a loose meshwork lined by flat or cuboidal cells, rounded or festooning pseudopapillary processes with central vessels (Schiller-Duval bodies), and solid undifferentiated areas. The mesenchyme-like component has pluripotent properties.

1.5.11 Embryonal Carcinoma

Embryonal carcinoma occurs in children and adolescents (with a median age of 15 years). Microscopically, it looks similar to the embryonal carcinoma of the testis, composed of solid sheets and nests of large primitive cells, occasionally forming papillae and abortive glandular structure. Syncytiotrophoblast-like tumor cells are frequently seen scattered among the smaller cells, immunoreactive for HCG.

1.6 Immunohistochemistry

H&E-stained sections represent the main approach of diagnosis, but usually require the support of ancillary techniques. Immunohistochemistry is the ancillary modality of choice for most diagnostic situations. To use immunostains in the most effective way, it is useful to have an algorithmic approach and to apply the markers in

panels. For example, a panel of antibodies to differentiate carcinomas, melanomas, sarcomas, and lymphomas from one another would be selected before a series of B- and T-cell markers.

1.7 Molecular Pathology

1.7.1 Genetic Profiling

Genetic profiling has been applied into the study of retroperitoneal tumors, including comparative genomic hybridization (CGH) and gene expression arrays. Antoine Italiano's study found that among soft tissue leiomyosarcomas, retroperitoneal leiomyosarcomas represent a specific clinical and molecular entity (Italiano et al. 2013). Indeed, in comparison with leiomyosarcomas of the extremities, retroperitoneal leiomyosarcomas are characterized by a higher risk of metastasis and a distinct genomic and expression profile. Most of the genes overexpressed in retroperitoneal leiomyosarcomas encode proteins involved in muscle differentiation. On the contrary, non-retroperitoneal leiomyosarcomas are characterized by overexpression of genes encoding proteins mainly involved in extracellular matrix, wounding, and adhesion pathways.

1.7.2 Fluorescence In Situ Hybridization (FISH)

Fluorescent in situ hybridization (FISH) is a powerful technique using fluorescent labeled DNA probes to target the given sequences within a nucleus, resulting in colored signals that are detected with a fluorescence microscope. It circumvents the needs for tumor cell culture (fresh or paraffin-embedded interphase nuclei can be analyzed directly) and provides a quick and precise screening approach over large quantities of cells.

It should be emphasized that for certain tumors, FISH studies are essential to make the diagnosis or help to predict its clinical behavior. For example, FISH is highly recommended for childhood neuroblastoma to measure N-myc amplification and for alveolar rhabdomyosarcoma to measure FOXO1 gene rearrangement (Bhargava et al. 2005).

1.7.3 DNA Sequencing

DNA sequencing is essential for some soft tissue tumors, for example, to check c-kit and PDGFRA gene mutation status in the gastrointestinal stromal tumors (GIST) especially when target therapy is applied.

1.7.4 Next-Generation Sequencing

As a revolutionary change to the traditional method, next-generation sequencing is a high-throughput sequencing technology, in which hundreds of thousands to millions of DNA molecules can be sequenced at the same time. High-throughput sequencing obtains a detailed picture of a species transcriptome, also known as deep sequencing. Next-generation sequencing offers a cost-efficient tool for analyzing hundreds of exons. Jenny Welander revealed that a germline mutation (c.223C_T, p.Arg75X) in *SDHA* gene in paraganglioma was validated by Sanger sequencing (Welander et al. 2013).

2 Techniques in Pathological Diagnosis of Various Retroperitoneal Tumors

Retroperitoneal tumors mostly originate from kidneys, adrenal gland, retroperitoneal lymph nodes, and soft tissues. They have a wide range of histological manifestations. Various subtypes often display overlapping morphological features; therefore, pathological techniques such as special staining, immunohistochemistry, and molecular testing are required to further confirm the diagnosis (Frans Graadt Van Roggen and Hogendoorn 2000).

2.1 Special Staining

Specific elements such as mucus, glycogen, collagen fibers, reticular fibers, and secretory granules can be revealed by special staining, which plays an important role in the differential diagnosis of retroperitoneal tumors. For example, characteristic periodic acid-Schiff (PAS)-positive needlelike crystals are visible in the alveolar soft tissue sar-

comas. Reticular fiber is stained to differentiate cancer and sarcomas; PTAH staining is used to label tumors with striated muscle differentiation.

2.2 Immunohistochemical Staining

Retroperitoneal tumors include a wide range of pathologic types and exhibit a variety of histological features. Immunohistochemistry plays a pivotal role in diagnosis and differential diagnosis, especially for poorly differentiated soft tissue tumors with atypical morphology. However, due to inherent limitations of immunohistochemistry, a comprehensive diagnosis should be made based on a combination of histological classification, special staining, and molecular genetic testing:

1. Epithelial markers, including epithelial membrane antigen (EMA) and cytokeratin (CK), are expressed in a number of biphasic tumors (such as synovial sarcoma, mesothelioma, and epithelioid sarcoma) and poorly differentiated tumors (such as malignant peripheral nerve sheath tumors, high-grade sarcoma-like renal carcinoma, and nephroblastoma) (Miettinen et al. 2000).
2. Mesothelial markers mainly include calretinin, D2-40, CK5/6, WT1, and mesothelin. D2-40 is used to label mesothelial and lymphatic endothelial cells assisting in the diagnosis of lymphangioma, Kaposiform hemangioendothelioma, Kaposi's sarcoma, and mesothelioma (Chu et al. 2005; Ordonez 2005).
3. Endothelial cell markers include CD31, CD34, D2-40, factor VIII-related antigen, and Fli-1. CD31 is mainly used to identify vascular neoplasms, whereas it is also expressed in macrophages, megakaryocytes, and small lymphocytic lymphoma. CD34 is often used to label blood vessels and lymphatic vessels for diagnosis of vascular tumors; it also aids in the diagnosis of lipoma, solitary fibrous tumor/hemangiopericytoma, dermatofibrosarcoma protuberans (DSFP), epithelioid sarcoma, and gastrointestinal stromal tumors (GIST) (Hasegawa et al. 1996). CD34 is also expressed in multiple soft tissue tumors, such as neurofibromatosis, dendritic fibromyxoid lipomas and spindle cell lipoma (Alawi and Freedman 2004; McNiff et al. 2005).
4. Nerve cell markers include S100, MBP, CD57, NSE, NF, GFAP, CgA, Syn, and calretinin (Gray et al. 1989). S100 is used to label neurogliocytes, Schwann cells, melanocytes, fat cells, myoepithelial cells, cartilage cells, Langerhans cells, and dendritic cells. S100-positive staining is localized in the nucleus and cytoplasm.
5. Muscle cell markers include desmin, MyoD1, myogenin, muscle-specific actin (MSA), smooth muscle actin (SMA), caldesmon, calponin, and myoglobin. Desmin is widely used in the diagnosis of tumors arising from striated and smooth muscles. It is also use to label tumors containing rhabdomyoblastic differentiation and myoblast component, such as malignant triton tumor, carcinosarcoma, fibroepithelial polyp, inflammatory myofibroblastic tumor, aggressive angiomyxoma, and malignant fibrous histiocytoma/undifferentiated sarcoma. Desmin can be used in the differential diagnosis of gastrointestinal smooth muscle tumors and stromal tumors. In desmoplastic small round cell tumor, typical desmin-positive punctate staining adjacent to the nucleus has diagnostic value. Myogenin and MyoD1 are used to label most of rhabdomyosarcomas and tumors containing striated muscle component. MSA mainly labels smooth muscle cells, vascular pericytes, striated muscle cells, and epithelial cells, and therefore, it is usually used for the diagnosis of leiomyoma, leiomyosarcoma, glomus tumor (angioneuromyoma), myoepithelioma, and rhabdomyosarcoma.
6. Histiocytic and dendritic cell markers include CD68, lysozyme, α1-antitrypsin, α1-antichymotrypsin, S100 protein, CD163, CD1a, CD21, CD23, and CD35.
7. Melanocyte and perivascular epithelioid cell markers include HMB45, melan-A, tyrosinase, S100 protein, and CD63.

8. Other markers: CD117 is a marker for gastrointestinal stromal tumor (GIST) cells, mast cells, and malignant melanoma. DOG1 and PDGFRA are used for the diagnosis of GIST. CD99 is mainly used to label synovial sarcoma, as well as bone Ewing's sarcoma/peripheral primitive ectoderm tumors. BCL-2 is mainly used to label solitary fibrous tumors, synovial sarcoma, Kaposi's sarcoma, and GIST (Hasegawa et al. 1996). ALK is used for inflammatory myofibroblastic tumor. Overexpression of EGFR correlates with a poor prognosis of sarcomas.

2.3 Electron Microscope

Since it can be used to observe the ultrastructure of cells, electron microscope plays an important role in the diagnosis of tumors. For example, a lipid droplet is visible near the squeezed nucleus in liposarcoma; pinocytosis vesicles in Langerhans cell histiocytosis and Birbeck granules in the cytoplasm are characteristic in Langerhans cell sarcoma; and numerous intertwined columnar protrusions on the cell surface are features of interdigital dendritic cell sarcoma.

2.4 Oncogenes and Tumor Suppressor Genes

Oncogenes and tumor suppressor genes play key roles in the formation, growth, and differentiation of tumors. Overgrowth of malignant cells results from activation of oncogenes and inhibition of tumor suppressor genes (negative regulators). Oncogenes and tumor suppressor genes are essential to the diagnosis and prognosis of soft tissue tumors. Those genes include *EWS* and related genes, *SYT*, *SSX*, *PAX*, *FKHR*, *protein tyrosine kinase*, *ASPL*, *TFE3*, *ALK*, and *NTRK3* (Argani et al. 2010). *EWS-FLI1* fusion gene arising from Ewing's sarcoma enables antiapoptosis of tumor cells. *SYT-SSX* fusion genes can be detected in synovial sarcomas, of which *SYT-SSX1* indicates high proliferation and a poor prognosis, whereas *SYT-SSX2* is suggestive of a relatively better prognosis.

2.5 Fluorescence In Situ Hybridization (FISH)

FISH can be used to detect specific DNA or RNA in tumor tissue on sections or smears using fluorescent-labeled complementary probes, so that the corresponding chromosomal segments or a whole chromosome can be displayed under a fluorescence microscope. FISH can detect cells in metaphase and interphase, to effectively quantify chromosomal translocations, deletions, and gene amplifications.

In soft tissue tumors, chromosomal translocation can be detected by both break-apart and dual fusion probes. It is used for diagnosis and differential diagnosis of various soft tissue tumors. For example, fusion between the *SYT* gene located on chromosome 18 and the *SSX* gene located on the X chromosome occurs in more than 90% of synovial sarcoma; thus, *SYT-SSX* fusion gene is of great diagnostic value.

3 Pathological Classification of Retroperitoneal Tumor

A variety of benign and malignant lesions, either primary or metastatic, can be found in the retroperitoneum, while malignant tumors occur four times more frequently than benign lesions. Primary retroperitoneal tumors can be of many types. Soft tissue sarcomas are rare tumors, with retroperitoneal sarcoma representing the second most common sites of origin of malignant mesenchymal tumors after the lower extremities. Sarcomas account for 90% of primary retroperitoneal malignancies, with liposarcoma and leiomyosarcoma making up more than 80% of these tumors. As a group, retroperitoneal soft tissue sarcomas are associated with a poor long-term survival rate. The main reason is the extreme difficulty encountered in performing a complete surgical removal with a rim of normal tissue around the tumor. Complete surgical excision at the time of the initial presentation offers the best chance of long-term survival.

The large majority of the retroperitoneal malignant lymphomas are of non-Hodgkin type

and B-cell derivation. Most are follicular center cell lymphomas. These tumors can be diagnosed by fine needle aspiration, supplemented if necessary by immunostaining.

3.1 Adipose Tissue Tumors

Adipose tissue tumors are the most frequent primary retroperitoneal soft tissue neoplasms. They are particularly prone to arise and grow in the perirenal region. At the time of excision, they are usually extremely large. Some cases present as multiple independent tumor nodules. Liposarcomas in this location present a worse prognosis than those located in the extremities. Total or near-total excision followed by radiation therapy offers the best chance of cure. Histologically, liposarcoma is classified into four subtypes with an increase in malignant nature: well-differentiated, dedifferentiated, myxoid/round cell, and pleomorphic.

The large majority of retroperitoneal liposarcomas are of well-differentiated type (also called atypical lipomatous tumors) or of dedifferentiated type. Myxoid liposarcomas are practically nonexistent at this site; before making this diagnosis, the alternative possibility of a well-differentiated tumor with secondary myxoid changes should be considered. A certain proportion of well-differentiated liposarcoma of the retroperitoneum (higher than at other sites) undergo dedifferentiation, sometimes associated with divergent differentiation in the form of rhabdomyosarcoma (Fig. 5.1). In the presence of a pleomorphic and not easily classifiable retroperitoneal sarcomas, this possibility should be considered, and sampling of the adjacent areas searching for well-differentiated liposarcoma elements (which may look grossly like normal fat) should be carried out. Indeed, the majority of retroperitoneal tumors diagnosed as malignant fibrous histiocytomas represent dedifferentiated liposarcomas. When theses tumors metastasize, the clinical course is rapidly fatal.

Truly benign lipomas of the retroperitoneum are very rare. They are usually very large at the time of diagnosis and can be multiple. Any adipose tissue tumor of the retroperitoneum with atypical features should be designated as well-differentiated liposarcoma, no matter how focal these features are, in view of its marked tendency for recurrence and poor long-term prognosis.

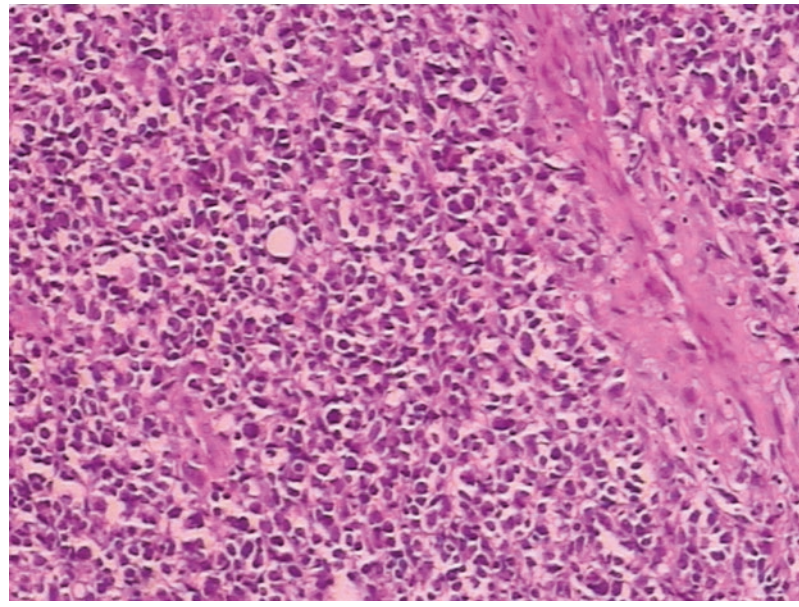

Fig. 5.1 Dedifferentiated liposarcoma, with the component of rhabdomyosarcoma

3.2 Pleomorphic Sarcoma

Pleomorphic sarcoma is the second most common retroperitoneal sarcoma. Three histological subtypes have been identified: undifferentiated high-grade, giant cell, and inflammatory pleomorphic sarcoma. The latter two are usually considered low-grade sarcomas. It is inadvisable to classify these deep-seated lesions as benign no matter how bland their microscopic appearance may be, in view of the fact that some of them will result in repeated recurrences and even metastases.

3.3 Leiomyosarcoma and Leiomyoma

Leiomyosarcoma is the third most common sarcomas, with a particular tendency to undergo massive cystic degeneration when occurring in the retroperitoneal region (Bharti et al. 2014). Retroperitoneal smooth muscle tumors containing ≥5 mitoses per 50 high-power fields should be classified as leiomyosarcomas. Tumor cell necrosis or a tumor size >10 cm is strongly suggestive of malignancy, even in the presence of a low mitotic count. When these criteria are applied to retroperitoneal tumors, nearly all of them qualify as leiomyosarcomas (Fig. 5.2). The local control is obtained with wide surgical excision and neoadjuvant or adjuvant radiation therapy. Chemotherapy is employed for the treatment of systemic disease. Peculiar morphologic variations in retroperitoneal leiomyosarcoma are granular cell changes and focal skeletal muscle differentiation.

Previous series focusing on retroperitoneal sarcomas have shown the higher metastatic risk of leiomyosarcomas in comparison with other retroperitoneal histologic subtypes including liposarcomas.

Leiomyoma is very rare as a primary retroperitoneal neoplasm. When encountering a tumor in this region with a leiomyomatous appearance, one should consider the alternative possibilities of uterine leiomyoma extending posteriorly, well-differentiated leiomyosarcoma, benign or malignant GIST, lymphangiomyoma, and angiomyolipoma. The majority of truly benign smooth muscle tumors presenting as retroperitoneal masses are anatomically and/or functionally related to the female genital tract.

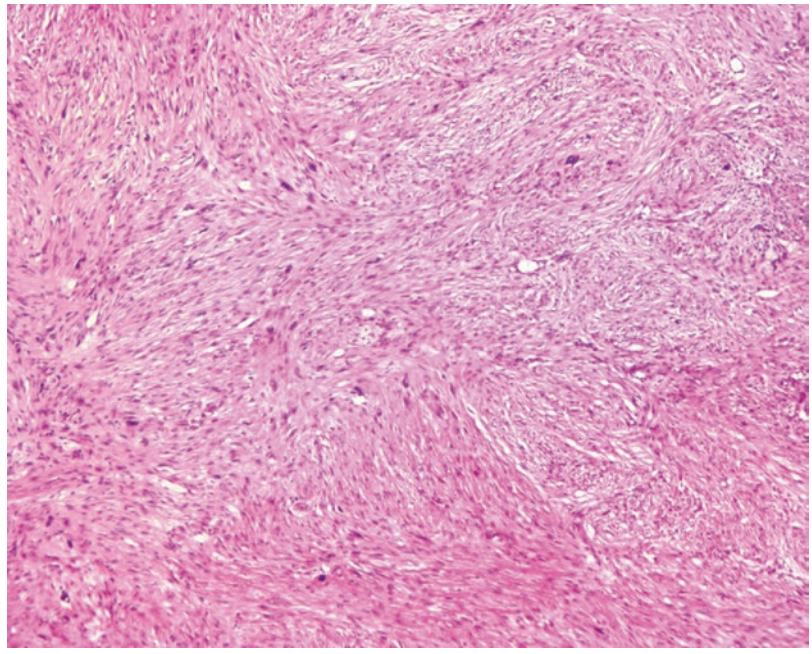

Fig. 5.2 Leiomyosarcoma

3.4 Renal Angiomyolipoma

Renal angiomyolipoma is a generally benign retroperitoneal tumor that can be easily confused with leiomyosarcoma in a biopsy specimen due to the atypia commonly seen in the smooth muscle elements (Fig. 5.3). The primarily intrarenal location, the admixture with mature fat and thick-walled blood vessels, and the immunoreactivity for HMB-45 should allow the recognition of this entity. Primary extrarenal examples of this tumor do exist; some of them are epithelioid and malignant.

3.5 Rhabdomyosarcoma

Rhabdomyosarcoma of the retroperitoneum is usually of the embryonal type (including its botryoid variety) and rarely of the alveolar type and mostly affects infants, children, and young adults. The differential diagnosis of retroperitoneal rhabdomyosarcoma includes malignant lymphoma, Ewing's sarcoma/PNET, and (intra-abdominal) desmoplastic small cell tumor. Adults are uncommonly afflicted with rhabdomyosarcoma (Simon et al. 2003). Local control is important in the curative treatment of adult RMS. Adult RMS carries a much worse prognosis compared to childhood RMS.

3.6 Rhabdomyoma

Rhabdomyoma is practically nonexistent in the retroperitoneum; however, a convincing case combining features of the fetal and adult types of this tumor has been reported in neonate (Whitten and Benjamin 1987).

3.7 Fibromatosis

Fibromatosis may occur in association with mediastinal involvement (Casillas et al. 1991). It is characterized by fibroblastic proliferation that disrupts soft tissue planes. This process occurs without any inflammation or signs of definite neoplasia.

In contrast to idiopathic retroperitoneal fibrosis (a disorder with which it is often confused), it lacks a prominent inflammatory component, except for perivascular lymphocytic cuffing at the growing edge.

3.8 Solitary Fibrous Tumor

Solitary fibrous tumor (SFT) can present as a primary retroperitoneal mass, accompanied by hypoglycemia (Demicco et al. 2012). The solitary fibrous tumor is a distinct spectrum of

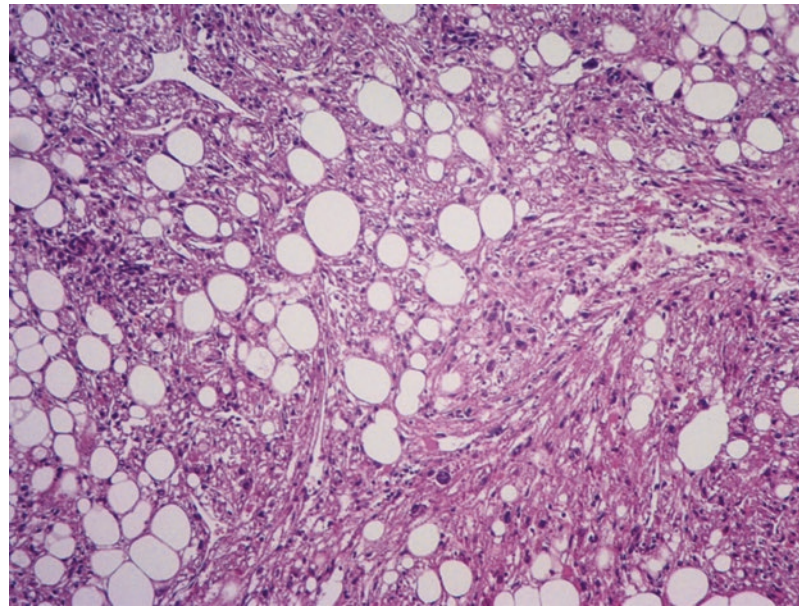

Fig. 5.3 Angioleiomyolipoma

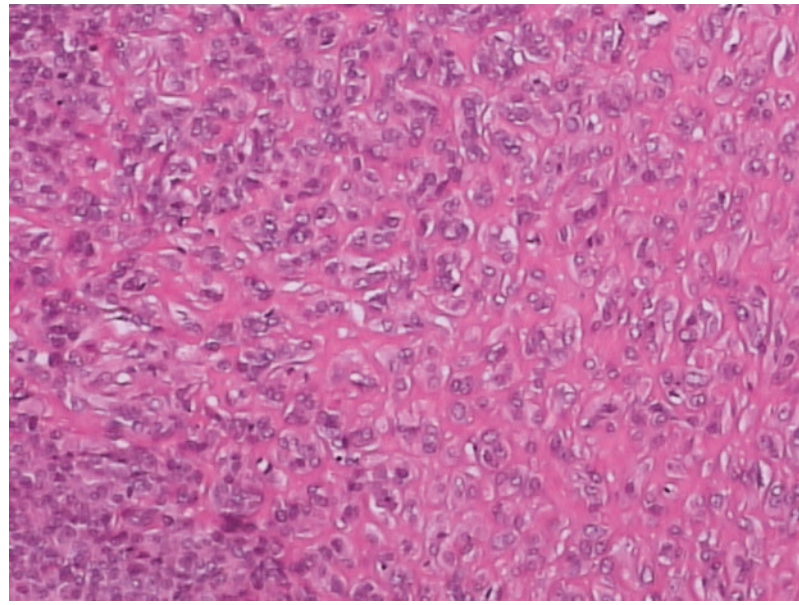

Fig. 5.4 Malignant solitary fibrous tumor

mesenchymal tumors, of which hemangiopericytoma is considered as a phenotypic variant. This tumor is composed of variably pleomorphic spindle cells admixed with collagen. The tumor is CD34 positive, with a dilated "staghorn"-like vascular network (Hasegawa et al. 1996). The solitary fibrous tumor is categorized as intermediate biological potential with low risk of metastasis and a relatively indolent course. The diagnostic criteria of malignant solitary fibrous tumors (MSFTs) (Fig. 5.4) include high cellularity, high mitotic activity (>4/10 HPF), pleomorphism, hemorrhage, and necrosis (England et al. 1989; Ito et al. 2008). Metastasis may occur even in benign SFTs. Even if the histological diagnosis of SFT is malignant, complete excision of the tumor is thought to have a favorable prognosis.

3.9 Vascular Tumors

Vascular tumors include hemangioma, lymphangioma, lymphangiomyoma, and angiosarcoma. Some of the angiosarcomas are of the epithelioid pattern (Fig. 5.5); prominent eosinophilic globules may be present in the cytoplasm of the tumor cells. A peculiar variant of infantile hemangioendothelioma mimicking Kaposi's sarcoma, accompanied by thrombocytopenia and hemorrhage (Kasabach-Merritt syndrome), has a special tendency for a retroperitoneal location.

3.10 Peripheral Nerve Tumors

Peripheral nerve tumors (PNSTs) of both benign and malignant types occur; as a matter of fact, the retroperitoneum is a relatively common site for their development. The benign tumors include schwannomas, neurofibromas, and (rarely but diagnosed with increasing frequency) perineuriomas. Malignant peripheral nerve tumors (MPNSTs) usually present as paraspinal masses and tend to behave in an aggressive fashion. They may directly invade the bone and metastasize distantly.

Synovial sarcoma, alveolar soft part sarcoma, extraskeletal osteosarcoma, and endometrial stromal sarcoma can present as primary retroperitoneal neoplasms.

3.11 Germ Cell Tumors

Primary extragonadal germ cell tumors are rare, accounting for approximately 5% of all primary retroperitoneal tumors (Su et al. 2012).

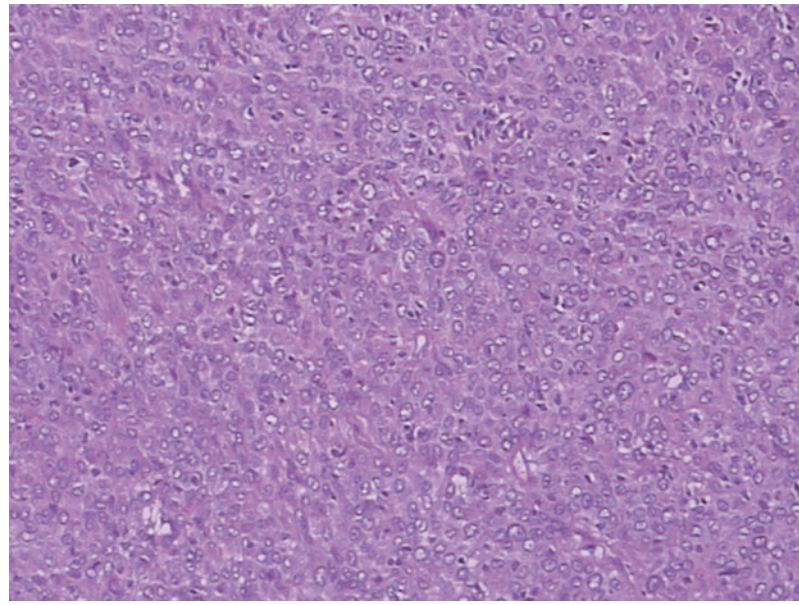

Fig. 5.5 Epithelioid hemangioendothelioma

The retroperitoneum is the second most common extragonadal sites for germ cell tumors, after mediastinum. Primary extragonadal germ cell tumors are predominantly non-seminomatous in histology.

Retroperitoneal germ cell tumors in children are represented by mature and immature teratoma, embryonal carcinoma, and yolk sac tumor. These tumors may occur in combination. Their features merge with those of sacrococcygeal teratomas.

Retroperitoneal germ cell tumors in adults can theoretically arise in this location or represent metastases from primaries in the gonads. Both types are much more common in males. The entire microscopic gamut includes seminoma (germinoma), embryonal carcinoma, teratocarcinoma, mature and immature teratoma, yolk sac tumor, and choriocarcinoma.

The chances of a retroperitoneal germ cell tumor in a male being metastatic from a small insidious testicular primary tumor are much higher than for a mediastinal tumor of the same type. The gross appearance of the tumor may give a clue in this regard: primary retroperitoneal neoplasms are formed by a single mass, whereas those metastatic from the testis tend to involve several nodes, often on both sides of the peritoneum. Also, seminomas are more likely to be primary than non-seminomatous germ cell tumors.

3.12 Other Primary Tumors and Tumorlike Conditions

3.12.1 Sympathetic Nervous System Tumors

Sympathetic nervous system tumors arise from adrenal sympathetic nervous system or outside the adrenal gland in the retroperitoneum, including neuroblastoma, ganglioneuroblastoma, ganglioneuroma and their variants. Retroperitoneal paragangliomas are originated outside of adrenal glands, accounting for 10% of paragangliomas. They may occur anywhere along the midline of the retroperitoneum.

3.12.2 Malignant Lymphoma

Malignant lymphoma can primarily arise from retroperitoneum and mostly belong to B-cell-derived non-Hodgkin's lymphoma. The major subtype is follicular lymphoma with prominent fibrosis.

3.12.3 Myelolipomas

Myelolipomas similar to those of the adrenal glands can be encountered in the presacral area. They are well circumscribed, can attain a huge size, and are composed of a mixture of fat cells and normal marrow hematopoietic elements.

3.12.4 Tumors of Mullerian Type

Tumors of mullerian type including mixed mullerian malignant tumor (mullerian carcinosarcoma) are occasionally seen as primary retroperitoneal masses in the pelvis or rectovaginal septum. They can be of serous, mucinous, or endometrioid subtype, either benign, borderline, or malignant.

3.12.5 Metastatic Tumors

Secondary neoplasms may appear in the retroperitoneal space as a result of local extension or lymph node involvement. The former is mainly represented by pancreatic carcinoma and primary bone neoplasms, notably sacrococcygeal chordoma.

The carcinomas most commonly giving rise to retroperitoneal lymph node metastases are those originating in the testis, prostate, pancreas, uterine cervix, endometrium, and kidney.

4 Grading and Staging of Soft Tissue Sarcomas

Besides histologic classification and subclassification, the grading and staging systems also provide important clues for predicting the biological behavior of soft tissue sarcomas. Grading is a useful tool for assessing the degree of malignancy based on histological indicators, whereas staging is determined by the scope of tumor involvement. Criteria for staging are relatively constant, whereas those for grading vary greatly depending on the types of tumors. For example, mitotic activity is important for the grading of leiomyosarcomas but not for the undifferentiated pleomorphic sarcomas.

4.1 Grading System of Soft Tissue Sarcomas

Grading of soft tissue tumors was first proposed specifically for fibrosarcomas by Borders et al. (1939). Studies over the years have emphasized the value of grading and identified necrosis and mitotic activity as its vital criteria. In a case study involving 1000 patients, the integration of grading with staging was proved to be an essential guide for predicating prognosis. Importantly, the study indicated that clinical staging would be determined basically by grading if no metastasis had occurred. Pitifully, a reliable grading system was not proposed in this study where grading was only judged subjectively according to the professional's experience. However, this study has proposed a concept that is still well-accepted today—some sarcomas are low grade in nature, while others are high grade essentially. This concept is not substantially fit for epithelial malignancies, in which precancerous lesions are commonly present.

Since then, a number of grading systems have been proposed internationally by Myrhe Jensen, Costa, Hashimoto, Van Unnik, Gustafson, and Markhede. Tumors are divided into two to four grades in some systems with individual strengths and weaknesses. None has been adopted by the World Health Organization (WHO), while the most common system used in China is the French grading which is proposed by Trojani et al. and improved by the French Federation of Cancer Centers Sarcoma Groups (FNCLCC), referred to as "FNCLCC grading" (Coindre et al. 1996; Stoeckle et al. 2001).

The FNCLCC grading system has integrated three parameters: tumor differentiation, mitotic index, and tumor necrosis. Grading is calculated by summing up the scores obtained for each of these parameters (Table 5.1). It has been shown that tumor grading is an independent and the most important prognostic factor. However, this system also has some limitations, including the determination of "differentiation score," due to difficulty in defining a well-differentiated vs. undifferentiated sarcoma, especially for specimens in response to chemotherapy.

Table 5.1 FNCLCC grading system

Parameter	Criteria
Tumor differentiation	Tumor differentiation
1	Sarcomas closely resembling normal adult mesenchymal tissue (e.g., well-differentiated liposarcoma)
2	Sarcomas for which histologic typing is certain (e.g., myxoid liposarcoma)
3	Embryonal and undifferentiated sarcomas, sarcomas of uncertain type (e.g., undifferentiated pleomorphic sarcoma)
Mitosis count	/10HPF
1	0–9
2	10–19
3	≥20
Tumor necrosis (under microscopy)	
0	No necrosis
1	≤50% tumor necrosis
2	>50% tumor necrosis
Histologic grade	Sum/total score
1	2–3
2	4–5
3	6–8

Additionally, none of the grading systems can be widely accepted because of specific characteristics of sarcomas. As mentioned before, it seems unnecessary to categorize some sarcomas of either low-grade malignancy or high-grade malignancy in nature. For example, well-differentiated liposarcoma itself is a low-grade and nonmetastatic tumor, whereas alveolar rhabdomyosarcoma itself is highly malignant. Another limitation of the system is the difficulty in grading rare sarcomas, such as epithelioid sarcomas. Moreover, clinical features of some tumors have more prognostic significance than histologic grading. Thus, the relevance between grading and biological behavior is significantly reduced. For example, the number and size of the lesions play a more important role than grading in predicting the prognosis of skin angiosarcomas.

Nevertheless, grading remains the most effective and economical tool in assessing the prognosis of sarcomas. Tumor specimens should be obtained prior to neoadjuvant therapy in order to avoid the effects of chemotherapy on grading parameters.

4.2 Staging System of Soft Tissue Tumor

Staging system refers to stratification of similar tumors based on histological grade, size, and location of tumors, as well as the presence or absence of distant metastases, to facilitate both prognostic evaluation and efficacy assessment. For adults with soft tissue sarcomas, the AJCC staging system developed by the American Joint Committee on Cancer is commonly used, which classifies soft tissue sarcomas with tumor size, lymph node involvement, presence of distant metastases, histologic subtype and grade, as well as invasive depth. Other staging systems include the Musculoskeletal Tumor Society staging system and the SIN staging system.

The disadvantage of the AJCC system is the difficulty in comparing various tumors originating from different sites, because it classifies tumors based on their individual lesions. The extent of resection during the surgery varies with the specific site of the tumor. Staging of soft tissue sarcomas requires a close multidisciplinary cooperation.

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6 Perioperative Anesthetic Management and Preoperative Precautions for Retroperitoneal Tumors

Lei Guan, Tianzuo Li, Bin Zhu, and Lan Yao

1 Anesthetic Risk Assessment and Preparation for Retroperitoneal Tumor Surgery

Retroperitoneal tumors (RPTs) refer to neoplasms that occur in the retroperitoneal space, mainly arising from fat, loose connective tissue, muscle, fascia, blood vessels, nerves, and lymph tissue, within the retroperitoneum, but excluding the origin from retroperitoneal organs (such as the kidney, pancreas, suprarenal gland, and ureter). They are a relatively rare entity of tumor and mostly malignant (accounting for about 70% of total cases). Common benign RPTs include teratoma, nerve sheath tumor, and fibroma. Malignant RPTs include liposarcoma, fibrosarcoma, leiomyosarcoma, embryonal carcinoma, neurofibrosarcoma, and malignant lymphoma. These tumors are located deeply inside the abdominal cavity with a certain space for expansion. It is tough to diagnose these tumors at the early stage due to lack of typical signs or symptoms. As they grow larger, tumors may compress or invade the surrounding organs and tissues, resulting in subsequent presentations in patients. All of these factors contribute to a challenge for surgeons to radically remove RPTs. The key points in the assessments of anesthetic risk for patients include clinical presentations at baseline, concomitant diseases, current treatment, and organ system function. The preexisting disease of patients must be well controlled in order to create optimal conditions for surgery.

1.1 Patient Assessment

To ensure safe and smooth implementation of anesthesia procedure, each patient should receive a detailed assessment before anesthesia in clinics.

1.1.1 Medical Records Review

To make a comprehensive assessment requires full understanding of the patient's surgery and anesthesia-related conditions:

1. General condition: age, gender, development, nutrition, mental state, spine and extremities, activity, blood pressure, heart rate, respiration, body temperature, and so on.
2. History of the present illness, past medical history, past history of anesthesia, family history of tumor, histories of drug allergy, cigarette smoking and alcohol consumption,

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as well as presence, severity, and pathologic effects of concomitant diseases such as neurological, respiratory, cardiovascular, endocrine, and other systemic disorders.
3. Routine blood, urine, and stool tests, blood biochemistry, water and electrolyte acid-base status, X-ray, ECG, liver and kidney function, as well as other special examinations.
4. Understand the administration of special anesthesia-related drugs and preoperative preparations.

1.1.2 Physical Examination

1. Give priority to reexamination of the nervous, circulatory, and respiratory systems.
2. Perform special tests depending on the specific type of anesthesia, e.g., patients who receive intrathecal block should be examined by X-ray, for the spine and skin of the chest and back; those who receive general anesthesia should be examined for dentures, dental caries and loose teeth, the extent of mouth opening, the activity of the head and neck, the height of the throat, and feasibility for tracheal intubation.
3. Understand the patients' mental state and anesthesia requirements.
4. Carefully explain to patients in order to eliminate their concerns and to enhance their confidence in the anesthetic procedure and their trust in anesthesiologists.
5. Determine the type and premedication of anesthesia according to physical condition and surgical requirements of the patients.
6. If any examination is not performed as scheduled or needs to be repeated or if the patient's physical condition does not allow undergoing anesthesia, anesthesiologists should directly notify the physician to seek for a resolution through consultation and report to the senior physician in the department.
7. Anesthesiologists must ask for advice from surgeons about the surgical site, requirements, options, and time length of duration, potential intraoperative risks, and anesthetic requirements.
8. Explain the choices of anesthesia, potential anesthesia complications, adverse effects of anesthetics, anesthesia accidents, as well as self-supporting drugs and supplies to the patients' relatives before anesthesia, in order to obtain their consent before asking them to sign the anesthesia consent form.

1.2 Preanesthetic Preparation for Patients with Common Concomitant Diseases

Anesthesia risk in hypertensive patients depends on the presence of secondary damages to vital organs and the extent of the damage, including the changes in the brain, heart, coronary blood supply, and renal function. Patients should be treated with antihypertensive drugs to keep their blood pressure below 160/90 mmHg, as well as with preoperative medication to improve the functions of vital organs and to maintain water and electrolyte balance before anesthesia.

Anesthesia is generally well tolerated in NYHA Class I and Class II patients whereas poorly tolerated in NYHA Class III and Class IV patients. It is necessary to improve the preoperative cardiac function and to control chronic heart failure for NYHA Class III and Class IV patients. The heart rate in atrial fibrillation should be controlled, with the ventricular rate of <100 bpm. Premature ventricular contractions (PVCs) should be less than 5 beats/min. Drugs that can effectively control PVCs should be administered appropriately except for multifocal PVCs or R on T. Patients with obvious ECG abnormalities should undergo consultation with cardiologists. For patients with ischemic heart disease, clinicians must clarify the patient's present history of angina and previous history of myocardial infarction, as well as the current status of cardiac decompensation. Patients should not undergo elective surgery anesthesia if they have experienced myocardial infarction within 6 months.

Respiratory diseases: As patients with acute respiratory infections are prone to developing atelectasis and pneumonia postoperatively, elective surgery should be scheduled 1–2 weeks after patients have shown complete response. Patients are asked to quit smoking 1–2 weeks before operation. Patients with pulmonary heart disease (cor pulmonale) should be treated with drugs to maintain an

optimal cardiac function. Prophylactic antibiotics may be administered 3–5 days before surgery.

For patients with diabetes, urine glucose should be basically controlled to be negatively or weakly positive, urine ketone bodies must be negative, and fasting blood glucose must be less than 8.0 mmol/L before operation. During the operation, these patients should be monitored for blood glucose and treated with insulin when appropriate, and attention should be paid to the maintenance of normal serum potassium. Before emergency surgery, blood glucose, serum potassium, sodium, chlorine, pH, urine glucose, and urine ketone bodies should be examined. Insulin should be administered accordingly. Anesthesia and surgery should not be considered until urine ketone bodies have been converted to negative and electrolyte levels have recovered to normal.

1.3 Physical Status Classification Before Anesthesia

Refer to physical status (PS) classification system of American Society of Anesthesiologists (ASA) (Table 6.1).

Table 6.1 ASA physical status (PS) classification system

Classification	Definition
I	Normal healthy
II	Mild systemic disease
III	Severe systemic disease that limits the daily activities but does not cause loss of working ability
IV	Severe systemic disease that causes loss of working ability and poses a threat to life
V	A moribund person who is not expected to survive for 24 h without or with the operation

Note: The addition of "E" denotes each class of emergency surgery. For Class I and Class II patients, anesthesia is generally well tolerated, while anesthesia poses a certain risk to Class III patients for whom clinicians should make appropriate preanesthesia preparation for the prevention and treatment of complications; anesthesia poses great risk to Class IV patients for whom active rescue should be given; simultaneously, the surgeons and the patients' families must be clearly informed of accidents that may occur during perianesthesia period before surgery.

1.4 Preparation of Anesthetic Instruments and Devices

Anesthesia devices are used to implement general anesthesia, supply oxygen, as well as assist in or control ventilation. Additionally, modern anesthesia devices are equipped with electronics and computer control and monitoring system, thus requiring better operative and management skills. Devices must be thoroughly examined before use in order to minimize accidents caused by mechanical failure.

1.4.1 Air Source

Oxygen, nitrous oxide, or compressed air has a distinctive mark. Gas source output pipeline should be connected to the corresponding gas source input joint of anesthesia machine, which cannot be mistakenly connected.

1.4.2 Anesthesia Machine

Anesthesia machine is the most important device in anesthesia. It has fast oxygen supply and assisted respiration and other special functions, which is an indispensable element of anesthetic procedure. Modern anesthesia machine must have the following functions:

1. Flowmeter: The scales should be accurate, the knob can be opened and closed freely, and the float can move up and down flexibly and shouldn't bounce when starting. Float should point to zero when the meter is turned off. Glass tube should be intact without steam, and the knob shouldn't be closed too tightly.
2. Evaporator: Inhaled anesthetics are placed into the corresponding evaporator after checking their names, and the volume should not exceed the "maximum" mark. Vaporizer's concentration dial should be rotating properly, and the dial can be closed by a "padlock." The accuracy of output concentration marker of the evaporator can be verified by anesthetic concentration monitor.
3. Loop system: Check the components for leaks before implementation of anesthesia. Inhalation and exhalation valves should be opened and closed flexibly, free from condensed water vapor or soda lime dust. Each

joint must be matched to each other. It should be noted that residual water in the loop during anesthesia should be removed timely if any; attention should be paid to the degree of discoloration or heating of soda lime; if any, soda lime should be timely replaced.
4. Attention should be paid to the activity of ventilator balloon. If any joggling or shaking occurs or the balloon does not empty completely, the fresh gas flow should be adjusted.
5. Once the respirator is disconnected from the connecting pipe of anesthesia machine and the nozzle is shut off with the palm, the pressure gauge rises immediately. When it is fully inflated, the balloon does not move up and down any longer, suggesting that it is intact without leakage.
6. Modern anesthesia machine is equipped with a variety of breathing patterns, adjustable respiratory parameters that can apply to both adults and children, perfect respiratory monitoring system (such as inhaled oxygen concentration, tidal volume, respiratory rate, respiratory ratio, peak airway pressure, and mean pressure), and even respiratory function monitoring feature.

1.4.3 Monitoring Equipment

Vital signs of patients should be monitored during surgery. Routine monitoring includes noninvasive blood pressure, ECG, and pulse wave oxygen saturation. Patients who undergo general anesthesia should also be monitored for end-tidal carbon dioxide and body temperature. Special operation may require special monitoring. Therefore, further requirements have been raised for monitors.

1. Invasive blood pressure monitoring: Monitors with blood pressure monitoring feature must be selected during major surgery, and those with multichannel invasive pressure monitoring features should be preferred as they can be used to monitor various pressures simultaneously, such as arterial pressure, central venous pressure, and pulmonary artery pressure.
2. Cardiac output monitoring: Cardiac output monitoring can be conducted as a part of the multifunctional monitor or by a separate monitor.
3. Neuromuscular monitoring: For patients with neuromuscular diseases or severe liver and kidney dysfunction, muscle relaxation monitoring is required during general anesthesia.
4. Monitoring depth of anesthesia: Adjust medication according to monitoring results.

1.4.4 Testing Device

As tests are often performed during anesthesia, including routine blood, biochemical, coagulation, and arterial blood gas (ABG) tests, appropriate devices should be equipped in the anesthesiology department.

1.4.5 Insulation Devices

Insulation devices include insulation mattress, hot air heater, and infusion warmer.

1.4.6 Infusion Set

Infusion set includes various infusion pumps, syringe pumps, target-controlled infusion pumps, and blood transfusion devices.

1.5 Preparation of Anesthetics

1.5.1 Preanesthetic Medication

1. Sedative hypnotics: such as phenobarbital sodium, diazepam, and midazolam.
2. Narcotic analgesics: such as meperidine and morphine.
3. Anticholinergics: such as atropine and scopolamine.
4. Antihistamines: hormones and gastric mucosal protective agents.

1.5.2 Local Anesthetics

1. Lipids: such as procaine, chloroprocaine, and tetracaine.
2. Amides: such as lidocaine, bupivacaine, and ropivacaine.

1.5.3 General Anesthetics

1. Intravenous anesthetics: such as propofol, ketamine, thiopental, midazolam, etomidate, and sodium oxybate (sodium γ-hydroxybutyrate).
2. Inhaled anesthetics: such as enflurane, isoflurane, sevoflurane, desflurane, halothane, and nitrous oxide.

3. Narcotic analgesics: such as morphine, pethidine, fentanyl, sufentanil, remifentanil, tramadol, and nonsteroidal anti-inflammatory drugs (NSAIDs).
4. Muscle relaxant: such as succinylcholine, mivacurium, vecuronium, pipecuronium bromide, atracurium, pancuronium, and rocuronium.

1.5.4 Autonomic Nervous System Drugs

1. Cholinergic drugs
   Atropine, scopolamine, anisodamine, neostigmine, and edrophonium chloride
2. Adrenergic drugs
   Norepinephrine, epinephrine, phenylephrine, dopamine, dobutamine, isoproterenol, ephedrine, metaraminol clonidine, phentolamine, urapidil, metoprolol, esmolol, and labetalol.

1.5.5 Vasoactive Drugs

1. Vasodilator

   Prazosin, urapidil, phentolamine, diazoxide, nitroprusside, nitroglycerin, hydralazine, and indapamide

2. Calcium channel blockers

   Nifedipine, nimodipine, nicardipine, felodipine, lacidipine, amlodipine, diltiazem, verapamil, and flunarizine

3. Antiarrhythmic drugs

   Quinidine, procainamide, lidocaine, phenytoin, mexiletine, propafenone, amiodarone, bretylium, and adenosine

1.5.6 Infusion

Infusion includes crystalloid solutions, colloidal solution, and electrolyte supplements, of which:

1. Crystalloid solution: such as normal saline, multiple electrolytes injection, balanced salt solution, and dextrose and sodium chloride injection.
2. Colloidal solution: such as hydroxyethyl starch (HEAS), all kinds of gelatin preparation, and dextran preparation.
3. Electrolyte supplements: such as sodium chloride, potassium chloride, calcium chloride, magnesium sulfate, and sodium bicarbonate at high concentration.
4. Dehydration diuretic drugs: such as furosemide and mannitol.

1.5.7 Drugs Acting on Coagulation System

Heparin such as unfractionated heparin and low molecular weight heparin; prothrombin complex; fibrinogen; V/VII factor preparation; and antifibrinolytic drugs, such as tranexamic acid injection, aminocaproic acid, and protamine.

In each operation requiring anesthesia, clinicians should fully assess patients' preoperative risks of anesthesia and surgery and thus prepare for appropriate medication according to perioperative accidents that may occur.

2 Selection of Anesthetic Method and Regulation of Intraoperatively Anesthetic Depth

2.1 Selection of Anesthetic Method

In general, the choice of anesthetic method for patients who undergo surgical procedures is determined by anesthesiologists based on the size of the surgery, the patient's physical condition, and their proficient in anesthesia.

In early stage, retroperitoneal tumors which are confined to relatively small areas with intact envelopes can be resected under epidural anesthesia. However, most of the tumors are located more deeply into the abdomen with greater space for expansion and generally asymptomatic in the early stage. When they grow larger and larger over time, tumors may fulfill the retroperitoneal space. Symptoms don't occur until the boundary between the tumor and intestine or blood vessels becomes ill-defined. At this point, general anesthesia is necessary because spinal anesthesia alone cannot meet the operative requirements. In addition, spinal anesthesia interferes with the compensatory mechanisms that are activated in

response to blood loss, as it can block the sympathetic ganglia, causing dilation of the blood vessels. Therefore, hypovolemic shock is a contraindication to spinal anesthesia. By contrast, general anesthesia not only alleviates the suffering of patients but also facilitates the maintenance of respiration and circulation as well as monitoring the changes in vital signs and hemodynamics. General anesthesia is a more popular choice for patients with retroperitoneal tumors who often experience loss of a large amount of blood intraoperatively. If necessary, general anesthesia may be combined with epidural anesthesia in order to reduce medication/dosage.

2.2 Regulation of Intraoperative Anesthetic Depth

Anesthesia is far more than maintaining hemodynamic stability and keeping patients in unconscious state. As postsurgical traumatic syndrome often occurs, forgetting and consciousness have become more and more important components in the field of anesthetic depth. A suitable anesthesia should at least meet two standards:

1. Loss of awareness and memory (implicit memory).
2. Blockage of noxious stimulation response (i.e., analgesia, muscle relaxation, loss of autonomic response) which has been shown to occur at a subcortical level and therefore may be unrelated to consciousness.

2.2.1 Anesthetic Depth and Noxious Stimulation Response

A variety of noxious stimulation responses during anesthesia may be acquired by somatic and autonomic responses of patients. Somatic responses can be reflected by pain and body movement, while autonomic responses can be reflected by sympathetic, parasympathetic, endocrine, and neural responses.

Clinical Presentations

With the wide use of muscle relaxants, the body movement and breathing types have lost their original indication. Clinically, the depth of anesthesia is estimated only based on the blood pressure, heart rate, and autonomic nervous reaction; however, such indicators vary greatly depending on individual differences, medication, diseases, and surgical procedures, thus causing certain difficulty in accurately determining the depth of anesthesia.

Pupillary Light Reflex

Pupillary light reflex is commonly used to evaluate the effects of anesthetics and the function of brain stem during the surgery. It can be used to assess surgical stimulation; however, its clinical reliability is affected by opioids, advanced age, the disease itself, and other factors.

Lower Esophageal Contractility (LEC)

In human, the lower esophageal sphincter is composed of smooth muscle, and its spontaneous contraction is controlled by the vagus nerve center and reticular activating system (RAS) within the brain stem. Spontaneous contraction of esophagus only occurs in patients who are awake and sober. Under anesthesia, the spontaneous contraction disappears, resulting in a decrease in waveform amplitude even with stimulation, which can be used to determine the depth of anesthesia.

Heart Rate Variability (HRV)

HRV refers to minor variation in the time interval between consecutive heartbeats. Under physiological conditions, HRV that originates from the self-regulatory activity of the sinoatrial node is regulated by advanced innervation of the brain as well as spontaneous rhythm and pressure chemoreceptor activities of central nervous system (CNS) via the sympathetic and vagal nerves. Heart rate variability may be used to assess quantitatively the tension and balance of cardiac sympathetic nerve and vagus nerve. When any harm or injury stimulates human body, the sympathetic system will be activated, thus increasing heart rate variability. Studies have indicated a correlation between the depth of anesthesia and the change in heart rate variability, which can serve as an index for objectively evaluating the depth of anesthesia.

2.2.2 Depth of Anesthetic and Level of Consciousness

How to prevent intraoperative awareness by reasonably regulating the depth of anesthesia has become a common concern in today's anesthesiology community. Indicators such as heart rate, blood pressure, respiration, eye symptoms, lacrimation, and sweating that were previously widely used in clinical judgment on the depth of anesthesia are independent of awareness, so the intraoperative awareness cannot be completely eliminated even if the depth of anesthesia is maintained stable during the surgery. The consciousness state under anesthesia can be divided by cognitive function into four stages as follows: (1) conscious awareness with explicit memory, (2) conscious awareness without explicit memory, (3) unconscious awareness with implicit memory but not explicit memory, and (4) no awareness. The elimination of implicit memory constitutes the sole basis for eliminating the underlying cause of awareness. Studies on electroneurophysiology (ENP) have proved that bispectral index (BIS), auditory evoked potential (AEP), auditory evoked potentials index (AEPI), and EEG-nonlinear are closely associated with alterations in consciousness during general anesthesia, thus providing supporting evidence for the objective monitoring of consciousness components under general anesthesia.

3 Intraoperative Monitoring of Patients with Retroperitoneal Tumors

During surgery, electrocardiogram (EKG), noninvasive blood pressure (NIBP), and noninvasive pulse oximetry (SpO_2) should be routinely monitored. For patients who undergo major surgery and are critically ill, invasive blood pressure (IBP), central venous pressure (CVP), pulmonary capillary wedge pressure, cardiac output, and even end-tidal carbon dioxide ($PETCO_2$) under general endotracheal anesthesia should be monitored. In the elderly, children, and patients who undergo major surgery, the body temperature should be monitored.

3.1 Monitoring of Respiratory Function

3.1.1 Tidal Volume (VT) and Minute Ventilation (VE)

These parameters are measured by the flowmeter of the anesthesia machine. Normal range in adults is as follows: VT: 350–500 mL and VE: 5000–8000 mL. During mechanical ventilation, the expiratory volume should be monitored.

3.1.2 Airway Pressure (Paw)

Airway pressure is related to tidal volume, inspiratory flow, airway resistance, and lung compliance. During mechanical ventilation, the peak inspiratory pressure is 12–15 cm H_2O in adults and 10–12 cm H_2O in children. The mean airway pressure may be raised by increasing tidal volume and inspiratory flow or using end-expiratory pressure (PEEP).

3.1.3 Noninvasive Pulse Oximetry (SPO_2)

The pulse oximeter probe is usually placed on a finger, and the light source is aligned with the fingernail; pediatric probe is placed around the fingers, toes, or dorsum of the hand and foot. SPO_2: normal range in inspiratory air is 96–97% in adults and 91–92% in newborns.

3.1.4 End-Tidal Carbon Dioxide Partial Pressure (PET CO_2)

The clinical significance of PET CO_2: Clinically, the monitoring of PET CO_2 is used in endotracheal intubation under general anesthesia, mechanical ventilation, critically ill patients, and cardiopulmonary resuscitation.

3.2 ECG Monitoring

During surgery requiring anesthesia, the purpose of routine ECG monitoring is to timely detect and prevent cardiac arrhythmias and cardiac arrest, to identify the presence of myocardial ischemia or electrolyte imbalance, as well as to evaluate pacemaker function. Common leads include chest lead V5 or modified lead CM5 which are

suitable for monitoring any changes in S-T segment and the presence of myocardial ischemia. Limb lead II showing clear P-wave is suitable for monitoring cardiac arrhythmias. Note: the instrument should have special anti-interference ability, the earth wire should be connected carefully, the integrity of the lead wire should be checked, and the electrode patch should be closely attached to the skin.

3.3 Blood Pressure Monitoring

Noninvasive blood pressure monitoring is suitable for all types of surgeries. Invasive blood pressure (IBP) monitoring can be used for cardiovascular and complex procedures, patients with shock and critical illness, hypothermia, and controlled hypotension (during hypotensive anesthesia).

3.3.1 Noninvasive Blood Pressure Monitoring (NIBP)

The ideal width of the cuff should be 40% of the limb circumference. The measured value is accurate when the cuff is deflated at a rate of 2–3 mmHg per second. If deflation is too rapid, the measured value may be underestimated.

3.3.2 Invasive Blood Pressure (IBP) Monitoring

Clinically, 22G and 20G catheters are usually inserted into the radial artery or dorsal pedal (dorsalis pedis) artery, or 18G catheter is inserted into the femoral artery for continuous measurement of arterial pressure. Normal blood pressure is 90–130/60–90 mmHg in adults and less than 140/90 mmHg in patients under 40 years without a history of hypertension; in patients over 40 years, systolic blood pressure (SBP) increases by 10 mmHg for each 10-year increment in age, whereas diastolic blood pressure (DBP) remains unchanged. In adults, the blood pressure of the lower limb is about 20–40 mmHg higher than that of the upper limb. The difference in blood pressure between the left and right limbs is about 10 mmHg. Normal SBP in children is calculated with the formula (mmHg) = age × 2 + 80, and DBP is calculated as 2/3 or 3/5 of SBP.

3.3.3 Central Venous Pressure (CVP)

The central veins most commonly used for catheter insertion are femoral vein, internal jugular vein, and subclavian vein. An accurate reading may be obtained when measuring CVP from the superior vena cava. Normal range of CVP is 6–12 cm H_2O.

CVP value of 0–5 cm H_2O indicates insufficient blood circulation. CVP > 15 cm H_2O suggests heart failure, cardiac tamponade, excessive infusion, or peripheral vascular contraction; clinicians should make the diagnosis combined with clinical symptoms and other hemodynamic monitoring indicators such as pulmonary capillary wedge pressure (PCWP).

3.4 Blood Gas Analysis

1. Acidity or alkalinity (pH value): The normal pH of arterial blood is between 7.35 and 7.45, while the venous blood pH is usually 0.05 units lower than the arterial. The pH below 6.8 or above 7.8 indicates severe acid-base imbalance, which can lead to severe, even life-threatening medical conditions.
2. Partial pressure of carbon dioxide (PCO_2) refers to the pressure exerted by the amount of CO_2 that is physically dissolved in the blood. It can reflect the acid-base status when breathing. The normal range for PCO_2 of arterial blood is 35–45 mmHg, and PCO_2 of the venous blood is 6–7 mmHg higher than that of arterial blood. The PCO2, along with the pH, can be used to distinguish among metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis.
3. Buffer base (BB) refers to the sum of all the buffer bases in the whole blood. Normal range is 45–50 mmol/L. BB can reflect the body's buffering capacity in response to acid-base disorders.
4. Base excess (BE) refers to the amount of acid or base required to titrate whole blood at 37 degrees Celsius with $PaCO_2$ of 40 mmHg back to a standardized blood pH of 7.4. BE is an important indicator to reflect the metabolic acid-base status, with a normal range of +/− 3 mmol/L.

5. Partial pressure of oxygen (PO_2) refers to the pressure exerted by the amount of oxygen molecules that are physically dissolved in plasma. Normal range of PaO_2 is 80–110 mmHg; and normal mixed venous oxygen tension (PvO_2) value is 40 mmHg. It is a critical indicator in the diagnosis of hypoxia.
6. Arterial oxygen saturation (SaO_2) refers to the extent of oxygen binding to hemoglobin. Normal range of SaO_2 is greater than 95%, whereas 64 to 88% for venous blood.

3.5 Monitoring of Cardiac Output (CO) and Stroke Volume (SV)

Cardiac output (CO) is able to reflect the cardiac ejection function. The abnormality in cardiac output is related to insufficient preload as well as cardiac systolic and diastolic dysfunction. Monitoring of capacity indicators is helpful to rule out causal factors for inadequate capacity, analyze the etiology and pathophysiology of cardiac systolic and diastolic dysfunction, and thus implement individualized treatment during surgery. Both minimally invasive and noninvasive cardiac function monitoring devices can be used for monitoring CO and stroke volume (SV). Swan-Ganz catheter may be considered for critically ill patients who should be monitored for mixed venous oxygen saturation, pulmonary artery pressure, pulmonary vascular resistance, and pulmonary artery wedge pressure (PAWP), because of its high specificity in evaluating the abovementioned indicators. Pulse index continuous cardiac output (PiCCO) can be used to obtain pulse contour cardiac output (PCCO) and to calculate intrathoracic blood volume (ITBV) and extravascular lung water (EVLW), which is helpful to evaluate hemodynamic changes and distribution capacity of patients during surgery.

3.6 Urine Volume

Urine volume not only reliably reflects renal blood perfusion but also indirectly reflects the systemic circulation. The method for monitoring urine volume is simple. During surgery, the nature and total volume of urine are determined. The amount of creatinine, protein, and other chemicals released into the urine during this period is often tested.

3.7 Monitoring of Body Temperature

If the patient's body temperature rises during anesthesia, firstly, several factors should be ruled out, such as ambient over-temperature, malignant hyperthermia, carbon dioxide accumulation, transfusion reaction, septic shock or sepsis, and thyroid crisis. If hypothermia occurs during anesthesia, first of all, the following factors should be ruled out: uncontrollable rewarming after hypothermic anesthesia, liver dysfunction after liver transplantation, disease progression, long-term exposure of body chamber to low-temperature environment, and a large amount of blood transfusion.

3.8 Monitoring of Effects of Muscle Relaxants

The commonly used patterns of electrical nerve stimulation are single twitch, train of four (TOF), tetanic, post-tetanic count (PTC), and double-burst stimulus (DBS). Monitoring of muscle relaxants is helpful to identify the cause for postoperative respiratory depression and to provide guidance for the administration of antagonists. The respiratory depression induced by residual muscle relaxants should be prevented.

3.9 Monitoring of Concentration of General Anesthetics

The concentration of volatile anesthetics (such as enflurane, isoflurane, sevoflurane, desflurane, and nitrous oxide) in breathing air is usually determined by an infrared analyzer. Clinically, the monitoring of inspired and expired concentration of anesthetics is helpful to evaluate the

uptake and distribution of anesthetics, depth of anesthesia, as well as tolerance and response of patients to the specific concentration of anesthetics.

4 Anesthesia for Patients with Retroperitoneal Tumors with Endocrine Function

Retroperitoneal tumors (RPTs) can be divided into benign and malignant categories, of which malignant RPT accounts for about 60–80% (~80% reported in international literatures vs. 56% reported in Chinese literatures). Common malignant RPTs include liposarcoma, fibrosarcoma, nerve fiber sarcoma, and malignant lymphoma, whereas benign RPTs include fibroma and teratoma. Generally, cystic RPTs are benign, whereas solid RPTs are malignant. Retroperitoneal space is a huge compartment of the extraperitoneal space located in the posterior abdomen, which extends from the diaphragm superiorly to the pelvis inferiorly. RPTs may be derived from fat, connective tissue, fascia, muscles, blood vessels, nerves, and lymphatic tissue or residual embryonic tissues in the retroperitoneal space, of which two-thirds are malignant in nature. Therefore, there are a variety pathological subtypes of RPTs. Several RPTs derived from chromaffin tissue with endocrine function can secrete norepinephrine and epinephrine, also known as pheochromocytoma.

4.1 Clinical Characteristics of Pheochromocytoma

1. Hypertension: Hypertension is the most important clinical symptom of pheochromocytoma and mostly paroxysmal. At the time of onset, SBP may rise up to 300 mmHg and DBP up to 180 mmHg, accompanied by headache, palpitations, nausea, vomiting, sweating, paleness, anxiety, panic attacks, blurred vision, tachycardia, arrhythmia, and precordial distress (sense of urgency). In severe cases, hypertension can induce left ventricular failure and cerebral stroke.
2. Arrhythmia: Symptoms of arrhythmia include tachycardia and atrial fibrillation.
3. Metabolic disorder syndrome: Patients may experience increased basal metabolic rate (BMR), low-grade fever, sweating, elevated blood glucose (hyperglycemia) and impaired glucose tolerance (IGT), glycosuria, limb weakness, weight loss, and skinny (for those with history of chronic disease).

4.2 Preoperative Preparation

1. Preoperative depressurization, volume expansion, and correction of arrhythmia: Pheochromocytoma not only secretes large amounts of catecholamines but also results in changes in renin-angiotensin-aldosterone system, thus maintaining contraction of peripheral vascular vessels. Although pheochromocytoma presents with increased blood pressure, patient's blood volume can be decreased by ~30% as compared to the normal physiological state. Two weeks before surgery, selective α1-blockers are used to decrease the blood pressure by gradually dilating the peripheral vascular beds in contracted state. If a desired effect is not achieved by α1-blocker monotherapy, the concomitant administration of Ca^{2+} channel blockers such as nifedipine may be used to block the source of intracellular Ca^{2+}, thus achieving a satisfactory effect. An ideal preoperative blood pressure is within or close to normal range, at which the patients do not experience obvious discomfort such as dizziness and palpitations after minor activities. Long-acting α-blocker should be discontinued 1 day before surgery in order to prevent the occurrence of sustained hypotension after adrenalectomy.
2. When part of the interstitial fluid moves into the blood vessels due to the decline in blood pressure, the intravascular blood volume is partially complementary but remains in an insufficient state. Therefore, a certain amount of liquids such as colloidal solutions and plasma is required for volume expansion,

which should be performed at least 3 days before surgery, with daily volume of no less than 1500 mL and maintaining hematocrit level below 45%. However, attention should be paid to the blood pressure during the preoperative volume expansion; otherwise patients are susceptible to suffer from increased cardiac loading and subsequently induced heart failure.

3. Tachycardia (>100 beats per min) is the most common type of arrhythmia observed in pheochromocytoma. Concomitant administration of propranolol can reduce the patient's heart rate. However, the addition of β-blockers cannot be given less than 1 week after the administration of α-blockers. Domestic scholars believe that the heart rate should be controlled at less than 90 beats/min during preoperative preparation.
4. Preoperative medication: Atropine is not recommended because it inhibits the vagus nerve, thus causing an increase in heart rate and arrhythmia. Scopolamine is commonly used before operation.
5. Anesthesia method

An ideal anesthetic method is expected to properly suppress or relieve stress response caused by surgical trauma.

a. Epidural anesthesia has been gradually abandoned due to its obvious disadvantages, such as induction of anxiety, fear and other psychological stress response in patients during the operation, incomplete block, traction reaction, and high incidence of hypotension after tumor resection.
b. General anesthesia can make up for deficiencies of epidural anesthesia but has its limitations in inhibition of the perioperative traumatic stress. Now, it is commonly used in surgery.
c. The combination of general anesthesia and epidural anesthesia is worth advocating because it can draw upon each other's strengths while removing their respective shortcomings. Epidural puncture is firstly conducted. Until a plateau is reached, the induction of general anesthesia won't be performed. The stable induction and smooth catheterization should be guaranteed during general anesthesia. Succinylcholine is not recommended as it can cause muscle tremors, easily leading to an increase in the secretion of catecholamine or potassium. Fentanyl is an ideal drug due to its role in slowing heart rate.

4.3 Intraoperative Anesthetic Management

Once entering the operation room, patients will undergo opening of venous access route. Patients with mental stress or sympathetic hyperactivity can be given a small dose of midazolam and intravenous pump infusion of sodium nitroprusside (1–5 μg kg^{-1} min^{-1}) or nitroglycerin (5–20 μg • kg^{-1} • min^{-1}) in order to control the rapid rise in blood pressure and maintain it within the normal range before surgery. Simultaneously, phentolamine, metoprolol, esmolol, cedilanid, dopamine, norepinephrine, and other first-line drugs are diluted and labeled until use. Invasive monitoring of mean arterial pressure (MAP) and CVP, as well as noninvasive monitoring of heart rate, ECG, SpO_2, $PETCO_2$, minimum alveolar concentration (MAC), and urine volume should be initiated.

Patients with pheochromocytoma may encounter risks during surgery, such as arrhythmia and severe fluctuations in blood pressure, which frequently occur in the catheterization under induction of anesthesia, especially during surgical resection and vascular ligation of tumor. Therefore, the maintenance of stable hemodynamics during these periods is pivotal to guarantee the surgical safety.

1. Treatment of hypertensive crisis: Once hypertensive crisis occurs, monitor the patient's heart rate, MAP, CVP, and ECG; maintain the original controlled hypotension medicine such as nitroglycerin or sodium nitroglycerine, while immediately administering 0.5–3 mg of phentolamine via intravenous bolus; and expand the blood volume slowly.

The above intervention is able to prevent a sudden drop in the blood pressure as well as a sharp rise in compensatory heart rate resulting from the dilating effect of phentolamine. When the blood volume of patients is slowly expanded with crystalloid solution and crystalloid solution during controlled hypotension, the incidence of hypotension and shock after tumor excision may be effectively reduced. Usually, the blood pressure and heart rate would be gradually declined following the abovementioned treatment. If the ventricular rate remains fast (greater than 140 beats/min), slow speed and low-dose administration of propranolol, metoprolol, or esmolol may be given under ECG monitoring. Notably β-blockers are not recommended for controlling heart rate of patients with hypertension accompanied by tachycardia due to its risk of inducing heart failure. Thus, α-blockers such as phentolamine are preferred as the first treatment option when hypertension and tachycardia occur simultaneously. Phentolamine should be intravenously administered, while gradual expansion is conducted. If necessary, β-blockers may be employed to control heart rate.

2. Prevention and treatment of hypotension after tumor resection: Slow expansion is performed before tumor resection, while the blocking test is conducted to observe the changes in blood pressure, and the expansion volume is adjusted accordingly. After removal of the tumor, the endogenous catecholamine levels are expected to drop suddenly; therefore, norepinephrine (dopamine or dobutamine) should be supplemented. The administration dose should be adjusted according to blood pressure. The volume is timely expanded by rapid infusion of blood and liquid according to CVP and urine volume to maintain systolic blood pressure above 100 mmHg. Patients with preexisting heart failure may be given cedilanid and a small dose of dopamine or dobutamine (2–10 μg kg^{-1} min^{-1}) after tumor resection to maintain stable hemodynamics.
3. Blood transfusion and liquid infusion during surgery: While monitoring the CVP and urine volume, an appropriate volume of blood or liquid may be transfused or infused. During the infusion, the filling extent of external jugular vein should be carefully monitored. The breath sounds at the base of lung should be auscultated. In addition, attention should be paid to maintain cardiac function.
4. Monitoring of blood glucose is conducted intraoperatively. Hypoglycemia induced by tumor resection should be prevented. Metabolic homeostasis of blood glucose and carbohydrate should be maintained.

4.4 Postoperative Management and Analgesia

Heart failure and hypotension are common postoperative risks. Since malignant hypertension caused by pheochromocytoma results in cardiovascular damage, patients are susceptible to die because of poor compensatory capability in response to excessive cardiac load and hypovolemia. Clinicians should pay attention to this serious problem. Close monitoring and careful adjustment are guaranteed. Effective postoperative pain management not only alleviates the stress response but also blocks the cardiac sympathetic nerve and improves the balance between supply and demand of myocardial oxygen, thus providing better conditions for recovery of patients.

5 Bloodless Medicine and Surgery for Retroperitoneal Tumor

In recent years, the shortage in blood supply is becoming more and more severe with a sharp increase in blood consumption. With in-depth exploration of blood transfusion, clinical studies have shown that blood transfusion may arouse more serious problems in cancer patients, such as tumor recurrence and metastasis, poor quality of life, and reduced survival time. To alleviate the shortage in blood supply, reduce the occurrence of transfusion-related complications and improve long-term prognosis of patients with tumors; a concept of bloodless medicine has been proposed

by scholars worldwide. The bloodless medicine refers to a variety of techniques that allow a patient to be treated without blood transfusions through optimal blood manipulation. The purpose of bloodless medicine is to reduce blood transfusion-related complications and prolong survival of patients by minimizing or avoiding allogeneic blood transfusion. Common approaches applied in bloodless medicine include correction of anemia before surgery, autologous blood reservation, control of perioperative bleeding, blood recovery and hemodilution by surgeons, strengthening of blood conservation for patients at high risk of bleeding, multidisciplinary collaboration, as well as sustained and effective continuing education. For patients with retroperitoneal tumors (RPTs), surgery remains the only effective therapeutic approach. Due to its special nature, RPT does not cause symptoms until it develops to an advanced stage. As it invades the large blood vessels and adjacent organs, advanced disease will bring extreme difficulty achieving a complete surgical resection, leading to a large amount of bleeding. Therefore, the bloodless medicine plays a pivotal role in reducing allogeneic blood transfusion and providing long-term prognosis in patients with RPTs.

5.1 Implementation of Bloodless Medicine

5.1.1 Implementation of Preoperative Autologous Blood Donation and Reservation

A certain amount of autologous blood can be collected from patients within the preoperative period (2–4 weeks) to prepare for blood transfusion during surgical procedures.

Case Selection

Generally, patients with Hb > 110 g/L and Hct > 33% are eligible to donate blood, without limitation on age. For a patient with body weight ≥50 kg, the volume of blood collection is about 450 mL each time, which may be appropriately reduced for a patient with body weight <50 kg. The volume of blood collection is usually controlled at 10–15% of circulating blood volume each time. Contraindications include combined congestive heart failure, unstable angina, severe coronary artery stenosis or myocardial infarction within 3 months, and severe aortic valve stenosis.

Detailed Implementation

Simple method is similar to ordinary blood donation; however, it is difficult to meet the requirement of retroperitoneal tumor surgery due to very limited volume of blood collection.

Switchback method can obtain sufficient autologous blood to meet the requirements of surgery within a certain period. The process is as follows: the first unit is collected for reservation at 4 weeks before operation; the second and third units are collected for reservation at 3 weeks before operation while the first unit is transfused back into the body; and the fourth, fifth, and sixth units are collected for reservation at 2 weeks before operation while the second and third units are transfused back into the body; finally, the seventh, eighth, ninth, and tenth units are collected for reservation at 1 week before operation while the fourth and fifth units are transfused back into the body. In such way, approximately 5 units of autologous blood can be obtained (about 1000–1500 mL), thus substantially meeting the surgical requirements.

Erythropoietin (EPO) as an enhancer for blood reservation: Clinical studies have shown that only one-thirds of red blood cells (RBCs) is compensated within 4 weeks when a moderate blood loss lasts for a short period (10 days). By contrast, the proliferative response of RBCs in bone marrow with the aid of EPO can be enhanced by 3–4 times, thus producing adequate amounts of RBCs that can meet the reservation requirements on autologous blood donation.

5.1.2 Implementation of Intraoperative Autologous Blood Donation and Blood Dilution

a. Preoperative management: Patients with deep vein thrombosis combined with chronic venous diseases should be excluded before operation. Tumor embolization should be

conducted for patients with large tumors preoperatively to reduce 50–90% of the blood supply to tumors. Drugs that can promote proliferation of RBCs should be given to patients with preoperative hemoglobin (Hb) <12 g/L until it recovers to normal. The erythropoietin (EPO) 300 U/kg plus iron sucrose 500 mg should be administered on days 1, 7, 14, and 21.

b. Management of intraoperative anesthesia: Catheterization via radial artery (the gauge on artery catheter needle must be >20G) and central vein is performed under local anesthesia. Patients' indicators such as blood pressure, heart rate, oxygen saturation, and end-tidal carbon dioxide should be monitored.
c. Blood donation: After patients are placed in a Trendelenburg (15°) position, radial artery blood is drawn for 15–30 min. Blood volume (mL) = body weight (kg) × 1000 × 7% × 2 × (actual Hct − target Hct)/(actual Hct + target Hct). Hct is hematocrit. The blood is stored in a collection bag containing ACD (antibiotic coagulate drug).
d. Fluid replacement: When 6% hydroxyethyl starch (Voluven at a dose of 15 mL/kg) and compound sodium lactate (at a dose of 10 mL/kg) are intravenously infused at a rate of 50 mL/min after blood donation, patient's Hct may decrease to 28.8%; however, the actual increase in volume is only 10–15% of circulation volume, thus exerting less effect on the load capacity of circulation.
e. Intraoperatively controlled hypotension: The combination of nitroglycerin at a dose of 1–6 μg/kg/min and esmolol may be used depending on patient's heart rate. MAP should be controlled at no less than 50–55 mmHg.
f. Blood transfusion: Blood gas, routine blood, and five indicators of blood coagulation should be reexamined intraoperatively. The target range of Hb or Hct is 6–7 g/L or 24–26%, respectively. When Hb is <6 g/dL or Hct is <24%, the autologous blood should be reinfused. If a large amount of bleeding (>3000 mL) occurs, the allogeneic blood should be transfused. The Hb should be controlled to be equal to or less than 7 g/L intraoperatively. Excessive blood transfusion should be avoided before tumor resection in order to prevent blood loss in the tumor. Artificial colloids (hydroxyethyl starch or gelatin) and vasoactive drugs (such as phenylephrine) may be used to maintain systemic blood pressure.
g. Postoperative management—modified iron shock therapy: Iron is a vital component in the production of erythropoiesis. Iron deficiency affects not only the hematopoiesis of bone marrow but also the synthesis of various key enzymes and coenzyme involved in cell metabolism. Clinically, patients are given intravenous infusion of iron sucrose 500 mg/500 mL or low molecular weight iron dextran 1 g/500 mL.

5.2 Key Technologies of Bloodless Medicine

5.2.1 Correction of Anemia

Patients with retroperitoneal tumors may experience weight loss, fatigue, sodium reduction, fever, ascites, jaundice, and even cachexia and severe anemia due to long duration, high consumption, as well as compression and displacement of adjacent organs caused by the increased tumor volume. Common medications include anti-anemia drug (iron, folic acid, and vitamin B12), erythropoietin (EPO), and traditional Chinese medicine (such as Siwu decoction, *Angelica sinensis* blood- supplementing decoction, and all nourishing decoction).

1. Iron supplements: As an essential component of hemoglobin, myoglobin, and cytochrome system, iron is the main raw material for hematopoiesis. Iron deficiency affects not only the hematopoiesis of bone marrow but also the synthesis of a variety of important enzymes and coenzyme involved in cell metabolism, causing microcytic hypochromic anemia (John et al. 2009). Iron is indicated for different types of iron deficiency anemia, while attention should be also paid to elimi-

nate the cause of anemia. Commonly used drugs include ferrous sulfate, iron dextran, and ammonium ferric citrate syrup. Folic acid and vitamin B12 are major therapies for megaloblastic anemia and malignant anemia.

2. Erythropoietin (EPO): EPO is an endocrine hormone that acts on the bone marrow hematopoietic cells to promote proliferation, differentiation, and ultimate nature of erythroid progenitor cells. It plays an important role in oxygen supply to the body. In the early embryo development, EPO is generated by the liver, and then the production site of EPO gradually shifts to the kidney after birth. In practice, EPO has been widely used in the treatment of various anemias. It is mostly effective in treating anemia caused by renal failure and uremia. EPO also shows efficacy in cancer-related anemia, anemia of prematurity, and maternal anemia, as well as reduction in perioperative allogeneic blood transfusion. In previous studies on cancer-related anemia, a single dose of EPO was 100–150 U/kg, which cannot meet the surgical requirements due to long-treatment duration and low efficacy. For this reason, an alternative regimen was implemented, namely, single dose of erythropoietin (EPO) of 300 U/kg plus iron sucrose of 500 mg on days 1, 7, 14, and 21, respectively. As its role in enhancing the production of RBCs may cause long-term tumor recurrence, EPO is only indicated for patients with Hb of less than 12 g/L. In order to avoid the adverse effect of EPO postoperatively, we apply pulse therapy with low molecular weight iron dextran at a dose of 1 g/500 mL and periodically reexamine the serum iron concentration afterward.
3. Traditional Chinese medicine: In Chinese medicine theory, blood is generated by transforming the vital energy from water and food. Its generation is closely associated with the functions of the heart, spleen, stomach, and kidney. The generated blood is dominated by and stored in the heart, spleen, and liver, respectively, i.e., the blood is generated by the heart, stored in the liver, and governed by the spleen. Vital energy that is closely related to blood plays a key role in promoting its generation and circulation. Therefore, deficiency of vital energy often leads to blood deficiency and vice versa. Promoting vital energy and replenishing blood are mutually beneficial. Commonly used blood-replenishing recipes include Siwu decoction, *Angelica sinensis* blood-supplementing decoction, and all nourishing decoction. Commonly used blood-replenishing traditional medicine includes blood-supplementing *Angelica sinensis* extract, mulberry-honey extract, blood-supplementing donkey-hide gelatin extract, blood-nourishing granule, promising longevity extract, blood-nourishing and hair growth capsule, Angelicae sinensis, and herbaceous peony and rehmannia pill.

5.2.2 Autologous Blood Transfusion

Preoperative Autologous Blood Donation

It is applicable to patients with good performance status, weight of 45 kg (maternal weight of 55 kg) and above; blood pressure of 90–140/60–90 mmHg, pulse difference of >30 mmHg; normal function of the heart, lung, liver, and kidney; Hb > 110 g/L or Hct > 33%; and platelet count > 100×10^9/L. For patients with low platelet count for a long term, without bleeding tendency, platelet restriction may be relaxed to >80×10^9/L, with normal platelet function and normal blood coagulation.

Specific procedures: Doctors should estimate the possible blood loss during surgery and accordingly make decision on the amount, method, and timing of blood collection. Each blood collection volume should be controlled at about 8 mL/kg. Simple blood collection is suitable for patients with a small amount of expected blood loss and blood donation. If 400 mL of blood is required, the collection should be conducted 3–5 days before surgery; if 800–1200 mL of blood is required, the collection should be conducted 14–21 days before surgery. Leapfrog blood collection is suitable for patients with a large amount of expected blood loss and blood donation. Conversion/switchback blood collection: Firstly, 400 mL of blood is collected 30 days

before surgery. Secondly, 800 mL of blood is collected 7 days later, while the previously collected blood is transfused back into the body. Thirdly, 1200 mL of blood is collected thereafter, while the whole blood volume collected in the second time is transfused back into the body and so forth. Before and after blood collection, patients may be given iron, vitamin B12, folic acid, and recombinant human erythropoietin. Relevant examinations should be conducted before blood collection, and patients are asked to sign the consent form for autologous blood donation and fill in the application form by themselves (Sanders et al. 2004).

Previous studies have reported leapfrog blood collection, namely, the conversion of the preoperative blood collection within the wards. Autologous blood is collected before surgery, with the volume not exceeding 12% of the total generally. The amount of collected blood accounting for 10% of the total is equivalent to the amount of blood collected from donors with the same blood group in blood bank. For patients who are not dehydrated, liquid supplementation is not necessary; if a single blood volume collected reaches 12%, supplementation of appropriate crystalloid solution is recommended. Collected blood can be stored in blood bank generally for not more than 10 days. If the plasma is removed, the remaining packed RBCs may be stored in the −80 °C freezer for several months to years. During the blood collection, oral administration of ferrous sulfate at a dose of 200–300 mg 3 times a day is effective for regenerating RBCs and preventing anemia. After 4 weeks of treatment, 1000 mL blood can be reserved (Arthur and Bracey 2008). However, this method also has disadvantages, i.e., the cycle is long, and the patients remain in a state of iatrogenic anemia.

Acute Hemodilution Technique

It mainly consists of three types: a) acute normovolemic hemodilution (ANH), b) acute non-normovolemic hemodilution (ANNH), and c) hypervolemic hemodilution (HVH). ANH is the most commonly used method in anesthesiology department. The principle of ANH is as follows: while removing a portion of RBCs, plasma, or blood, substitute will be transfused into the patients' body to maintain their intravascular volume and oxygen-carrying capacity. Specific procedures are as follows: blood is collected from arteries or deep veins, and the collection volume is calculated based on the initial and target Hct in combination with the patient's height, weight, and gender. Meanwhile, equivalent volume of crystalline or colloidal solution is rapidly infused via the unobstructed venous access. In general, crystalloids are replaced in a ratio of 3:1 (crystalloid/blood, v/v) whereas colloids in a ratio of 1:1 (colloids/blood, v/v). Dilution can be achieved by mixing crystalloid solution and colloidal solution.

Acute hypervolemic hemodilution (AHH): When a certain amount of mixture of crystalloid and colloidal solution (usually 20–30% of blood volume) is rapidly infused using reserved elasticity of blood vessels after anesthesia, the intravascular volume may increase above the baseline level, thereby achieving the purpose of hemodilution. Thanks to its easy accessibility, this method has been widely used in the early management of cerebral infarction.

Theoretically, any degree of hemodilution may be achieved by normovolemic hemodilution. However, with the higher degree of hemodilution, blood volume and fluid volume will be dramatically raised, thus increasing the difficulty for the operation. The extent of AHH depends on the ability of dilation of capacity vessels in patients. Fluid dynamics have indicated that the expansion efficiency of hypervolemic hemodilution can be improved only when the blood vessels are effectively dilated under general anesthesia or epidural block; otherwise a considerable amount of the expansion liquid may affect the efficiency of expansion and cause interstitial edema after entering the blood vessels according to Starling's laws.

In view of the abovementioned facts, the concept of non-normovolemic hemodilution has been proposed, i.e., the blood donation is performed before fluid expansion on the day of surgery, and the volume of blood collection is 10–15% of the patient's total circulating blood volume, and then the liquid equal to 2–2.5 times the volume of blood donation is administered for

rapid expansion during induction of general anesthesia. Since a portion of intravascular volume has been reduced prior to hemodilution, the actual preload increment of the system is only one-half of the expansion volume, thus improving the safety of hemodilution. As blood donation performed prior to hemodilution removes a portion of RBCs, a greater degree of hemodilution can be achieved more easily with non-normovolemic hemodilution as compared to AHH when supplementing the same volume of expansion liquid. Compared with ANH, the volume of blood donation required for non-normovolemic hemodilution is reduced by one-half when the same degree of blood dilution is achieved, which simplifies the procedures of the hemodilution. In addition, the blood volume of patients who receive acute non-normovolemic hemodilution is higher than the baseline level, while to the same extent of dilution, the blood volume of patients who receive ANH is essentially equal to the baseline level. Thus, acute non-normovolemic hemodilution may improve the tolerance of patients to bleeding.

Non-normovolemic hemodilution process: After induction of anesthesia, the volume of whole blood (mL) = body weight (kg) × 1000 × 7% × 2 × (actual Hct –target Hct)/(actual Hct + target Hct) is collected via arteries or veins before surgery. Following blood donation, 6% hydroxyethyl starch Voluven at a dose of 15 mL/kg and compound sodium lactate at a dose of 10 mL/kg are intravenously infused at a rate of 50 mL/min. On one hand, this method only exerts a minor effect on the circulating load capacity. As a portion of RBCs is removed prior to dilution, the patients' Hct may drop to 0.28 ± 0.09. In this sense, non-normovolemic hemodilution is superior to acute normovolemic hemodilution (ANH). On the other hand, this method has little effect on the hydrostatic pressure of the system, thus maintaining intravascular retention of expansion liquid at a higher level as compared with acute hypervolemic hemodilution (AHH). For example, the blood volume of an adult with body weight of 70 kg is 70 mL/kg, and the volume of blood collection is about 800–1200 mL; the changes in the patient's circulating blood volume is [(15 + 10/3) − 800/70]/70 × 100%, so the actual increase in capacity is only 10–15% of total circulating volume. As this method only exerts minor effect on the circulating volume, its indications for hemodilution may be widened. This method can obtain high-quality blood which is helpful for postoperative recovery of the blood coagulation function.

Controlled Hypotension

In order to reduce blood loss in surgical field, create favorable conditions for surgical procedures, and decrease the amount of blood transfusion, controlled hypotension is intentionally performed using various drugs and methods during surgery. However, the blood perfusion to vital tissues and organs must be guaranteed in the implementation process to meet the minimum needs of the body metabolism and to prevent hypoxic-ischemic damage (Spahn et al. 2008). Quick-acting vasoactive drugs with shorter half-life (e.g., nitroglycerin) in combination with β-blockers (e.g., esmolol) can be applied intraoperatively to reduce blood pressure as much as possible for the purpose of reducing blood loss as long as the mean arterial pressure (MAP) of the radial artery is not less than 50–55 mmHg. Controlled hypotension should be discontinued when substantial blood loss causes a sudden drop in blood pressure. Before tumor resection, blood transfusion should be minimized to prevent a large amount of blood loss in the surgery. Once heavy blood loss is encountered perioperatively, artificial colloids and vasopressors may be applied to maintain stable circulation. As for vasopressor, a combination of a small dose of norepinephrine and dobutamine is recommended for those patients.

Intraoperative Blood Doping Technology

Indications for autologous blood doping: a) Operative bleeding is estimated to be more than 600 mL, such as cardiovascular surgery, total hip replacement, spine surgery, and intracranial aneurysm clamping operation, b) liver and spleen rupture and rupture of the femoral artery with subsequent massive hemorrhage, and c) massive hemorrhage caused by ruptured ectopic pregnancy. Contraindications: a) sepsis, b) serious

bacterial contaminations in blood, and c) malignant cell contaminations in blood.

Nowadays, safety in blood transfusion during tumor surgery remains controversial. In the review of literatures involving intraoperative blood recycle in patients with tumors between 1968 and 2000, Elias pointed out via meta-analysis that tumor cells were present in all recycled blood and tumor spread was independent of collected blood. Leukocyte filter is expected to reduce the number of circulating tumor cells; however, in vitro experiments demonstrate that only 75% of liver tumor cells can be removed by leukocyte filter. X-ray irradiation can only inhibit tumor cell proliferation without killing them. Therefore, intraoperative blood in patients with malignant tumors may not be recycled in order to avoid the spread of cancer, but further investigation is guaranteed.

5.3 Treatment of Refractory Hypotension in Retroperitoneal Tumor Surgery

It is very difficult to completely resect retroperitoneal tumors due to its special location. Especially, malignant tumors do not cause symptoms until they are in the advanced stage. At the time of diagnosis, large blood vessels and adjacent organs have been invaded by tumors, resulting in a larger amount of blood loss during surgery. Therefore, intraoperative and postoperative refractory hypotension frequently occurs.

5.3.1 Definition of Refractory Hypotension

Refractory hypotension is a shock-like state. When experiencing hypotension during surgery, patients whose arterial pressure is less than 12/8 kpa (90/60 mmHg) or declined by more than 40 mmHg from baseline, with a low perfusion state (lactic acidosis, oliguria, or acute confusion) or organ dysfunction, can be diagnosed as refractory hypotension, if their blood pressure remains low after receiving blood transfusion, fluid replacement, vasopressors, and other anti-shock therapy. Refractory shock means decompensated shock lasting more than 1 h. Chinese scholars define refractory shock as decompensated shock lasting for more than 12 h or recurrent hypotension despite adequate treatment. Its occurrence is related to the decline in the reactivity of small arterial smooth muscle cells (ASMCs) to endogenous or exogenous vasoconstrictor.

Refractory hypotension that results in hypoperfusion of the brain, heart, and other vital organs is one of the critical causes of severe shock-related death. However, the mechanism has not yet been elucidated. According to literatures, severe shock may be possibly related to free radicals that lead to inactivation of endogenous catecholamines, desensitization of adrenergic receptor, metabolite accumulation, energy depletion, and action of cytokines (NO and ET).

5.3.2 Treatment of Refractory Hypotension

1. Vascular reactivity recovery agent: Refractory hypotension during the surgery is mainly caused by declined reactivity of arterial smooth muscle cells (ASMCs) to endogenous or exogenous vasoconstrictor. Hyperpolarization of ASMCs is a major factor responsible for decrease in vascular reactivity. Hyperpolarization inhibits the voltage-dependent calcium channels (potential-operated channels [POC]), so that the intracellular calcium level cannot rise appropriately (only 50% of normal) when stimulated by norepinephrine (NE), resulting in a decrease in contractile response. The potassium efflux via activated potassium channels (ATP-sensitive potassium channels KATP, large conductance calcium-activated potassium channels BKCa) results in cellular hyperpolarization. In patients with shock, KATP is activated due to lack of ATP, increase in H^+, and formation of peroxynitrite ($ONOO^-$) anion induced by excessive NO in ASMCs; meanwhile the release of Ca^{2+} sparks from sarcoplasmic reticulum (RyR), enhanced coupling with BKCa, and the action of $ONOO^-$ jointly mediate activation of BKCa and increase in

spontaneous transient outward current (STOC), thereby leading to hyperpolarization of cell membrane. Based on this mechanism, vascular reactivity may be restored with drugs (called vascular reactivity recovery agent restituting vasoreactivity agent, RVA). For example, glyburide can be used to antagonize the activation of potassium channels in order to recover vascular reactivity.

2. Vasoactive drugs: High-dose dopamine results in vascular spasm and internal organ ischemia and hypoxia by activating dopamine receptors in blood vessels. That is why dopamine can worsen hypoperfusion of internal organs instead of significantly boosting blood pressure in the treatment of patients with shock accompanied by refractory hypotension. Ideal vasoactive drugs should be able to a) quickly raise blood pressure and improve heart and brain perfusion and b) improve or increase blood flow and perfusion of kidneys, intestine, and other organs, as well as correct tissue hypoxia to prevent multiple organ dysfunction syndrome (MODS). As a strong α receptor agonist, norepinephrine is effective in increasing blood pressure. It can rapidly improve hemodynamic status in patients with septic shock. However, Meier Hellmann et al. pointed out that monotherapy with norepinephrine can reduce visceral perfusion in septic shock due to its strong vasoconstrictor effect. A reduction in organ perfusion is the main pathophysiological feature of shock. Hypoxia of internal organs remains in patients with shock even after their blood pressure has been corrected, thus leading to MODS. Therefore, reversion of tissue ischemia by improving organ and tissue perfusion, particularly visceral organ perfusion, is the key for shock recovery and administration of vasoactive drugs. When evaluating shock resuscitation and efficacy of vasoactive drugs, special emphasis should be laid on improving organ perfusion rather than simply increasing blood pressure. Hemodynamic support must be strengthened to normalize cellular metabolism by restoring tissue perfusion. Dobutamine is the preferred choice, started at the initial dose of 10 μg/kg/min, titrated by 5 μg/kg/min very 10 min to a maximum of 20 μg/kg/min within 30 min. If it is still difficult to maintain blood pressure, norepinephrine may be used concomitantly at an initial dose of 0.1 μg/kg/min and titrated upward until MAP is maintained between 65 and 70 mmHg.
3. Vasopressin: The purpose of vasoactive drugs is to boost the blood pressure without inducing excessive contraction of blood vessels whereas ensuring visceral perfusion in patients with hypotension. Vasopressin (AVP), also known as antidiuretic hormone, is a peptide synthesized in hypothalamic nucleus and paraventricular nucleus of hypothalamus. AVP acts as agonists for V1, V2, and oxytocin receptors (OTRs). Its effect on V1 receptor is even stronger than angiotensin II and norepinephrine. The excitation of V2 receptors that are distributed in renal collecting tubules may promote reabsorption of water to help maintain a constant osmotic pressure and fluid volume. The excitation of vasopressin OTRs that are mainly located in the umbilical vein, aorta, and pulmonary artery may dilate blood vessels. A low-plasma concentration of AVP was found in patients with severe shock, thus laying a theoretical basis for its treatment of refractory hypotension. AVP may elevate the blood pressure in severe shock via two mechanisms: a) direct effect, namely, inducing contraction of vascular smooth muscle by directly activating V1 receptors, and b) indirect effect, namely, enhancing vasoconstriction of catecholamines. Short-term use of vasopressin can reduce the need for norepinephrine while increasing urine volume and creatinine clearance in patients with severe shock. AVP is especially suitable for children who need large doses of vasoactive drugs to maintain blood pressure, as it can reduce the dose of catecholamines and selectively affect systemic vascular vessels. Animal models have shown that AVP reduces blood flow to skeletal muscle and skin while relaxing the brain, coronary, and pulmonary blood vessels. AVP is superior to catecholamines for increasing the vital organ blood flow. Low dose of 0.0003–

0.001 U/kg is recommended since higher doses may cause splanchnic vascular, coronary ischemia and consequent decrease in cardiac output. In the treatment of severe shock, low dose of AVP exhibits diuretic effect possibly due to the following facts: (a) The elevation in mean arterial pressure caused by AVP increases the renal perfusion pressure and subsequently enhances urine output; (b) AVP increases glomerular filtration pressure by relaxing the afferent arterioles and contracting efferent arterioles; and (c) AVP increases urine output by regulating the secretion of atrial natriuretic hormone, renin, angiotensin, aldosterone, and other mediators.

4. Endorphin receptor antagonist: Inflammatory mediators involved in severe shock include tumor necrosis factor (TNF) α, interleukins (ILs), platelet-activating factor, leukotrienes, thromboxane A2, adhesion molecules, bradykinin, thrombin, myocardial inhibitory substance, β-endorphin, and heat shock protein. Among them, β-endorphin receptors are universally present in the central nervous system, heart, liver, kidney, and small intestine. The inhibitory role for β-endorphin in the cardiovascular effects of prostaglandins and catecholamines constitutes a key pathophysiological component of shock, thus providing a theoretical basis for the clinical use of naloxone in anti-shock therapy. Naloxone can reverse endotoxin shock by improving hemodynamics due to its antagonistic effect on endorphins. It was reported that naloxone was only effective for some septic shock and possibly associated with onset of pulmonary edema and seizures; therefore, it is still controversial on the efficacy and safety of naloxone in the treatment of severe shock. High dose of naloxone is suitable for vasoactive drug-dependent severe shock, which can effectively correct shock without vasopressors. The plasma half-life of naloxone is 90 min, and duration of action is 45–90 min. Therefore, naloxone should be continuously infused within 24 h to maintain an effective blood concentration. In case of emergency, the initial dose of 2 mg can be rapidly administered via intravenous route followed by a continuous maintenance infusion.
5. Fluid resuscitation: The supplementation of large volume of liquid may cause hypervolemia and hyperviscosity in patient with shock, thereby leading to adverse effects. Hypervolemia refers to hemoglobin concentration <70 gPL or hematocrit <0.20 as a result of transfusion. As shear stress is the product of shear rate times blood viscosity, a decrease in blood viscosity may reduce blood viscosity, shear stress, and the release of NO from endothelial cells. The reduction in NO that causes constriction of microarteries may result in reduction in perfusion pressure and capillaries collapse, thus affecting the cure rate of shock. When a large volume of dextran and artificial blood is transfused in the treatment of hemorrhagic shock, animals who received 100% of lost blood volume or 1.5 times the lost blood volume showed significantly lower survival rate than those who only received 50% of the lost blood volume. This may be explained by different degrees of reduction in blood viscosity. Particularly, a large volume of transfusion is not recommended for the treatment of uncontrolled hemorrhagic shock, and blood pressure should be firstly raised up to about 70 mmHg, rather than rapidly increased to a normal level. That is because a large volume of transfusion may worsen the hemorrhage by increasing blood pressure if the bleeding is uncontrolled; the transfusion may reduce the survival rate in hemorrhagic state. Furthermore, scholars have put forward new concepts such as “controlled resuscitation for uncontrolled hemorrhagic shock” and “permissive hypotensive resuscitation techniques.”

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7 Perioperative Management of Patients with Retroperitoneal Tumors

Cheng-Hua Luo and Xiaobing Chen

In addition to the inaccessibility of the retroperitoneal region, retroperitoneal tumors (RPTs) present no or non-specific symptoms until they have grown to a substantial size and invaded many adjacent organs. As a result, the removal of RPTs is quite complex. A good clinical outcome depends on not only superb surgical technique but also comprehensively perioperative management. There are very few reports on the perioperative management for patients with RPTs in international literatures, and in-depth understanding of its importance is required for surgeons. The perioperative management of RPTs involves multidisciplinary knowledge on circulation, respiration, digestion, urinary system, nerves, and blood vessels, due to the prolonged operation time, more blood loss, frequent blood transfusion, major surgical trauma, and multiple organ resection; thus, only a multidisciplinary team with comprehensive knowledge can help patients smoothly pass through the perioperative period.

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1 Preoperative Preparation of Retroperitoneal Tumor

1.1 Assessment of the Difficulty of Surgery

Emphasis should be laid on the comprehensive and accurate imaging, such as ultrasound, CT, and MRI. If necessary, intravenous pyelogram (IVP) or digital selective angiography (DSA) is performed. The images should clearly provide accurate and reliable information on the disease, including tumor size, location, as well as relations with surrounding organs and blood vessels, thus helping surgeons predict the resectability of RPTs. Since there are several intestinal canals located anterior to RPTs, ultrasound can't exhibit obvious advantage in the diagnosis. Moreover, the relationship between the tumor and retroperitoneal blood vessels is difficult to be displayed with ultrasound due to the deep location of the tumor. Rich blood supply indicated by ultrasound often suggests great difficulty in tumor resection. CT scan can display the tumor size, shape, boundaries, density, necrosis, cystic degeneration, and relation with adjacent organ and tissues. After injection of contrast media, CT can better disclose the degree of tumor blood supply, so it is of great importance to the assessment of relationship between the tumor and major blood vessels. CT scan is the most important tool for assessing resectability. Significant displacement or invasiveness $\geq 1/2$ of abdominal

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aorta and other blood vessel, or inferior vena cava stenosis (to the extent of being invisible on image), suggests the extreme difficulty of surgery and the possibility of vascular resection and even transplantation. MRI offers abundant information, but it has limitations in abdominal examination due to the effects of gastrointestinal gas. For this reason, MRI is primarily used to understand the relationship between RPTs and major retroperitoneal blood vessels. Due to the special nature of imaging principle, many surgeons are not skilled in reading abdominal MR images. It is encouraged to conduct MDT discussions with radiologists before surgery, so that surgeons may accurately predict the difficulty of resectability. Before surgery, gastrointestinal barium contrast is used to detect compression and displacement of gastrointestinal tract, and multiple displacements with stenosis suggest the high difficulty of surgery.

1.2 Prediction of Postoperative Prognosis

Clinically, the prediction of prognosis is vital for RPT patients. If a patient who has received a surgical excision wouldn't be expected to survive for more than 1 year, the surgery may be meaningless. A major factor that determines clinical outcome is the tumor's biological behavior, i.e., malignant degree, which can be indirectly reflected by its growth rate. In our hospital, some patients who underwent R1 resection had experienced relapse 3 months later, with tumors occupying the whole abdominal cavity. In these patients, the resectability rate was extremely low, and postoperative prognosis was dismal.

1.3 Prediction of Patients' Tolerance to Surgery

Before removal of RPTs, an overall analysis must be performed on the patient's cardiopulmonary, hepatic and renal, and coagulation function, as well as nutritional status, in order to comprehensively assess the patient's tolerance to such major surgery. For patients who are expected to undergo the resection of one kidney, clinicians must confirm whether their contralateral kidney function is normal using renogram, IVP, or other reliable methods. If serum albumin is <30 mg/ml, the incidence of intestinal fistula, infection, and other postoperative complications would be high. The elderly patients with poor cardiopulmonary function generally cannot survive this type of surgery.

1.4 Preparation for Intestinal Cleansing

Preoperative intestinal preparation is essential to complex RPT surgery, since up to 29.8% of patients who undergo the resection of RPTs may receive combined gastrointestinal surgery. Preoperative intestinal obstruction is common, especially in those who experience a relapse following resection of RPTs. As abdominal wound is extensive, the incidence of postoperative intestinal adhesions is high. The residual stool left in the intestine should be completely removed when performing secondary operation. Patients without preoperative gastrointestinal obstruction can be given laxatives to empty gastrointestinal contents and parenteral antibiotics for anti-inflammation. Intestinal preparation of patients with gastrointestinal obstruction is mainly performed by cleansing enema.

1.5 Improvement of Nutritional Status

As patients with RPTs often present with malnutrition and gastrointestinal obstruction before surgery, supportive enteral nutrition should be administered while monitoring indicators such as serum albumin, prealbumin, and hemoglobin. If these patients cannot take food by mouth, total parenteral nutrition (TPN) support is required to raise albumin to more than 30 mg/ml. In addition to big three macronutrients (carbohydrate, protein, and fat), sufficient dose of vitamins and trace elements is also needed, especially vitamin

K. For patients with anemia, a small amount of red blood cells should be infused successively to improve oxygen metabolism.

1.6 Sufficient Reserves in Blood Bank

Due to a lot of uncertainties during surgery of RPTs, it is difficult to predict the amount of blood loss before operation. Large surgical wounds and long operation duration increase the risk of accidental injuries to major blood vessels during surgery. On the one hand, a large tumor itself can facilitate the growth through the feeding vessels, making it difficult to stop bleeding due to very thin walls of blood vessels. Thus, available source of blood supply for patients must be guaranteed before surgery. Generally, the amount of blood reserve should be three times the expected transfusion amount to ensure enough reserve blood supply once unexpected bleeding occurs. In addition to sufficient RBCs, plenty of plasma will be needed, which can provide coagulating substances if coagulation disorder occurs following infusion of a large number of RBCs.

1.7 Preparation of Vascular Devices and Vascular Repair Materials

As RPT surgery often involves injury and repair of major blood vessels, clinicians should prepare vascular devices, various types of vascular sutures, and artificial blood vessel materials required for repairing vascular defects before surgery, especially when preoperative imaging findings suggest a close relationship between the tumor and major retroperitoneal blood vessels.

1.8 Selective Embolization

Digital subtraction angiography (DSA) is used to assess blood supply to RTPs and identify blood source, which plays an important role in demonstrating cellular origin of the tumor and richness of blood supply, as well as predicting benign vs. malignant predisposition. Angiography is also of diagnostic value for compression and displacement of blood vessels, wrapping and infiltration of blood vessel walls, vascular stenosis, and intraluminal thrombosis. In addition, angiography is essential to help guide repair of vascular damage and reduce or control blood loss during resection of RPTs. Patients who have hypervascular primary RPTs are advised to receive preoperative embolization. Selective embolization, that causes tumor ischemia or reduces blood supply, is conducive to the management of blood vessels during surgery. This strategy can significantly reduce intraoperative blood loss, increase operational safety, and improve rate of complete resection. Generally, the surgery should be performed within 1–3 days after embolization. If the interval is more than 3 days, the revascularization will increase inflammation, thus leading to heavier wound bleeding. That may explain why long interval will adversely affect the surgery. Patients with large hypervascular RPTs following effective embolization will present a certain degree of heat absorption, resulting in tumor shrinkage (presenting with gray surface) and tension reduction intraoperatively.

1.9 Preparation of Special Case

Functional pheochromocytoma is a special type of RPTs, which is mostly located adjacent to abdominal aorta and inferior vena cava, with rich blood supply. The resection on functional pheochromocytoma is very risky due to sharp fluctuations in blood pressure. Catecholamine metabolites should be determined preoperatively. If the levels of catecholamine metabolites are elevated, the preparation for surgery will be conducted as the same as that for pheochromocytoma. The preoperative preparations of retroperitoneal paraganglioma with functional properties similar to pheochromocytoma are described in relevant sections herein.

2 Intraoperative Management and Surgical Strategy

2.1 Surgical Approach and Intraoperative Exposure

For RPTs located deeply in abdominal cavity, the surgery is usually complicated and requires a longer period of time, and the surgical approach varies from the tumor location. The first principle is that the surgical incision should be large enough to achieve adequate exposure for good visualization of the operative field. A midline longitudinal incision can be used as the main surgical incision in most cases of RPTs, with transverse incision as an auxiliary incision when appropriate. The midline longitudinal incision with high flexibility can be supplemented by different auxiliary incisions during surgery if necessary. Surgeons may rapidly open and close abdomen via midline abdominal incision, thus shortening operation duration, minimizing incision bleeding, and reducing postoperative wound complications. The second principle is that surgeons should try to access retroperitoneal space without intermesenteric dissection. In general, peritoneal incision should be made via paracolic gutter, or the access into the retroperitoneal space is made by cutting gastrocolic ligament, diaphragm, and spleen ligament or flipping colon, duodenum, head and tails of the pancreas, or other organs, thus creating large enough surgical fields in order to prevent damages to the abdominal and mesenteric arteries.

2.2 Adhesion Separation Technology in Retroperitoneal Tumor Surgery

The separation of adhesions should be performed during the surgery of RPTs, especially in those with large and recurrent tumors. The most common adhesion occurs between the tumor and gastrointestinal tract and its mesentery. Liposarcoma is one of RPTs that most frequently generate adhesion. After repeated surgeries, the gap between the bowel and the tumor almost disappears in patients with intra-abdominal multiple tumors; therefore, the separation of adhesions will be a key step of the surgery. If it is difficult to separate the adhesion between the bowel and the tumor, combined removal of partial bowel can be performed; keep in mind that more than 1 m of the small intestine should be retained in order to avoid postoperative short bowel syndrome. After the separation of extensive abdominal adhesions, the entire digestive tract should be repeatedly checked for cracks, which should not be missed, and any crack must be repaired immediately. Adhesions are separated usually by sharp dissection and rarely by blunt dissection (only for loose space). If any adhesion between tumor and blood vessels occurs, traveling route of the blood vessels should be identified prior to sharp separation outside of the vessel wall.

2.3 En Bloc vs. Piecemeal Resection

The principle for surgery of RPTs is to strive for a complete and en bloc resection of the tumor, together with involved tissues and organs adjacent to the tumor, namely, R0 resection. R0 resection, representing the highest level of surgery, is a pivotal step in reducing postoperative recurrence. Alternatively, piecemeal resection should be selected if it is hard to perform R0 complete resection when a large tumor seriously affects the visualization of surgical field and exposure or the identification of major blood vessels and adjacent organs. The residual tumor should not be removed until most of the tumor body has been resected and the boundaries with major blood vessels and adjacent structures have been clearly identified. During the surgery, surgeons may predict the extent of tumor blood supply and estimate the controllable degree of bleeding after oncotomy base on their own experience. Considering the difficulty in stopping bleeding, en bloc resection rather than piecemeal resection should be performed.

2.4 Combined Organ Resection and Palliative Resection

The purpose of surgery for RPTs should emphasize complete resection of the tumor, leaving no evidence of residual tumor around the margin under the microscope. Retroperitoneal tumor frequently invades adjacent organs, so a combined resection of involved organs should be performed in order to achieve R0 resection. Organs that usually require combined resection include the colon, kidney, small intestine, pancreatic body and tail, ureter, and bladder. In our hospital, 132 out of 687 cases of primary RPTs underwent the combined organ resection (19%), including colorectal (12.8%), kidney (10.6%), and small bowel resection (7.4%). Other organs resected during RPT surgery include suprarenal gland, ureter, partial stomach, duodenum, head of pancreas, spleen, uterus, and adnexa. No matter combined resection is performed on organs or blood vessels, the possibility of reconstruction and the incidence of complications after reconstruction must be taken into account. If it is very risky, combined resection should be given up. If a tumor cannot be completely resected, a palliative resection will be performed for the following purposes: (a) firstly reducing the tumor burden and prolonging the patient's survival time and (b) removing the tumor compression, relieving the patient's symptoms, and improving the patient's quality of life. Due to high-grade malignancy and rapid growth speed, pathological remission of RPTs cannot be achieved even with palliative resection, so it might be wise to give up surgery.

2.5 Prevention and Treatment of Bleeding During Surgery

As a large amount of blood loss frequently occurs during surgery of RPTs, effective prevention and control of bleeding are the keys to successful operation. Surgeons and anesthesiologists must strengthen their skills and knowledge compared to those who perform conventional surgery and work together to deal with emergencies. Normally, in order to avoid failure of transfusion via lower extremity caused by intraoperative blockage of the inferior vena cava or iliac vein, two rapid infusion passages that doesn't pass through lower limbs should be established. In emergencies, multichannel, pressurized, and intravenous bolus of blood transfusion should be implemented. The backup person should be ready to respond to emergencies (Feng et al. 2015; Mishra and Joshi 2015).

3 Postoperative Management

During the surgery of RPTs that requires longer operative time, with higher incidence of combined organ resection and major surgical trauma, patients may experience bleeding, shock, and other severe complications. Therefore, the postoperative management is an important link to clinical outcome during the perioperative period (Flynn et al. 2007).

3.1 Strict Monitoring of Vital Signs

Patients with RPTs who have experienced major surgical trauma and large blood loss definitely need high volume of liquid and blood transfusion. As the blood loss cannot be accurately estimated, the usual volume of blood transfusion is far from equivalent to that of blood loss. Meanwhile the larger surgical wound increases the risk of persistent bleeding and exudates postoperatively. As a result, strict monitoring of vital signs and maintenance of blood volume balance are the most important tasks in the first 24 h after surgery. Central venous pressure is of significance to determine blood volume and to guide fluid infusion, while dynamic changes in hemoglobin concentration and hematocrit are critical indicators for objectively estimating the volume of bleeding and re-bleeding as well as guiding postoperative blood transfusion.

3.2 Observation and Interpretation of Quantitative and Qualitative Changes in Intraperitoneal Drainage

A heavy blood loss may occur during surgery of RPTs. The excessive consumption of coagulation factors during the operation leads to significant decline in postoperative coagulation function. Moreover, large surgical wounds may cause continuous bleeding postoperatively. Therefore, close observation of changes in volume and nature of peritoneal drainage is vital to discover postoperative bleeding. Based on our years of experience, in the absence of bleeding of major blood vessels, with the estimated amount of bleeding of less than 100 ml/h, conservative treatment may be considered, while dynamic changes in the patient's condition should be closely observed. Two large accesses for liquid and blood transfusion should be kept available after operation. Hemostatic treatment includes expansion of blood volume with fluid replacement. If hemoglobin and hematocrit decrease by 20% as compared with preoperative levels, supplementation of physical ingredients should be preferred to maintain the plasma colloid osmotic pressure. Appropriate blood coagulant drugs, vasoactive drugs, and coagulation factors may be used to improve blood coagulation function. Patients with heavy bleeding, especially those with severe liver impairment, will significantly benefit from fibrinogen. Patients with rapid bleeding postoperatively may show little response to short-term hemostatic transfusion therapy and thus experience a progressive decline in hemoglobin. Patients with decreased and unstable blood pressure should undergo an exploratory surgery timely to stop bleeding.

3.3 Maintenance of Balance Between Water and Electrolyte

During RPT surgery, infusion of large volume of liquid and blood may be needed, and it is difficult to accurately determine the amount of supplementation. On the one hand, the amount of blood loss may be too large to be accurately estimated. On the other hand, large surgical wounds and long-term intraperitoneal exposure may lead to more water evaporates which are not apparent fluid loss and often ignored by surgeons. In addition, patients with RPTs usually undergo intestinal preparation before surgery, so they are already in the dehydrated state. The above factors should be fully considered when fluid is supplemented intraoperatively and postoperatively. To maintain the balance between water and electrolyte, it is necessary to monitor the patient's vital signs, central venous pressure, and biochemistry parameters. The amount of fluid replacement is adjusted to maintain the balance between intake and output, and vital signs are kept stable intraoperatively and postoperatively. Since blood volume expansion during the surgery can result in hemodilution and water retention, diuretics should be administered appropriately based on stable vital signs to remove excessive water, especially in patients who present lower leg swelling before surgery.

3.4 Strengthening of Nutritional Support

The resection of RPTs is a major surgery, requiring excellent postoperative nutritional support, especially in patients who undergo intestinal resection or repair during the surgery. More importantly, the level of serum albumin in these patients must be maintained at above 35 mg/ml to avoid large amounts of exudates in the operative field, reduce tissue edema, and prevent intestinal leakage and infection postoperatively.

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8 Prevention and Treatment of Surgical Complications in Patients with Retroperitoneal Tumor

Cheng-Hua Luo and Xueyan Lv

According to our recent studies, the rate of combined multiple organ resection was 25.2% among 523 cases of retroperitoneal tumor (RPT) surgeries. The most common combined abdominal and pelvic organ resections include kidney resection (n = 73, 13.96%), partial resection of small bowel (n = 51, 9.75%), adrenalectomy (n = 25, 4.78%), partial ureteral resection n = 22, 4.21%), resection of pancreatic body and tail (n = 20, 3.82%), adnexal resection (n = 15, 2.87%), splenectomy (n = 13, 2.49%), partial duodenal resection (n = 10, 1.91%), cystectomy (n = 10, 1.91%), distal gastrectomy (n = 7, 1.34%), and hysterectomy (n = 5, 0.96%). Major blood vessel excision and reconstruction are common during RPT surgery. Therefore, the complication rate of RPT surgery is relatively high. The proper treatment of intraoperative and postoperative complications is essential to RPT therapy.

1 Massive Bleeding

The most common and severe complications of RPTs are macrovascular damage and massive bleeding. Due to a large size and deep location, RPT frequently compresses and squeezes blood vessels. Furthermore, because of the limited size of incision, the compressed blood vessels are not well exposed during the tumor separation. As a result, blood vessels are easily damaged, thus causing bleeding.

1.1 Systemic Treatment of Bleeding

Bleeding is the most serious complication of RPT surgery, which may be attributed to the following factors: (a) accidental injury resulting in rupture of major retroperitoneal vessels, such as abdominal aorta, inferior vena cava, iliac vessels, mesenteric vessels, and vessels supplying blood to retroperitoneal organs, (b) rupture or bleeding of large thick tumor-supplied blood vessels surrounding the tumor during the separation, (c) isolation of RPT through presacral space leading to presacral vessel rupture and bleeding, and (d) coagulation dysfunction causing persistent errhysis from tumor bed following excision.

If massive bleeding (such as more than 3000 ml) occurs during RPT surgery, patients may experience hemorrhagic shock, characterized by dramatic drop in blood pressure and increase in heart rate, due to hypovolemia. Under such condition, patients should be closely monitored for vital signs by anesthesiologists, for whom invasive arterial pressure monitoring is the preferred choice. Meanwhile, rapid supplementation of

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plasma, RBCs, plasma substitute, and other anti-shock strategies should be applied. Surgeons must keep calm and not blindly clip bleeding points with forceps in order to avoid accidental injury to important major blood vessels or retroperitoneal organs if unexplained bleeding occurs. Furthermore, the rupture of major retroperitoneal blood vessels may become wider and wider due to the forceps, thus causing heavier and heavier or even life-threatening bleeding. At this point, surgeons should immediately stop bleeding with fingers, gauze, or gauze pad while quickly ascertaining the causes of bleeding. If bleeding occurs to major blood vessels, the rupture zone is generally small and should be pressed by the first assistant gently. The repair should not be performed until the tumor has been separated from the ruptured blood vessel, making it extremely difficult to repair the vessel without free ends. Conversely, the repair will cause the rupture zone to become wider and eventually fail. As a result, the ruptured blood vessel has to be sacrificed, leading to the removal of tissues that lose blood supply. Until the tumor is successfully separated from blood vessel to a certain extent, the ruptured blood vessel cannot be controlled and sutured with noninvasive techniques under direct vision.

Postoperative bleeding is the most common complication following the surgery of RPTs, and if not treated promptly, it can result in serious consequences. The causes of postoperative bleeding include (a) bleeding of RPT surgical wound. Although a thorough hemostasis is performed before the end of surgery, patients with large surgical wounds may experience severe bleeding postoperatively due to coagulation dysfunction, especially within 24 h after surgery; (b) individual small vessel bleeds due to failure of ligature; and (c) since the intraoperative angiorrhaphy is not performed precisely, anticoagulant therapy that is conducted to prevent postoperative thrombosis may cause bleeding at the repair site. Patients with RPTs usually receive large doses of conventional hemostatic substance after surgery. Dynamic changes in hemoglobin level as well as the nature and amount of peritoneal drainage should be closely observed. If the abdominal drainage is dark bloody with an increase in quantity, coupled with continuous decline in hemoglobin level, abdominal bleeding may be highly suspected. If no improvement has been observed following volume expansion with appropriate blood transfusion, exploratory surgery should be considered to stop bleeding. In most cases, no significant vascular hemorrhage is seen in the secondary exploratory surgery; however, numerous blood clots can be identified locally, which consume large amounts of coagulation factors. Thus, blood clots are removed intraoperatively, and the bleeding area is fully burnt with argon knife or electric knife. After flushing with a large volume of normal saline, the drainage is repositioned, and then a sufficient number of platelets or fresh blood are infused, supplemented with hemostatic drugs. The above approaches can be used effectively to stop bleeding. If vascular ligature falls off and active bleeding persists locally, the bleeding points should be carefully sutured. If the vascular repair site bleeds, the vessel rupture should be completely closed with Prolene (polypropylene) suture. The bleeding from vessels supplying blood to tumors around RPTs may be controlled with clamps and by suture or ligation.

1.2 Topical Treatment of Bleeding

Major retroperitoneal arteries have thick walls. The outer membrane closely attached to the tumor should be separated for complete resection of RPTs, so the artery is usually intact during the separation. However, local vascular wall may be damaged due to a long-term compression of artery. Sometimes, even the separation of outer membrane can break the fragile blood vessels, leading to heavy bleeding. This phenomenon is frequently seen in RPTs located in the lower abdomen and pelvis. For example, the iliac arteries, including the common iliac artery and external iliac artery, may be squeezed into a bow-like shape. These arteries are partially wrapped and occasionally even wholly enclosed by the tumor. If arterial bleeding occurs, surgeons should try to fully separate the arteries, dissociate, and block the proximal and distal ends of the compressed arteries in principle to avoid heavy bleeding. In

case of severe damage, the suture and repair can cause a tear in the arterial wall, so vascular transplantation is required following resection of such vessel segment. The separation may accidentally damage the inferior vena cava; however, the repair is not difficult thanks to its wide diameter, thick wall, and easy dissociation, which can be conducted after clamping with noninvasive vascular forceps, and the suture rarely results in stenosis of the blood vessels. Once it is broken and bleeds during the separation, renal vein is mostly repaired under direct vision, and if it is difficult to repair, the renal vein may be alternatively pressed by surgeons' fingers. The repair cannot be resumed until the tumor is removed. Once the superior mesenteric vein is broken and bleeds, surgeons must keep calm and not blindly clamp the blood vessel with forceps. In such case, part of the mesentery can be clamped with noninvasive vascular forceps. The repair should be appropriately conducted only after the resection or dissociation of the tumor has been completed. Improper suture can often cause stenosis of blood vessels and subsequently lead to postoperative thrombosis.

1.3 Prevention and Treatment of Wound Bleeding and Coagulation Dysfunction

Since the surgery of RPTs usually generates larger wounds, the hemostasis for the wounds is vital to the safety of the operation. Wound bleeding is more common than major vascular bleeding, which may exceed 5000 ~ 10,000 ml in volume. Causes of bleeding include (a) the presence of rich collateral circulation between the tumor and abdomen or internal organs, and especially collateral circulation opened in tumors with active metabolism, leads to exposure of wound vascular network; (b) the surgery that requires a long time causes consumption of large amounts of coagulation factors, while lots of coagulation substances are transfused into bodies, coupled with hemodilution after infusion of large volume of liquid, jointly resulting in postoperative coagulation disorders. Emphasis should be laid on comprehensive treatment of oozing wound. The important factors associated with the coagulation dysfunction include the operation time of more than 4 h, intraoperative blood loss of more than 3000 ml, infusion of liquid volume of more than 5000 ml, and transfusion of blood reserve of more than 3000 ml. Preoperative malnutrition, liver dysfunction, or history of chronic liver impairment can adversely affect the synthesis of coagulation substances in the liver, making patients more susceptible to coagulopathy. Most of patients with RPTs need vitamin K supplements intraoperatively and procoagulant drugs intraoperatively. If there is a significant bleeding tendency, with more wound bleeding and fewer blood clots, one to two vials of fibrinogens should be intravenously infused to rapidly and effectively improve coagulation function. If it is difficult to correct coagulation abnormalities, the surgery should be completed as soon as possible. Spray coagulation with argon knife achieves good effects on minor wound oozing, which can be used together with various hemostatic sponge and gauze. For severe and extensive wound bleeding during RPT surgery, complete hemostasis is often infeasible. Never attempt to stop bleeding for a long time intraoperatively. The longer the operation time, the worse the coagulation function and the heavier the bleeding. When the speed of blood transfusion cannot keep up with that of bleeding, serious circulatory failure may occur. In this case, the wound should be packed with gauze to quickly terminate the surgery. Abdominal bandage compression strategy may be a preferred option for alleviating the crisis. Hemostasis with packs (tamponade) can gain time for saving patients' lives while creating conditions for the improvement of coagulation.

Key points of hemostasis with packs (tamponade) include clearing uncoagulated blood in surgical field and then quickly packing the wound with gauze. Intrauterine packing with gauze is a commonly used method, namely, placing one end of continuous strip of gauze into the deepest wound and the other end outside the abdominal wall for convenience of removal. The blood vessels may be directly compressed by multiple large gauze pads. The number of gauze used for

packing depends on the expected compression volume, usually 3 ~ 5 strips for a small volume and more than 8 ~ 10 strips for a large volume. All gauzes should be dry and packed promptly to reduce and prevent failure caused by blood soaking.

Gauze removal: the gauze is generally removed 3–5 days after the surgery. If the general condition of the patient is improved with basically normal blood clotting function and occlusion of small bleeding vessel, the gauze may be removed at 3 days after operation. If the gauze is removed at more than 5 days after surgery, secondary abdominal infection may occur. The timing to remove the gauze is determined by the intraoperative bleeding and postoperative improvement of general condition. If minor bleeding occurs intraoperatively, intrauterine gauze for packing should be placed in an orderly manner to ensure good accessibility and hemostasis effect, which can be removed under inhalation or intravenous anesthesia. If a secondary surgery is expected to stop bleeding, the patient should be under general anesthesia and gauze removed under direct vision with the incision opening.

1.4 Injury and Bleeding of Presacral Venous Plexus

The risk of resection of pelvic RPTs is very high due to the large tumor volume and difficulty in surgical field exposure. If RPT adheres to or invades presacral tissue, bleeding of presacral venous plexus will frequently occur in the separation process of tumors. Presacral venous plexus is an "H"-shaped blood pool that is comprised of inferior vena cava system, transverse sacral venous system, and sacral vertebral venous system, which lacks venous valve and allows blood to flow bidirectionally. During the resection of pelvic RPTs, torrential bleeding may occur if presacral fascia is injured or the presacral venous plexus is torn, which may be life threatening. The bleeding of presacral space is often difficult to be controlled by suturing due to lack of soft tissue. If possible, the bleeding vessels should be clearly identified before ligation or suture, or otherwise the blind ligament or suture may lead to heavier bleeding. Clinically, we always firstly stop bleeding with gauze packing oppression, using a small piece of gauze shaped like a peanut; secondly, we apply large curved forceps to rapidly block bleeding by accurate oppression. Under direct vision, the smaller the oppression range, the better the hemostatic effect. Bleeding points are then clamped with titanium clips or absorbable clip or stapled with thumbtacks plus hemostatic sponge. Alternatively, the bone surface is directly sutured with a small triangular needle and thin thread. Keep in mind that bleeding points are difficult to be controlled with circular needles, which may even cause heavier bleeding. If the hemostasis for presacral bleeding can't be achieved during the surgery of RPTs, surgeons should decisively stop bleeding by gauze packing to complete the surgery as soon as possible in order to prevent excessive blood loss, rather than repeatedly attempting to use other methods.

The author has reported one case of external iliac artery sigmoid resection and transplantation combined with sigmoid resection and anastomosis, whose arterial anastomotic site was close to colonic anastomotic site. On day 7 after the surgery, a large amount of blood in the stool was detected. After exploration, two anastomotic sites were confirmed to be channeled. Colostomy was conducted to repair the anastomotic sites of the blood vessels. If two anastomotic sites had been separated by omentum during the first surgery, this complication would have been avoided.

2 Injuries and Fistula of Digestive Organs

Any part of the digestive system that is pushed or compressed by RPTs may be damaged accidentally during tumor resection.

As a large RPT in the upper right abdomen can cause significant displacement of the duodenum, the wall of duodenum that may be damaged in the separation process should be carefully sutured. Retroperitoneal tumors located in the left upper abdomen sometimes can cause significant displacement of the body and tail of the pancreas or spleen. If spleen is broken during the surgery, it

can be repaired with clogging agent or suture after tumor resection; occasionally, subsequent splenectomy is necessary. If pancreatic injury occurs, the damaged area should be sutured carefully.

Risky factors attributed to the high incidence of digestive fistula after resection of RPTs include postoperative hypoproteinemia and other malnutrition; distal intestinal obstruction syndrome after surgery, coupled with high pressure in proximal intestine; intestinal rupture without being repaired during the separation of adhesion, or only intestinal serosa and muscle are damaged but high pressure in the intestine after surgery leading to rupture; multiple intestinal repair and anastomosis intraoperatively; and anastomosis and repair of gastrointestinal tracts that have not been subtly conducted by surgeons. Preventive procedures are as follows: (a) improve the postoperative nutritional status as possible; (b) strictly check if any intestinal injury is missed by chance; (c) if intestinal resection and anastomosis are performed, ensure good intestinal blood supply and tension-free anastomosis; (d) guarantee that distal intestine is smooth and the adhesion is fully loosened; and (e) if high-risk factors attributed to fistula still exist, establish intraoperative bypass through the stoma, or place a plurality of drainage catheter or double catheter if necessary. Once gastrointestinal fistula occurs after surgery, complete drainage should be conducted timely, and reoperation with supplementary cannulation or establishment of bypass through proximal intestinal stoma should be performed if necessary.

If the resection of RPT is incomplete and the distal obstruction is suspected, duodenal injury will increase the risk of fistula. Duodenal fistula with very high mortality is extremely difficult to treat once it occurs. Therefore, in terms of duodenal injury, gastrostomy for decompression, "T"-tube drainage of common bile duct, and placement of jejunal feeding tube should be considered on the basis of repair, in order to improve the healing rate of the fistula.

Pancreatic fistula is associated with pancreatic injury caused by RPTs. If pancreas is damaged or partial pancreas is resected intraoperatively, drainage catheter should be placed locally to maintain unobstructed drainage and to prevent abscess formation. If intractable pancreatic fistula is expected after surgery, silver clip marker is placed intraoperatively for future radiotherapy. For patients with minor pancreatic fistula, partial drainage is mostly effective, and for those with severe pancreatic fistula, double-catheter flushing can reduce the corrosive effects of pancreatic juice on the surrounding tissue, thus facilitating healing process. Patients who remain unhealed after receiving more than 6 weeks of drainage may be treated with a low dose of radiation. Patients who develop pancreatic pseudocyst may undergo ultrasonic intervention and subsequently receive electively internal drainage if ineffective.

Artery-intestinal fistula (fistula between arteries and the gastrointestinal tract) after RPT resection combined with intestinal and arterial resection and reconstruction is the most serious and dangerous complication in RPT surgery. It prevails in gastrointestinal anastomosis while overlapping vascular anastomosis. The interaction between vascular pulsation and inflammation of gastrointestinal anastomosis leads to intravascular gastrointestinal fistula. Clinically, patients present with sudden gastrointestinal bleeding. If postoperative gastrointestinal bleeding occurs in patients who undergo RPT surgery with gastrointestinal anastomotic site located close to suture points of blood vessels, intravascular gastrointestinal fistula rather than simple anastomotic bleeding or stress ulcer bleeding should be considered. Once intravascular gastrointestinal fistula is suspected, an emergency surgical exploration should be conducted firstly to stop bleeding. The purpose of preventive strategy is to maintain a certain distance between gastrointestinal anastomosis and vascular anastomosis as possible; if it is impossible, omentum or peritoneum should be used to keep them apart. If sigmoid colon and rectum anastomotic site overlaps iliac artery anastomotic site, colostomy is a much safer choice.

3 Cardiopulmonary Complications

Large RPTs often compress iliac vein or inferior vena cava. Removal of the tumor relieves the oppression; consequently a lot of water reflux

may lead to heart failure in patients who have already presented with lower extremity edema before operation. Common clinical presentation is refractory heart failure, characterized by temporary improvement after treatment with diuretics and recurrence in 3–4 h later. These patients should be closely monitored for central venous pressure in the first 3 days after surgery. In addition to limiting fluid intake, appropriate diuretics are administered. Major RPT surgery requires high oxygen consumption, thus causing relative myocardial hypoxia, and sometimes a decline in blood volume may result from blood loss. All these risk factors can contribute to heart failure, so this surgery is not suitable for elderly patients or those with cardiac dysfunction.

Pulmonary infection, atelectasis, and pulmonary embolism are common postoperative pulmonary complications in RPT surgery. Pulmonary infection is related to long operation time, major trauma, and trauma reaction-induced sodium retention, heart failure, pulmonary edema, reactive pleural effusion, and poor pulmonary reserve function caused by major abdominal surgery especially partial diaphragm resection. Those with pulmonary dysfunction and large RPTs are susceptible to pulmonary complications; thus, appropriate antibiotic prophylaxis should be performed preoperatively. Patients whose surgeries require a longer duration or frail elderly patients who have difficulties in excreting sputum are prone to developing postoperative atelectasis, and therapists may assist these patients with sputum expectoration or perform sputum suctioning with a bronchoscope if necessary.

The risk factors for postoperative pulmonary embolism include invasion or oppression of major veins caused by RPTs, intraoperative injury of veins, or pre-existing venous thrombosis and tumor thrombus. As pulmonary embolism caused by RPTs is often a fatal complication, emphasis should be laid on prevention, including preoperative prevention of hypovolemia, preventive placement of inferior vena cava filter, intraoperative prevention of damage or excessive mechanical compression of vein wall, and postoperatively preventive anticoagulation.

4 Damage and Complications of the Urinary System

Ureter can be pushed forward or moved to contralateral abdomen by RPT, thus presenting a bow-like shape. Ureteral catheters should be placed before surgery in such a way that they are easily identified during the surgery. It is not difficult to separate the tumor capsule from the ureter; however, special care should be taken to prevent injury to ureteral blood supply. Once it is injured intraoperatively, the ureter should be repaired after tumor resection. If a ureteral segment is resected, the broken free ends of the segment should be gathered together and anastomosed; if all else fails, the free proximal end of the ureter may be anastomosed to the contralateral ureter. If patients undergo repair and anastomosis, a double-pigtail "D"-shaped catheter should be placed in the ureter, with the upper end positioned in the pelvis and the lower end inserted into the bladder. The drainage must be placed at the site of repair as leakage of urine frequently occurs at the early stage after operation and gradually reduces until healed. Usually, the catheter used as a stent can be removed from the bladder with cystoscopy within 3–4 weeks. As large RPTs located in the pelvis can compress and squeeze the bladder, it is challenging to identify the ureter that has run into the triangular area. Surgeons should localize the ureter in the proximity and then trace back to the triangular area in the bladder and finally separate it from the tumors. If the tumor involves the triangular area in bladder and the bladder wall in the triangular area is injured intraoperatively, including partial resection of this portion, the anastomosis of bilateral ureters and apex urocyst can be performed. If it is hard to perform anastomosis, ureterosigmoidostomy and ileum fistulation or ostomy by which ureter directly runs in vitro may offer alternative options.

The surgery of retroperitoneal liposarcoma that is mostly derived from perirenal fat tissue is often accompanied by unilateral nephrectomy; in conjunction with a long-term intraoperative hypotension and large surgical trauma, patients

are susceptible to postoperative renal dysfunction. Patients should be closely observed for changes in renal function and any drugs that may be harmful to kidneys should be contraindicated.

Leiomyosarcoma located in inferior vena cava may involve the entire right and left renal veins. En bloc resection of the tumor together with inferior vena cava, as well as right and left renal veins, may be performed without reconstruction and transplantation of inferior vena cava; however, the urine in the bladder should be emptied after disruption of inferior vena cava and right kidney during surgery, and then the left renal vein is blocked, and 20 mg furosemide is administered intravenously. After half an hour's observation, the discharge of more than 100 ml of urine indicates that the left kidney loop can flow back via the established collateral vein and recover to normal function. Most patients can maintain normal renal function postoperatively.

5 Damage of Nerve Tissue

Primary RPTs can arise from nerve tissue. If the basal part of tumor is located at the intervertebral foramen, complete resection is likely to injure spinal nerves. The damage to unilateral single nerve root generally does not cause serious complications, but the involvement of multiple spinal nerves may result in corresponding symptoms of nerve injury. Sometimes, if the base of neurofibromas is located in the spinal canal, joint surgery should be performed in cooperation with neurosurgeons. During the surgery, surgeons firstly remove the outer layer of the spinal canal followed by partial tumor within the spinal canal.

Retroperitoneal tumors located in the lower abdomen and pelvis often compress sciatic nerve or femoral nerve. In some cases, femoral nerve can be completely wrapped by RPTs. If femoral nerve is resected together with the tumor, resulting in complete loss of function, patients will be unable to contract quadriceps muscle or to walk without the aid of crutches postoperatively. However, some patients do walk without the aid of crutches and require no further treatment during 1 or 2 years of follow-up. If symptoms are not improved, patients may undergo secondary surgery which transfers partial knee flexors into extensors in order to correct the extension function of the knee joint.

Some RPTs in the pelvic sidewall, which grow backward through the greater sciatic foramen, can compress the sciatic nerve. For this reason, the sciatic nerve is easily damaged during the removal of the tumor. Complete resection of sciatic nerve that is partially injured is rarely performed. Sciatic nerve injury may cause drop foot complication or intractable lower-limb pain and even inability to stand. If the RPT causes an extensive damage of peritoneum plexus, postoperative gastrointestinal paralysis and intestinal pseudo-obstruction can be observed when the injury is located in the upper abdomen, whereas voiding dysfunction, urinary incontinence, fecal incontinence, and other symptoms will be expected when the injury is located in the lower abdomen and pelvis.

Surgery for Left Upper Abdominal Retroperitoneal Tumors

9

Cheng-Hua Luo and Xiaobing Chen

1 Clinical Characteristics of Left Upper Abdominal Retroperitoneal Tumors (RPTs)

The author has summarized the clinical characteristics of 71 cases of left upper RPTs (age range, 0.5–76 years; median, 39.1 years). The incidence is about equal between men and women. The most common pathological types include liposarcoma, nerve sheath tumor, teratomas, leiomyoma, ganglioneuromatosis, and neuroblastoma. Other reported types include paraganglioma, malignant lymphoma, malignant stromal tumors, metastatic tumors, primitive neuroectodermal tumors, malignant fibrous histiocytoma, malignant hemangiopericytoma, synovial sarcoma, malignant Brenner tumor, and choriocarcinoma (Felix et al. 1981).

The most common clinical symptoms are upper abdominal or left upper abdominal pain or discomfort, accompanied by the left lumbar back soreness and abdominal distension. The upper abdominal pain with distension may be mitigated by the right lateral supine position, and the back pain may radiate to the left lower abdomen, occasionally accompanied by discomfort in the left shoulder, left upper limb numbness, or left thigh pain and numbness. Patients have obvious postprandial bloating in left upper abdomen and oppression feeling. Symptoms such as fever, anorexia, vomiting, fatigue, weight loss, chest tightness, shortness of breath, and trouble breathing in supine position are also seen in patients with the left upper abdominal RPTs, which are mostly associated with the compression of the surrounding organs, involvement of the nerves, or growth into the left side of the chest.

When growing to a certain extent, the left upper RPTs may involve surrounding organs. Tumors may result in reactive left pleural effusion when they reach upwardly the top of the left diaphragm. Tumors may adhere to and invade left diaphragm or metastasize to the dorsal portion of inferior mediastinum through the diaphragmatic hiatus. The left hepatic lobe can be invaded, and the left kidney and suprarenal gland are often squeezed, wrapped, and invaded by tumors located in this area. If it is neurogenic tumor, vertebrae and vertebral foramen are often involved. The stomach, spleen, pancreas body, and tail are usually pushed up by left upper abdominal RPTs, thereby resulting in eating disorders, enlarged spleen, and other symptoms.

About 20% of patients with left upper RPTs have palpable masses. Sometimes, these patients visit clinic when they found left abdominal mass by chance. Preoperative imaging such as B ultrasound, CT, and MRI may reveal lesions and

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display the location, size, shape, nature of the tumor, and changes in surrounding organs, with almost 100% of accuracy in diagnostic localization. It is reported that the qualitative diagnosis is challenging in 11% of patients with left upper RPTs (Karakousis and Pourshahmir 1999). The majority of those are tumors with specific features such as liposarcoma and teratoma (Furukawa et al. 1997).

2 Treatment and Prognosis of Left Upper Abdominal RPTs

The operative incision is essential to successful and complete resection of the left upper RPTs. Thoracoabdominal incision is the most common incision, which may be inverted "L" shaped, "L" shaped, arc shaped, and "┤" shaped. The vertical incision may pass through midline of the abdomen or rectus abdominis, while the thoracic incision may pass through the sixth or the seventh intercostal space. Alternative incisions include large roof-shaped incision under the bilateral costal margin, oblique incision from spinous process of the 11th thoracic vertebra to the anterior superior iliac spine, and a large "cross"-shaped incision in the left upper quadrant. During the surgery, elevate the left lumber region with pad, or secure the patient in the right lateral recumbent position as required.

A complete resection of the left upper abdominal RPTs depends on the surgeon's familiarity with the anatomy and professional skills in combined organ resection. Due to invasion of the tumor, combined left kidney resection is common in patients with RPTs, especially in those with liposarcoma derived from perirenal adipose capsule. The resection of the left kidney can be performed only when the preoperative kidney function is normal. If the tumor involves the renal cortex, partial nephrectomy is another option. If the tumor involves simply the renal vasculature, surgeons can remove this specific segment. Vascular graft is suitable for arteries, while ovarian vascular anastomosis or left renal collateral vein reflux is suitable for veins. Simple vascular rupture can be repaired. If diaphragm is invaded by the tumor, partial resection is feasible, or the diaphragm is opened for removal of thoracic tumor. After surgery, the closed thoracic drainage must be placed. Other common combined resected organs are partial or whole stomach, pancreatic body and tail, left lobe of spleen and liver, splenic flexure, left psoas major, partial vertebral body, and left suprarenal gland.

The author has found that the visually complete resection rate was 96% in 71 cases of left upper abdominal RPTs, with bleeding up to 6000 ml and blood transfusion up to 5400 ml and the longest operation time up to 12 h. The postoperative follow-up demonstrated that 59 cases survived more than 1 year, and 15 cases underwent reoperation due to recurrence, with a 3-year survival rate of 83%.

3 Surgical Procedure of Left Upper Abdominal RPTs

3.1 Preoperative Preparation

Preoperative preparation as per the principles described in relevant sections hereof and preoperative imaging reveal that the tumor is located in the left upper abdominal retroperitoneum (Fig. 9.1).

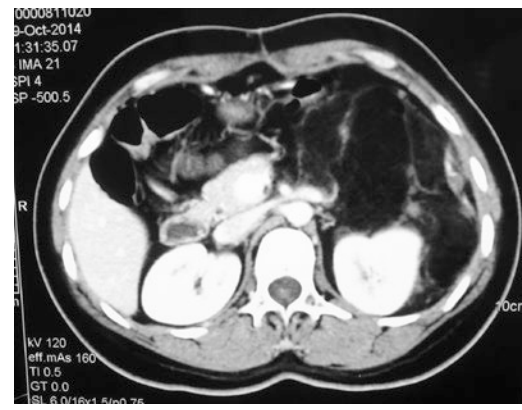

Fig. 9.1 Image (CT) of the retroperitoneal tumor in the left upper quadrant

3.2 Anesthesia

Endotracheal intubation under general anesthesia.

3.3 Position

Lie in supine position, and elevate the left side if necessary.

3.4 Incision

The midline incision in the upper abdomen is the most common choice. For those who have undergone surgery previously, the original surgical incision should be selected in principle (Fig. 9.2).

3.5 Surgical Procedures

1. Resect each layer of abdominal wall to gain access into the abdomen; pay attention to potential bowel adhesions under the incision, and carefully separate the tumor to guarantee no damage to the bowel and other structures (Fig. 9.3).
2. Abdominal adhesions are common in patients with RPTs, especially in those who underwent previous surgical treatment. Lift up one side of abdominal wall with multiple Alice forceps to separate the adhesion on the identical side. Prefer to remove part of the peritoneum rather than damaging intraperitoneal intestinal tract and other vital structures. Separate the adhesion on the opposite side (Fig. 9.4).
3. Explore the location and size of left upper abdominal RPT and its relationship with the surrounding organs, which is important to determine the next surgical approach (Fig. 9.5).
4. Protect the incision, retract the abdominal wall with large frame retractor to expose splenic flexure of the colon, and block off small intestine with gauze pad (Fig. 9.6).

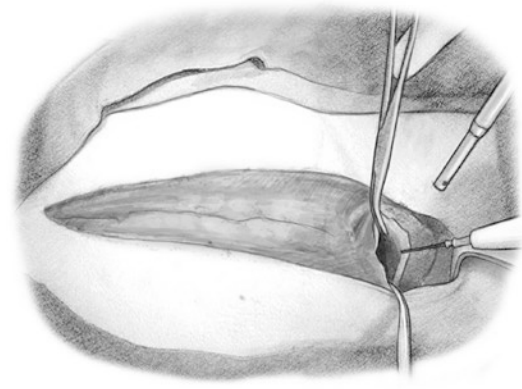

Fig. 9.3 Cut layers of abdominal wall and pay attention to inferior adhesions

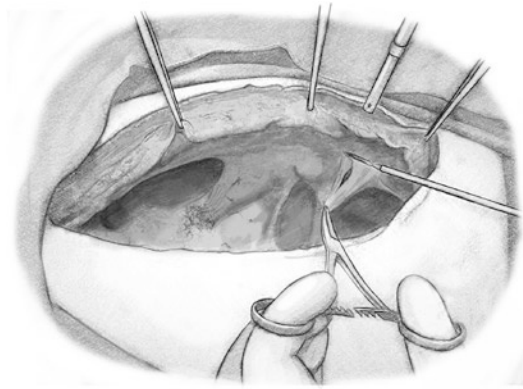

Fig. 9.4 Separate the adhesion between the abdominal wall and the intra-abdominal structure during the surgery of recurrent tumors

Fig. 9.2 Common surgical incisions for the surgery of retroperitoneal tumors in the left upper quadrant

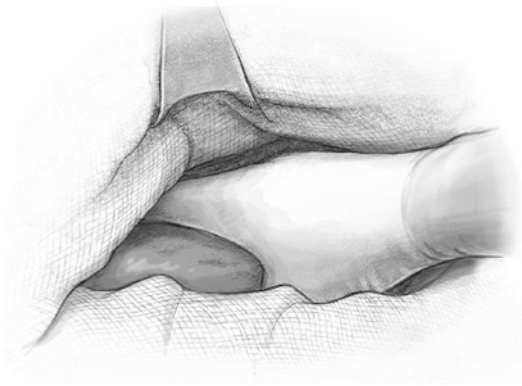

Fig. 9.5 Left upper abdominal exploration

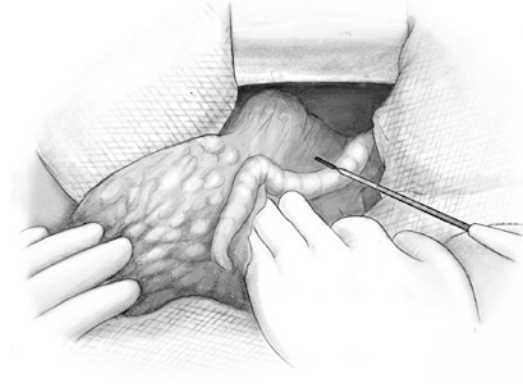

Fig. 9.7 Separate the splenic flexure

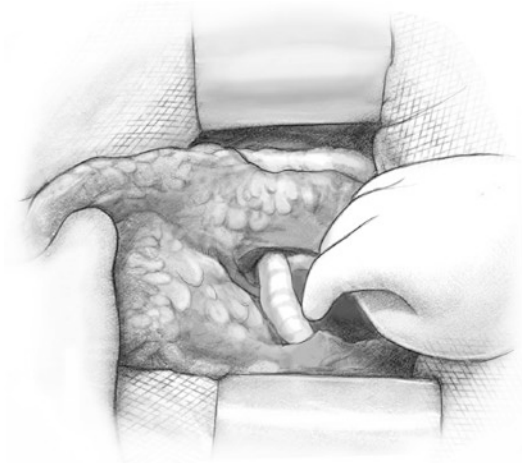

Fig. 9.6 Expose the tumor in the surgical field

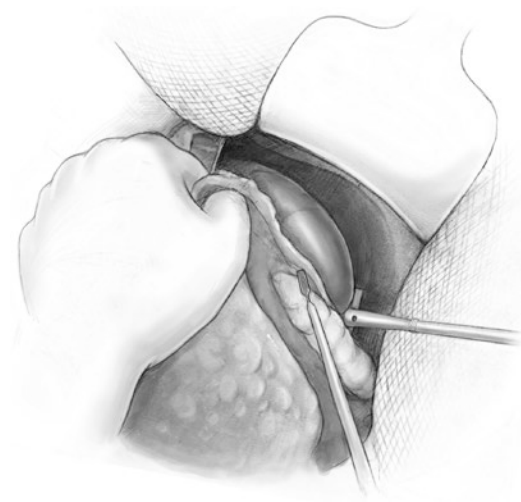

Fig. 9.8 Cut the colon and splenic ligament to obtain an access into the tumor area

5. Initiate sharp separation of the paracolic gutter of the descending colon, and then dissociate and separate splenic flexure (Fig. 9.7). How to gain access to RPTs through the gastrocolic space and splenocolic space approaches is the key to tumor resection, which requires cutting off gastrocolic ligament and splenocolic ligament (Fig. 9.8).
6. Now, expose the anterior portion of the tumor, which is medially close to inferior mesenteric vein, inferiorly to body and tail of pancreas and lower margin of spleen, whereas anteriorly and superiorly to the left kidney and renal blood vessels (Fig. 9.9).
7. Next, separate the adhesion between the left kidney and the tumor. For liposarcoma, remove perirenal fat capsule which may be the primary site of the tumor (Fig. 9.10).
8. Separate the lateral side of the tumor from the lateral abdominal wall due to relatively simple operation, and resect together with the adipose tissue around the tumor as much as possible, which is the key to reduce relapse of retroperitoneal liposarcoma (Fig. 9.11).
9. The medial side of the tumor is closely adjacent to descending mesocolon and transverse mesocolon, anterior to duodenojejunal flexure and abdominal aorta, and thus it is difficult to separate the tumor from these

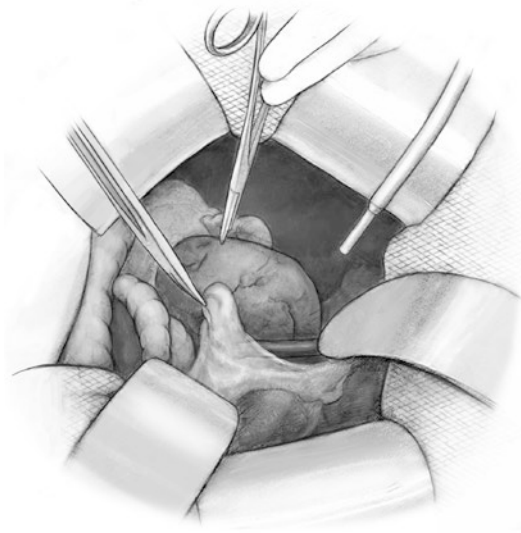

Fig. 9.9 The relation between the left retroperitoneal tumor and adjacent structure is clearly visible

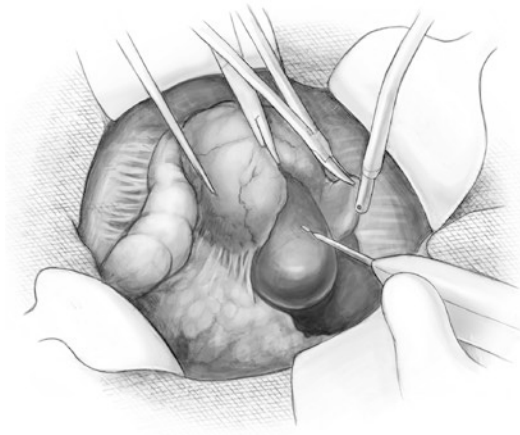

Fig. 9.10 Remove the pararenal adipose capsule to dissociate the kidney

structures. Close attention should be paid to protecting them from being damaged (Fig. 9.12).

10. Continuously separate the superior portion of the tumor to expose the lower margin of the pancreas and mesocolon structure (Fig. 9.13).
11. Continuously separate the tumor from pancreas laterally along the superior portion of the tumor, and cut off left splenorenal ligament (Fig. 9.14).

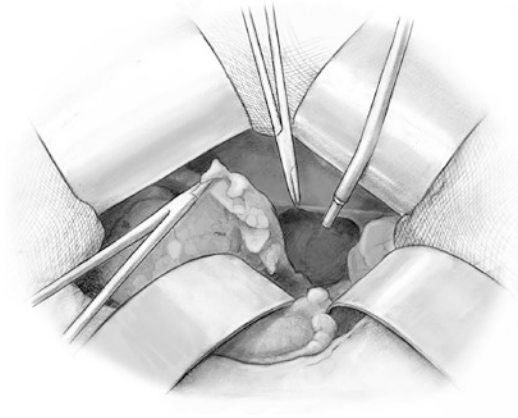

Fig. 9.11 Flush and separate the lateral area that is relatively easily accessible during the surgery of a retroperitoneal tumor

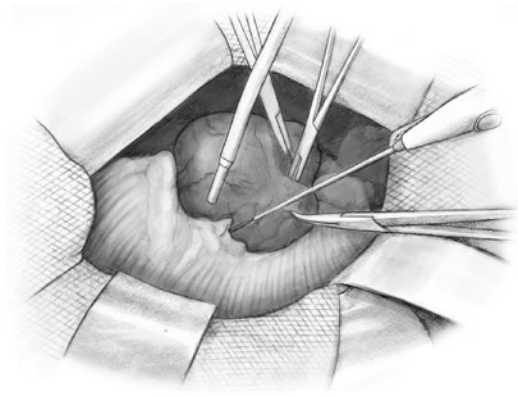

Fig. 9.12 Separate the duodenum from the mesocolon

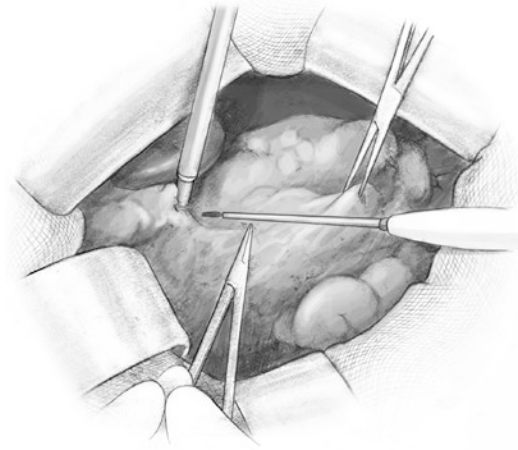

Fig. 9.13 Separate the pancreas

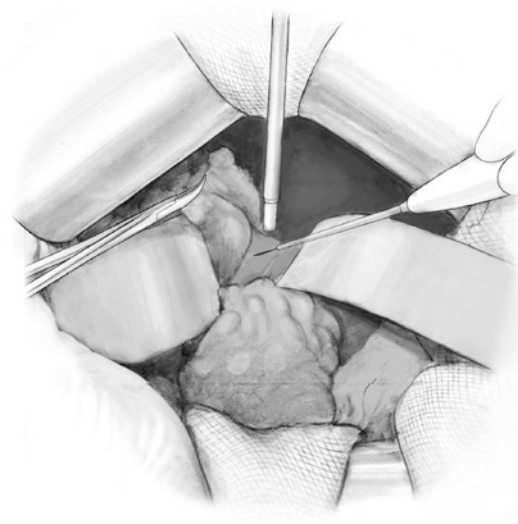

Fig. 9.14 Separate the tumor from the spleen

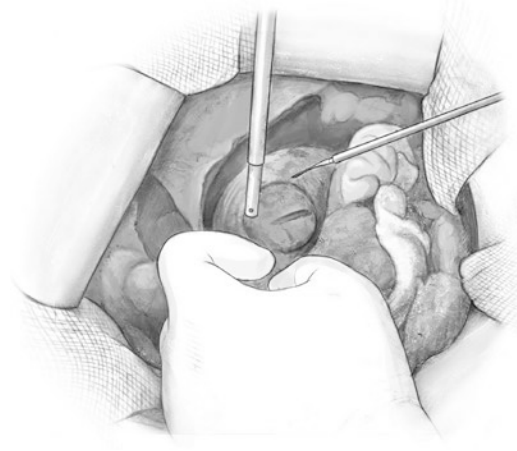

Fig. 9.16 Hemostasis at the bleeding points on the surface of the pararenal adipose capsule during its removal

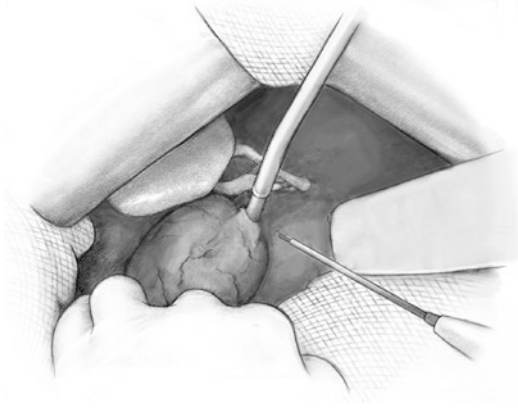

Fig. 9.15 Separate the tumor from the left kidney

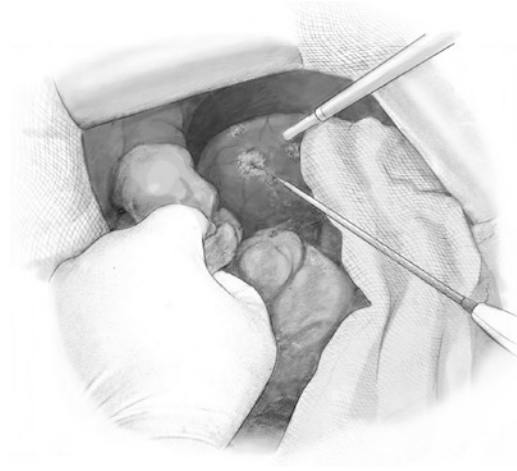

Fig. 9.17 A complete hemostasis of the bleeding points on the renal surface

12. After complete dissociation of the tumor from surrounding tissue, continuously dissociate along the space between the posterior portion of the tumor and the surface of the left kidney to separate the tumor from entire anterior portion of the kidney (Fig. 9.15).
13. When separating perirenal adipose capsule anterior to the kidney, spotlike bleeding may occur on renal surface; successive cauterization may be applied for hemostasis (Fig. 9.16).
14. After the adipose capsule is separated from the entire surface of the kidney, the renal hilum remains unseparated from the tumor. Check the bleeding points on the surface of the naked kidney again, and completely stop bleeding (Fig. 9.17).
15. When separating the tumor anterior to the renal hilum, pay attention to protecting renal artery and vein, suprarenal artery, left gonadal vein, and left ureter. During the surgery, prepare vascular devices, and make endovascular repair if necessary (Fig. 9.18).
16. After full dissociation between the structure of renal hilum and the tumor, only the tumor located anterior to inferior mesenteric vein

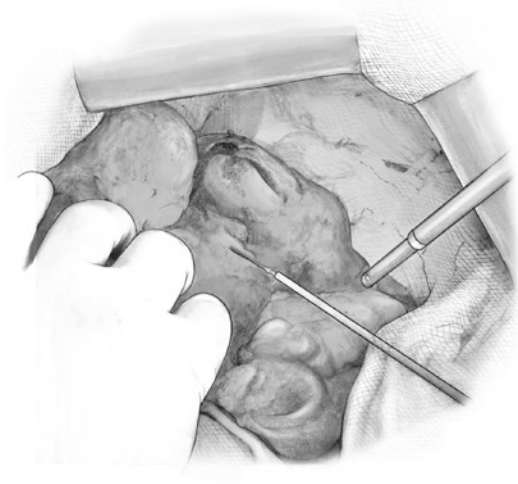

Fig. 9.18 Separate the tumor from blood vessels in the renal hilum and protect the structure of the renal hilum

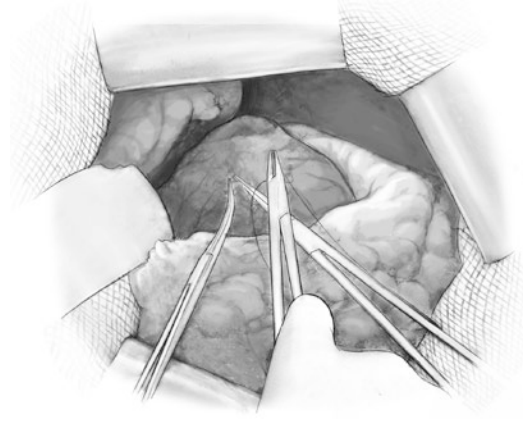

Fig. 9.20 Suture the wound and stop bleeding after tumor resection

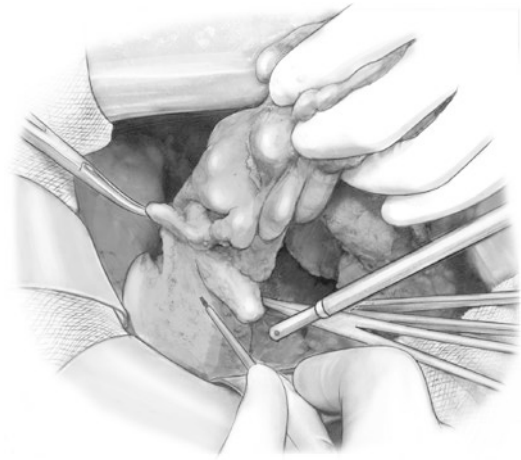

Fig. 9.19 Separate the inferior mesenteric vein medial to the tumor from the splenic flexure

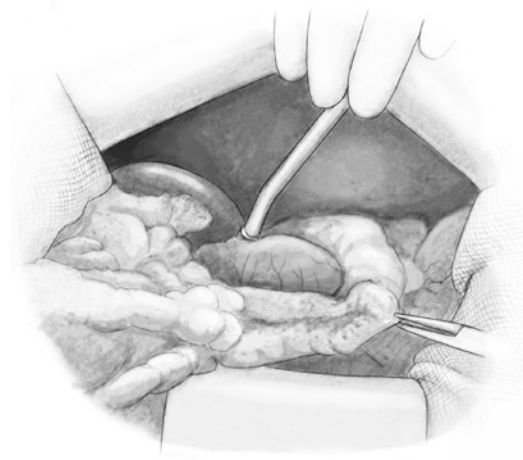

Fig. 9.21 Restore the splenic flexure to normal anatomic position

and splenic flexure mesangium is not separated. Lift up the tumor to expose the residual pedicle-shaped connection, carefully separate, and completely resect the tumor (Fig. 9.19).

17. After resection of RPTs in the left upper abdomen and prerenal zone (Fig. 9.20), if bleeding occurs due to vascular injury in the separation of the tumor anterior to the renal hilum, firstly stop bleeding with clamps, and then suture bleeding points after the tumor is completely removed.
18. Wash the wound, restore the separated and retracted splenic flexure of the colon (Fig. 9.21), place abdominal drainage catheter, accurately count the number of gauzes used for the surgery, and then suture abdominal incision layer by layer (Fig. 9.22).

3.6 Postoperative Treatment

For details, please refer to perioperative treatment of RPTs hereof.

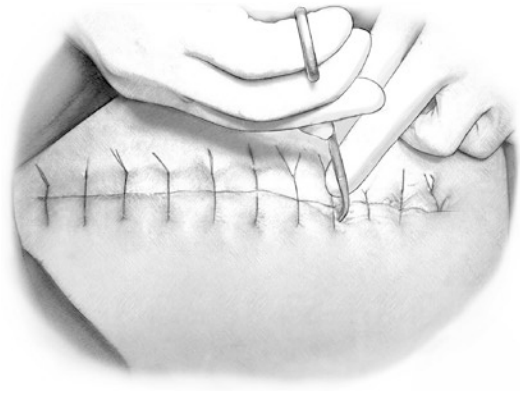

Fig. 9.22 Suture the wound and stop bleeding after surgery

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Surgery for Right Upper Retroperitoneal Tumors

10

Cheng-Hua Luo and Jia Zeng

It has been suggested that a lower resection rate of the right upper retroperitoneal tumors (RPTs) compared to left upper RPTs can be attributed to more frequent tumor invasion of the inferior vena cava. In our hospital, invasion of inferior vena cava in right upper RPTs is comparable to that of left upper RPTs. However, it is challenging to resect the right upper RPT due to the fact that the tumor is located close to the liver, including important structures such as the first, second, and third hepatic hila, and is adjacent to the head of pancreas, duodenum, common bile duct, and portal vein. Invasion of the above structures brings tremendous difficulties to surgical resection of RPTs located in this area (Facciuto et al. 2008; Felix et al. 1981).

1 Clinical Characteristics of the Right Upper Retroperitoneal Tumors

A total of 63 patients underwent resection of right upper RPTs in our hospital in the past 2 years, including 36 women and 27 men with median age of 40.5 years, range from 3 to 73 years.

Pathohistological classification of right upper RPTs is complex; retroperitoneal leiomyosarcoma, teratoma, nerve sheath tumor, liposarcoma, and paraganglioma are very common. Other pathological types include neuroblastoma, ganglioneuroma and neurofibroma, leiomyosarcoma of the inferior vena cava, seminoma, malignant fibrous histiocytoma, chemodectoma, fibrosarcoma, chondrosarcoma, sarcoma, lymphatic tumors, malignant stromal tumor, unspecified genital tumors, poorly differentiated sarcoma, and metastatic adenocarcinoma and squamous cell carcinoma (Weiss and Goldblun 2002).

Clinical presentation of right upper RPTs is similar to that of the left upper RPTs. Common symptoms are right upper abdominal pain and right back aching pain (swelling and dull in nature). Such tumors often compress the duodenum, leading to acid reflux, nausea, vomiting, and abdominal distension. Abdominal pain can radiate toward the right lower quadrant, causing chest pain, hip pain, and pain in the right thigh and even a right lower limb movement disorder. Systemic symptoms include fever and weight loss. Neuroblastoma can result in exophthalmos. Paraganglioma may cause sweating and hypertension (Raut and Pisters 2006).

Most of the right upper RPTs can be diagnosed and localized prior to surgery (Lim et al. 1990). However, some cases are misdiagnosed as duodenal tumor, liver cancer, gallbladder tumor, and left and right suprarenal tumors which are also derived from retroperitoneum. Thus, patients should be comprehensively evaluated preoperatively to avoid misdiagnosis (Raut and Pisters 2006).

Surgical resection is the major therapeutic choice for the right upper retroperitoneal tumor.

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The author has summarized that complete resection rate of right upper RPTs was obtained 73%, which is the lowest among all RPTs.

2 Surgical Procedures for Removal of a Retroperitoneal Tumor in the Right Upper Quadrant

2.1 Preoperative Preparation

The preoperative preparation depends on the involvement of adjacent organs. For patients with a retroperitoneal tumor complicated by duodenal obstruction, the upper gastrointestinal tract (contrast) radiography should be performed, together with warm saline lavage. For those with complicated biliary obstruction, cholangiography should be employed to demonstrate the site and scope of the obstruction. For those with a tumor invading the inferior vena cava, venography should be conducted to identify the retroperitoneal collateral circulation. Individual renal function should be examined separately to identify the potential risks for resecting one kidney. Routine bowel preparation and prophylactic use of antibiotics are similar to those in a major surgery for a retroperitoneal tumor in other parts of the body (Raut and Pisters 2006).

2.2 Anesthesia

General anesthesia with endotracheal intubation.

2.3 Position

Keep the patient in the supine position. His/her waist on the right side of the back can be raised under the pad if necessary.

2.4 Incision

A median upper abdominal incision is the most commonly employed, followed by a transverse incision through the rectus abdominis on the right side, and sometimes an oblique incision along the costal margin is an option. For patients who have undergone surgery, the original surgical incision should be selected in principle and extended according to the actual condition during the surgery (Fig. 10.1).

2.5 Surgical Procedures

1. Cut layer by layer of the abdominal wall. As abdominal adhesion is commonly encountered, special care should be taken to protect the abdominal wall and the bowel from accidental injury during surgery (Fig. 10.2) (Felix et al. 1981).
2. After access into the abdominal cavity, carefully separate the adhesion, especially the

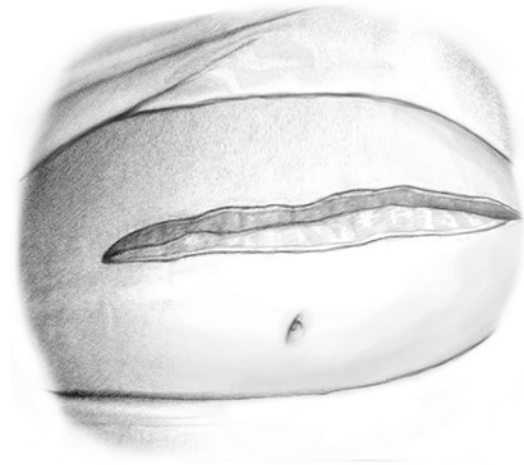

Fig. 10.1 An abdominal incision

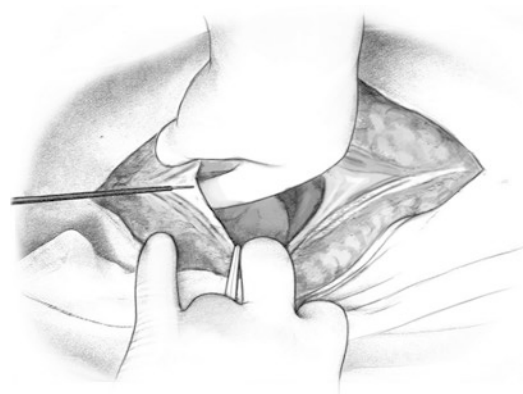

Fig. 10.2 Cut layer by layer of the abdominal wall

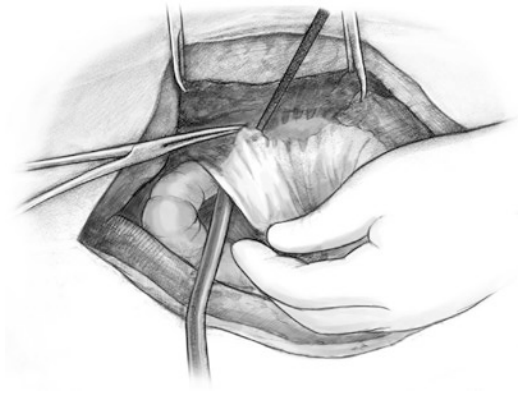

Fig. 10.3 Access to the abdominal cavity in order to separate the adhesions

Fig. 10.4 Separate the hepatic flexure

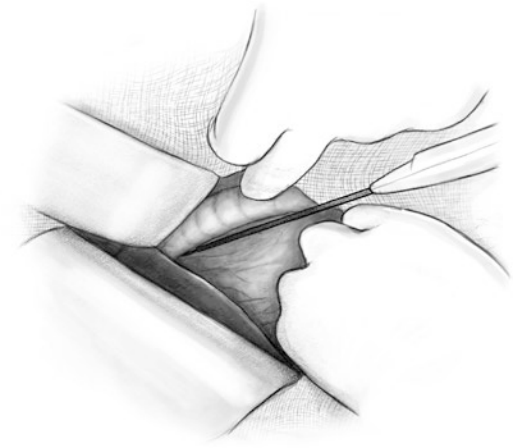

Fig. 10.5 Separate the duodenum

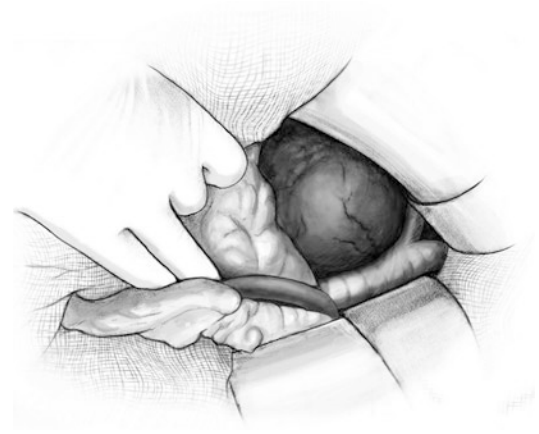

Fig. 10.6 Expose the inferior vena cava

one between the bowel and surrounding organs (Fig. 10.3).

3. The surgical approach to a retroperitoneal tumor is essential. For a retroperitoneal tumor in the right upper quadrant, the intrahepatocolic approach is usually chosen, which passes through the parapsidal groove in the ascending colon into the retroperitoneal area, in an attempt to separate the hepatic flexure inward inferiorly (Fig. 10.4) (Facciuto et al. 2008).
4. The posterior peritoneum from the posterolateral duodenum is cut to separate and pull the duodenum to the left side, in order to expose the inferior margin of the liver (Fig. 10.5). Once the duodenum is separated from the surface of the tumor, the inferior vena cava located posteriorly is exposed, which is also compressed by the tumor toward to the left (Fig. 10.6) and thus should be separated with an extreme caution during the surgery.
5. The right kidney should be treated properly during the removal of a retroperitoneal tumor in the right upper quadrant. After identifying the space between the tumor and the right kidney (the kidney is located lateral and posterior to the tumor), the adipose capsule of the right kidney should be separated by sharp dissection to reduce the bleeding. The use of an ultrasound scalpel is highly recommended (Fig. 10.7). The dissociation is continued toward to the right side in order

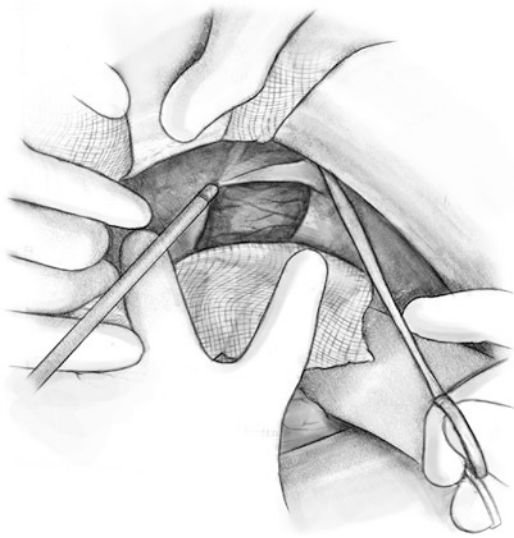

Fig. 10.7 Sharply dissect the pararenal adipose capsule

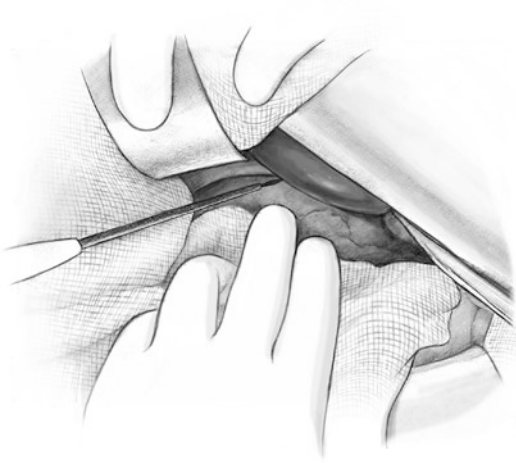

Fig. 10.8 Carefully separate the adhesion between the right kidney and the tumor

to expose the kidney that is closely connected to the tumor and should be carefully separated (Fig. 10.8).

6. Pay special attention to the structure of the right ureter when dissociating the inferior portion of the tumor (Fig. 10.9).
7. Carefully dissociate the loose tissue space between the medial portion of the tumor and the inferior vena cava, in an attempt to separate the inferior vena cava (Fig. 10.10). A complete separation of the inferior vena cava makes the dissociation of the tumor much safer (Fig. 10.11).

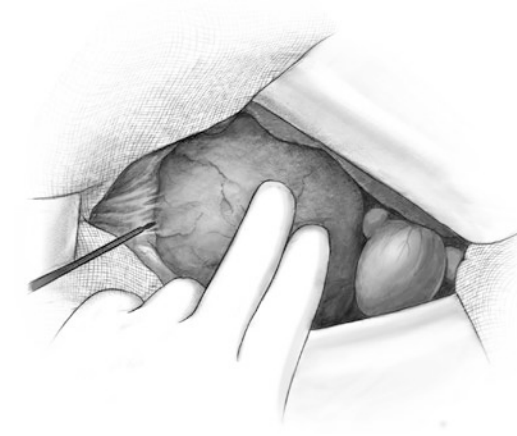

Fig. 10.9 Separate the ureter below the tumor

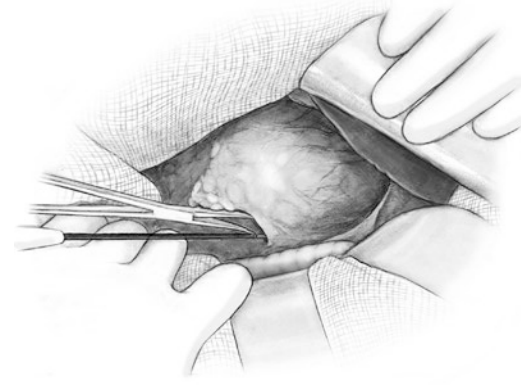

Fig. 10.10 Separate the inferior vena cava medial to the tumor

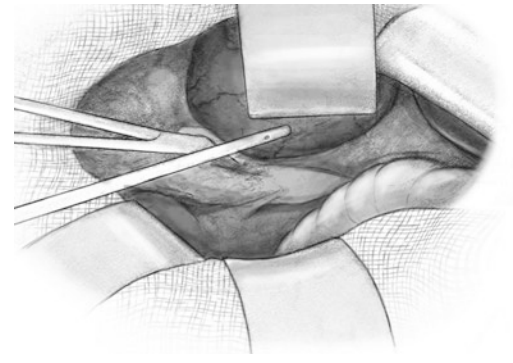

Fig. 10.11 Completely separate the inferior vena cava from the tumor

8. The last step is to dissociate the posterior aspect of the tumor: drag the tumor to one side, and then separate it under a direct vision

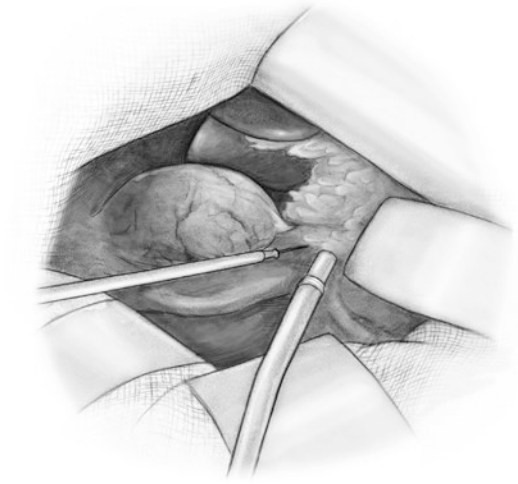

Fig. 10.12 Separate the posterior aspect of the tumor after the separation of adjacent structures

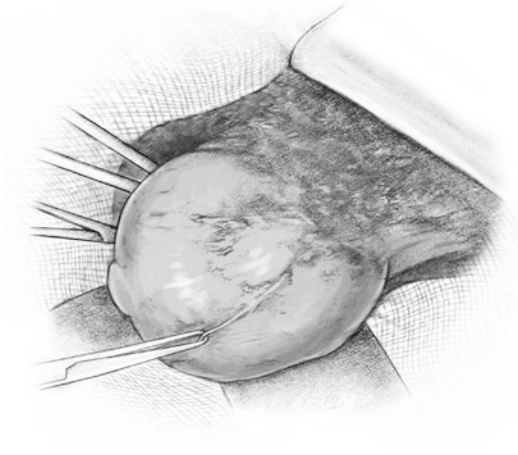

Fig. 10.13 Completely remove the tumor

using an ultrasonic scalpel (Fig. 10.12), and, finally, remove the tumor from the tumor bed (Fig. 10.13).

9. If the vasculature wall is injured during the separation of inferior vena cava, the surgeon should stay calm, clamp the rupture with Ellis forceps, and then calmly close/repair the rupture after the tumor is removed (Fig. 10.14).
10. Flush the wound and abdominal cavity with normal saline (Fig. 10.15), place a drainage tube into the abdominal cavity, and then suture the abdominal incision (Fig. 10.16).

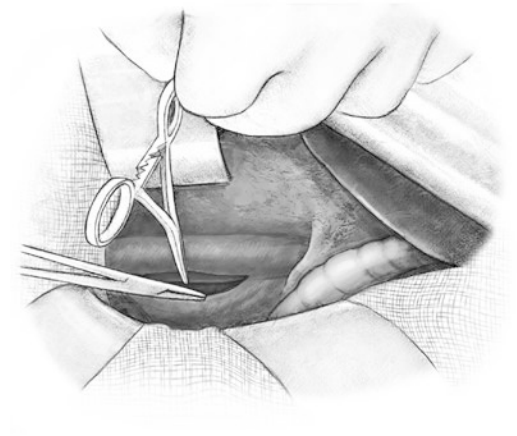

Fig. 10.14 Suture and repair the rupture of the inferior vena cava

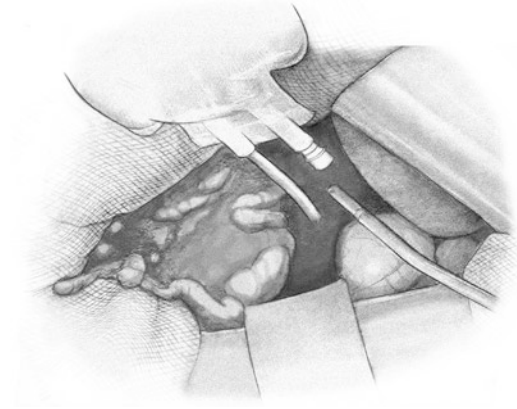

Fig. 10.15 Flush the abdominal cavity and the wound

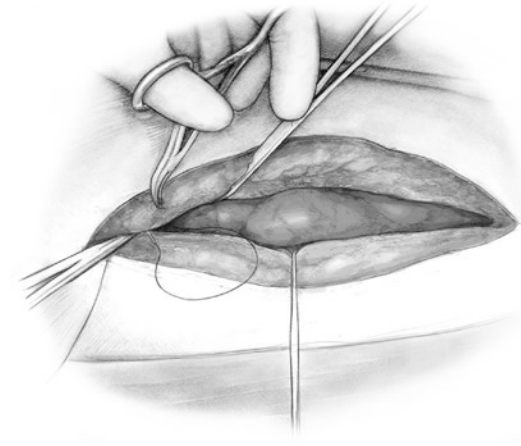

Fig. 10.16 Close the incision and the surgery is accomplished

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Surgery for Retroperitoneal Tumors in the Lower Abdomen

11

Cheng-Hua Luo and Shiwen Mei

The lower abdomen is comprised of the left lower abdomen, right lower abdomen, and bilateral iliac fossa, with the horizontal line over the umbilicus as the upper boundary and true pelvic inlet as the lower boundary. Lower abdominal retroperitoneal structure includes the lower section of the abdominal aorta and iliac artery and lower segment of the inferior vena cava and bilateral iliac vein, bilateral ureters, and bilateral retroperitoneal muscle nerves. Ileocecum and ascending colon are located in the right lower quadrant whereas descending colon and sigmoid colon in the left lower quadrant. The retroperitoneal tumors (RPTs) in the lower abdomen can involve all of the above structures which may require resection during surgery, making the procedure extremely challenging (Felix et al. 1981).

In our database 108 (13.2%) out of 818 cases of RPTs are located in the lower abdomen, including 24 located in the left lower abdomen exclusively, 26 located in the right lower abdomen exclusively, and 58 located in the lower abdomen simultaneously occupying other parts of the abdomen. Among these 108 cases who underwent RPTs combined with lower abdominal organ resection, 2 received resection of the abdominal aorta and iliac artery, 2 received resection of the inferior vena cava and iliac vein, 12 received resection of the ureter, 3 received resection of the femoral nerve, and 23 received resection of bowel. Out of these 108 cases, 20 underwent total resection R0, 4 underwent R1 resection, 3 did not undergo resection, and the rest underwent partial resection. The most common pathological types of RPTs in the lower abdomen are liposarcoma, schwannoma, and leiomyosarcoma.

R0 resection is the key to complete removal of RPTs in the lower abdomen with good prognosis. To the best of our knowledge, no studies have been reported on RPTs located in this area about key points for surgery due to the specificity of surgical treatment. In China, RPTs are often not diagnosed until they have grown to a large size. Furthermore, RPTs in lower abdomen can extend to the left upper abdomen, to the right upper quadrant or pelvic presacral space, and even to the bilateral inguinal region and thighs. Retroperitoneal tumors derived from the above sites may also spread to the lower abdomen. Therefore, surgeons are required to receive professional training of typically surgical technique for tumors located in both retroperitoneum and other sites of the abdomen or pelvis (An et al. 2007).

1 Surgical Indications

1. RPTs in lower abdomens without extensively systemic metastasis.
2. Tumors involving major vessels below the level of renal vessels, preoperative evaluation indicating possible vascular grafts.

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3. Tumors presenting with lower limb neurological symptoms, intestinal obstruction, or hydronephrosis.
4. Clinically diagnosed as soft tissue tumors after ruling out epithelial cancer peritoneal metastasis.
5. Primary RPTs in the lower abdomen or recurrence in more than 6 months after the operation.
6. Tumors unable to be removed during the exploratory surgery that was performed in another hospital more than 3 months ago, and now the patient has been admitted to the hospital that claims to have the technical capability to make a complete resection.

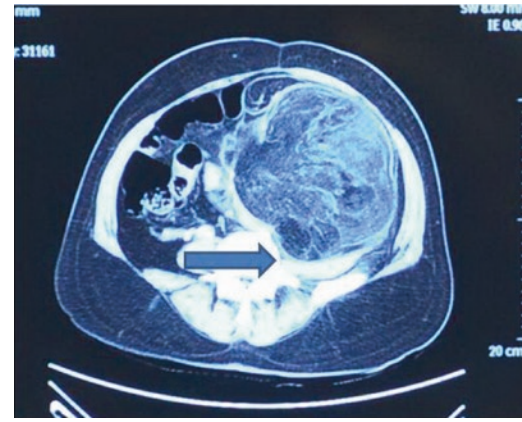

Fig. 11.1 CT image of a liposarcoma in the lower abdomen

2 Surgical Contraindications

1. Evidence has supported that the RPTs in the lower abdomen are metastatic from other sites, and primary tumors cannot be completely resected.
2. RPTs in the lower abdomen invade major retroperitoneal vessels, superior mesenteric artery, portal vein, or other vessels above the renal level, and the separation is impractical.
3. Tumors with widespread systemic metastasis.
4. Patients with concomitant severe cardia, pulmonary, and hematologic diseases, so that they cannot tolerate the surgery.
5. It's impossible to prepare enough blood reserves, artificial blood vessels, equipment, and devices to guarantee the safety of patients for various reasons.

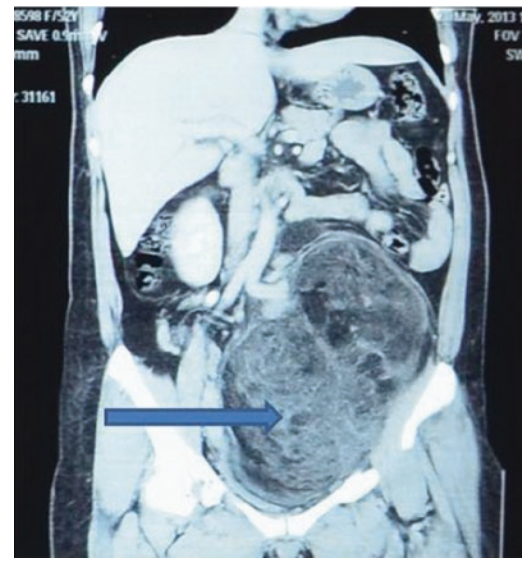

Fig. 11.2 Coronal CT scan image can clearly display the location of the retroperitoneal tumor in the lower abdomen

3 Preoperative Preparation

Three conventional tests (blood, urine, and stool), blood biochemistry, ECG, and chest X-rays should be performed before surgery.

CT and MRI scans demonstrate the size and location of the tumors, as well as their relationship with adjacent organs. Enhanced CT scanning should be performed in order to clarify the relation of the tumor with abdominal aorta and iliac arteries. If necessary, inferior vena cava angiography or the whole digestive tract imaging should be performed in order to identify potential involvement of retroperitoneal vein and gastrointestinal tract.

Predict blood loss based on the condition of tumors, and prepare sufficient red blood cells, plasma, and other components for transfusion.

Prepare postoperative care facilities and custodial staff.

Prepare sufficient artificial blood vessels, stapler, ureteral stents, and necessary materials. Before surgery, it is very important for surgeons to repeatedly interpret imaging findings. For example, CT scan (Fig. 11.1) and coronal scan (Fig. 11.2) display that lower left RPT inwardly

pushes sigmoid colon, thus squeezing forward the iliac vessels. Therefore, imaging diagnosis plays a crucial role in guiding the operation.

4 Anesthesia and Position

Generally, tracheal intubation is performed under general anesthesia during resection of RPTs located in the lower abdomen. Patients are lying in the supine position and may be elevated on the identical side intraoperatively with the abdomen obliquely facing the surgeon if the tumor spreads from the unilateral lower abdomen posteriorly into the dorsal part of the psoas major. If the removal of the sigmoid colon is expected, descending colon rectal anastomosis will be performed. Patients may lie in "A"-shaped supine position with their legs wide open, thus facilitating the placement of stapler through the anus intraoperatively.

5 Surgical Procedures

1. Incision: straight incision along ventral midline is commonly adopted during resection of RPTs in the lower abdomen and may be extended to xiphoid or pubic symphysis if necessary. If the tumor has deeply invaded into the dorsal structure unilaterally, an additional transverse incision that crosses the midline of the tumor will be performed on the same side, or transverse incision applied bilaterally, making a plus sign (+)-shaped incision. For patients with history of surgical resection, the original incision should be preferred and the scar removed. During skin preparation, disinfection scope should be adequate to cover the entire abdomen, perineum, and 1/3 of upper thighs, extending bilaterally to the posterior axillary line and superiorly to the nipple level (Fig. 11.3).
2. Cut the skin, subcutaneous fat, and white line. If it is a transverse incision, cut musculus obliquus externus abdominis, obliquus internus, transversus abdominis, transverse fascia, peritoneal fat, and peritoneum. For recurrent patients who undergo reoperation, it will take longer time to separate peritoneum that is adhered to abdominal organs—such as the bowel and omentum. Tumors extensively adhered to the abdominal wall should be carefully and completely separated. Sharp separation is recommended. The first step is to identify a free area from where the space between peritoneum and abdominal structure is retracted, so that the structure to be separated at the adhesion site may generate tension toward the opposite direction to facilitate the separation. RPTs covered with intact retroperitoneum can often be exposed after cutting the abdominal wall (Fig. 11.4).
3. Protect the incision, and carefully identify surrounding structures of the tumor. In general, firstly dissociate the tumor margin with good exposure, less blood supply, and fewer adjacent vital organs. Surgeons

Fig. 11.3 An incision for surgery on a retroperitoneal tumor in the lower abdomen

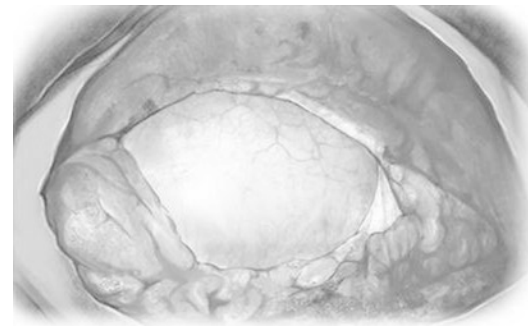

Fig. 11.4 An intact peritoneum on the surface of a retroperitoneal tumor

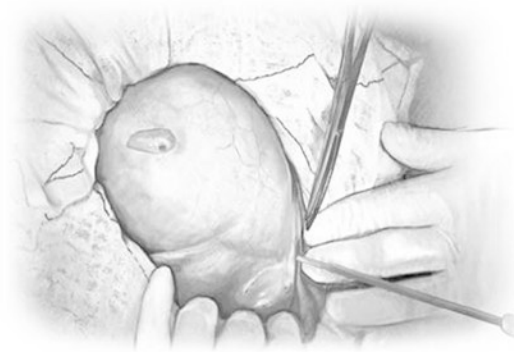

Fig. 11.5 Start the separation from the relative safe direction outside the tumor margin

should have a strong capability to clarify normal tissue structure of the lower abdomen as well as the displacement direction of surrounding structures pushed by larger tumors (Fig. 11.5).

4. Firstly open the retroperitoneum between RPT and normal tissue. Try to incise the normal tissue at the outer margin of the tumor to obtain a distance of about 0.5 cm away from the normal tissue. Most of retroperitoneal sarcoma exhibits expansive growth patterns, and the outer surface of the tumor is often covered with false capsule which must be intact in the process of separation. How to distinguish sarcomas from normal tissue depends on individual nature, e.g., it is sometimes difficult to distinguish liposarcoma from normal adipose tissue, so attention should be paid to the separation process (Fig. 11.6).
5. When dissociating the medial-inferior portion of the tumor, iliac vessels, ureter, and colon are occasionally encountered, which may be pushed by the tumor inwardly, posteriorly, or forwardly, while the tumor grows into the posterior portion of the abovementioned structures. Iliac vessels and ureter are sometimes wrapped within the tumors, making it extremely difficult to separate them (Fig. 11.7).
6. In women, the medial-inferior portion of RPT in the lower abdomen may be adherent to accessories, which should be carefully dissected. The preservation of ovarian is important, especially for young female

Fig. 11.6 Pay special attention to the tumor resection margin for R0 resection

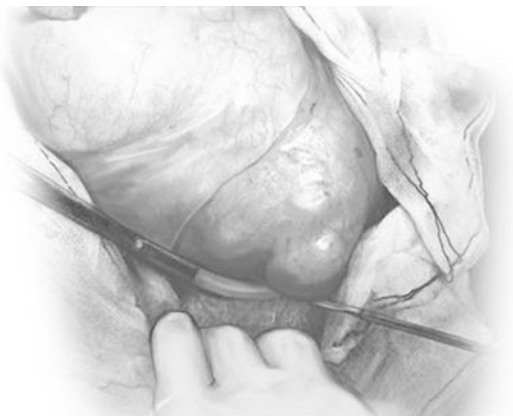

Fig. 11.7 Carefully identify the iliac vessels and ureter, and then separate them from the tumor

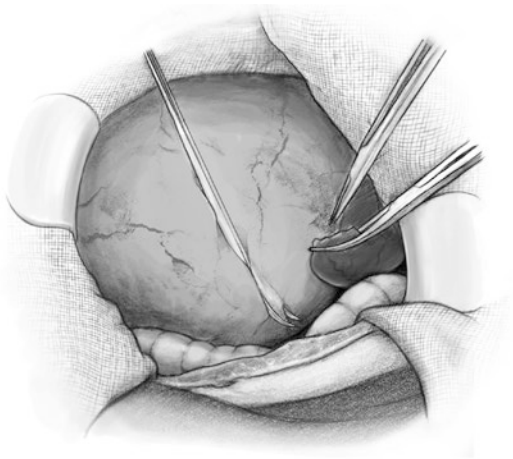

Fig. 11.8 Separate the tumor from its adjacent adhesions

patients, so ligation and excision are commonly performed to prevent bleeding during the separation (Fig. 11.8).

Fig. 11.9 To separate the lateral aspect of the retroperitoneal tumor in the lower abdomen is relatively safe

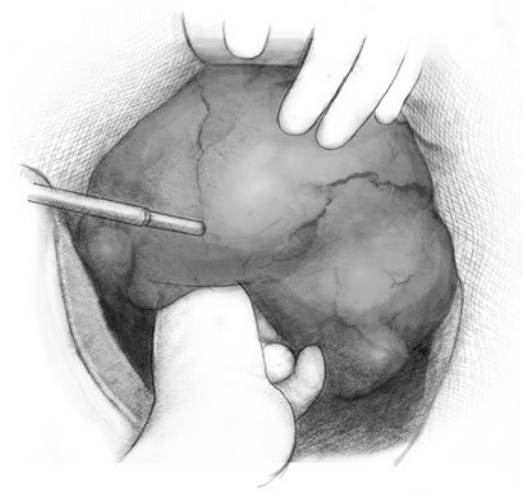

Fig. 11.10 Blunt separation of the posterior aspect of the tumor can be performed with fingers when encountering a tumor present with expansive growth or a capsule

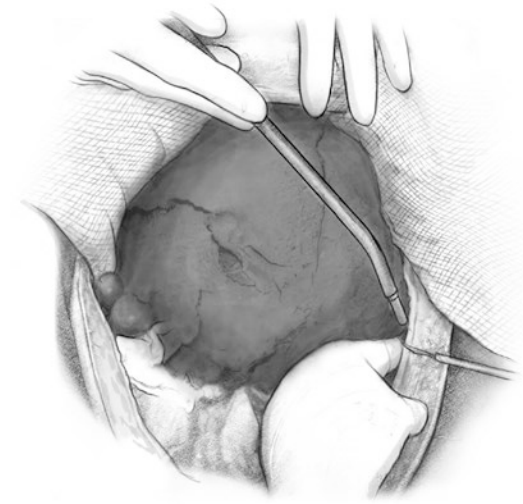

Fig. 11.11 The incision may be extended based on specific conditions of the tumor during the surgery

7. Dissociation of RPTs in the lower abdomen from medial side is relatively safe (Fig. 11.9). Surgeons firstly cut the peritoneum open at the included angle adjacent to the tumor and lateral abdominal wall and then separate it backward to the surface of the back muscles. For large tumors, it is difficult to separate them from one side to the furthest posterior part at one time. In principle, the separation is shifted from one side to the other side until it cannot be continued. During the surgery, the separation shall always start from the area where the separation is most easily performed.
8. One of the most difficult processes in separating RPTs is the posterior dissociation. Because of large volume, the posterior tumor bed is extensively adhered and attached. The separation cannot be performed under direct vision due to the fact that the tumor body cannot be overturned, which is only feasible after separating the posterior portion of the tumor. In such case, surgeons often apply blunt dissection with the fingers extending into the rear of the tumor (Fig. 11.10). Prerequisite of this operation is that the surgeon should be very familiar with the anatomical relationship of the area to be separated. Based on this, the surgeon needs to confirm whether major blood vessels and other critical structure are located posteriorly to the tumor.
9. RPTs in the lower abdomen vary greatly in size, location, and relationship with surrounding structures. Therefore, the surgical procedure for this type of tumor is not entirely consistent. During the surgery, extension of the incision or change in incision direction is often required based on the exposure (Fig. 11.11).
10. Sometimes, iliac vessels pass through the middle of the tumor, which should be carefully identified. To protect these vital structures, it is necessary to dissect the tumor located on their surface. To prevent damages to important structures located deeply in the tumor, putting fingers of the left hand into the rear of the tumor

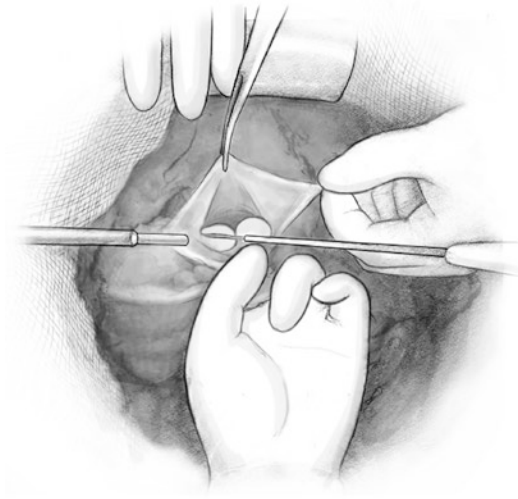

Fig. 11.12 Cut the tumor to expose the blood vessels which are wrapped by the tumor

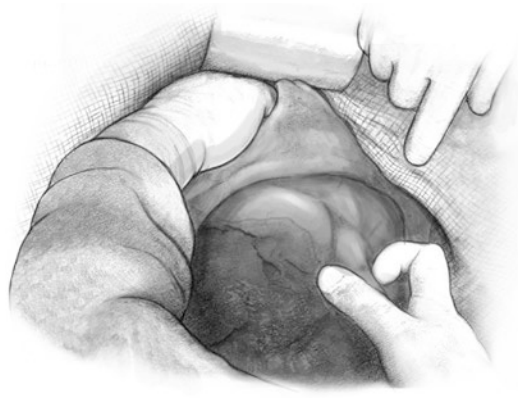

Fig. 11.13 Sometimes, the tumor is required to be bluntly dissected within the capsule and removed

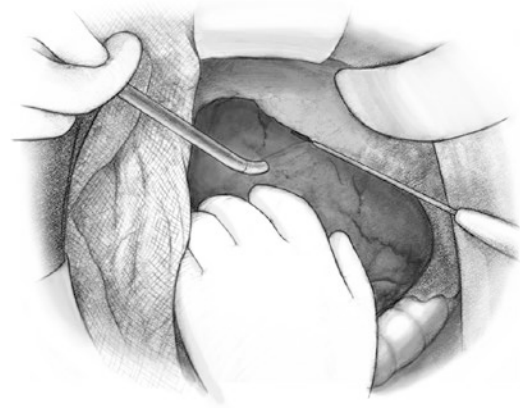

Fig. 11.14 The outside tumor margin should be separated from the normal tissue space after the central portion of the tumor has been removed

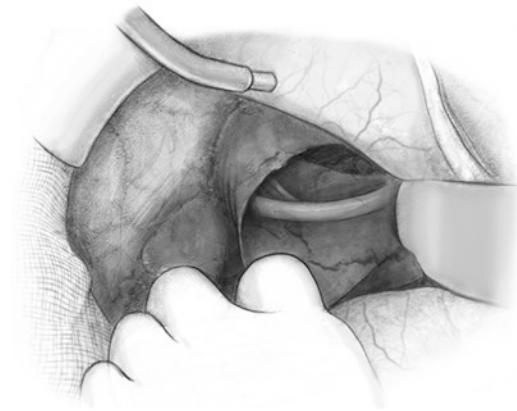

Fig. 11.15 Carefully separate the femoral nerve posterior to the tumor

to be dissected to guide the operation is a quite important skill for the surgeons (Fig. 11.12).

11. If it is difficult to completely separate and resect the tumor from the surrounding, or it is impossible to dissociate and remove the tumor due to vital structures surrounding the tumor, surgeons may alternatively perform blunt dissection to remove part of the tumor within the capsule. If iliac vessels are straddling anteriorly to the tumor, blunt dissociation and resection of the enclosed tumor body should be firstly performed followed by removal of the capsular wall (Fig. 11.13).
12. Due to significant decrease in tumor load after the majority of the tumor has been removed, the space between the surrounding structures of the tumor and normal tissue is exposed clearly, thus making the separation of the surface of the tumor easier (Fig. 11.14). Femoral nerve passing through lateral abdominal RPT is located deeply in the iliac fossa, which may be pushed up by the tumor growing into the rear. During the separation, femoral nerves should be exposed adequately and protected carefully. Any damage to femoral nerves can cause difficulties in raising ipsilateral thigh (Fig. 11.15).
13. Ureter attached to the surface of the tumor (Fig. 11.16) needs to be carefully distinguished. Ureter may be pushed inwardly, posteriorly, laterally, or forwardly by RPTs in the lower abdomen, which should be identified by preoperative angiography. Usually,

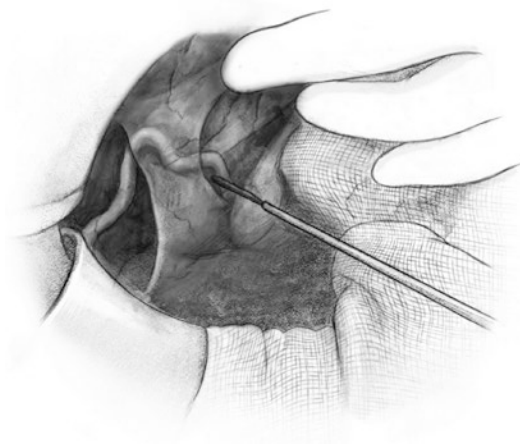

Fig. 11.16 Separate the ureter

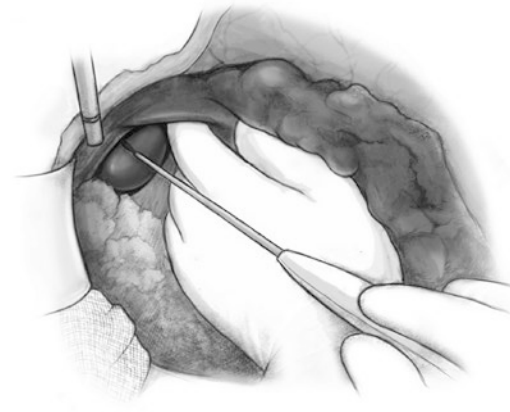

Fig. 11.18 Separate the superior portion of the retroperitoneal tumor from the kidney

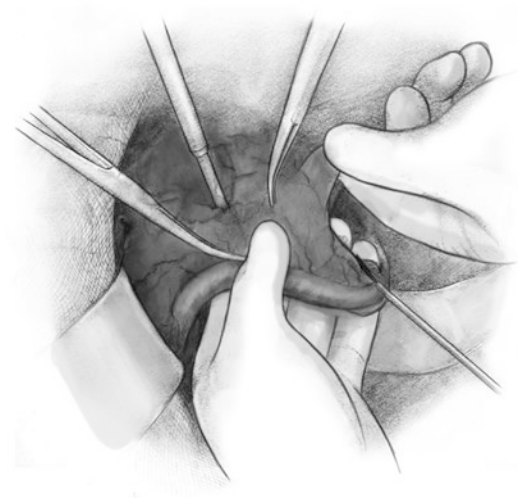

Fig. 11.17 Separate the femoral artery and vein from the tumor

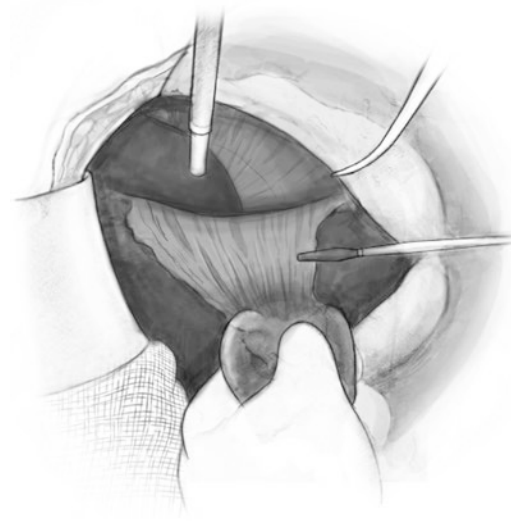

Fig. 11.19 Separate the inferior portion of the tumor from the fiber surface of psoas major muscle

ureter is rarely invaded by RPTs, so it can always be separated after careful dissociation. If ureteral injury and poor blood supply are detected, surgeons can place ureteral stents and then repair the ureter.

14. Femoral arteries and veins may be wrapped by RPTs, which should be carefully dissociated from the tumors to avoid any damage to the blood vessels. After complete dissociation is performed in other regions, it is advised to dissociate the femoral artery to a safe location based on optimal conditions (Fig. 11.17) before continuing the separation of the tumor. Usually the thin-walled femoral vein located posteriorly is vulnerable to damage, so unilateral ligation should be performed if it is difficult to repair. The collateral circulation is gradually established in 1 month after surgery.
15. Attention should be paid to the space between the tumor and kidney when separating the superior part of lower abdominal RPT in order to avoid any damage to the ureter and blood vessels at renal hilum. It is critical to carefully identify perirenal adipose capsule (Fig. 11.18) because un-identification of kidney can cause renal cortex damage and bleeding.
16. As psoas major is located bilaterally posterior to lower abdominal RPT, surgeons often need to completely resect the tumor (Fig. 11.19) from the surface of the muscle.

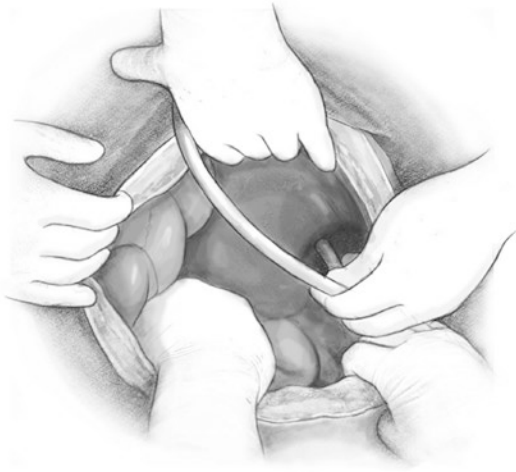

Fig. 11.20 Flush the wound with normal saline after tumor resection

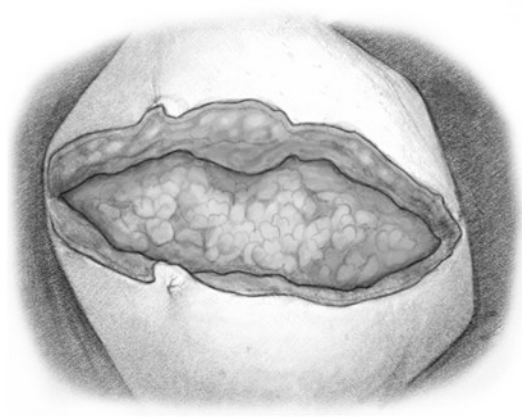

Fig. 11.22 Place the greater omentum beneath the incision

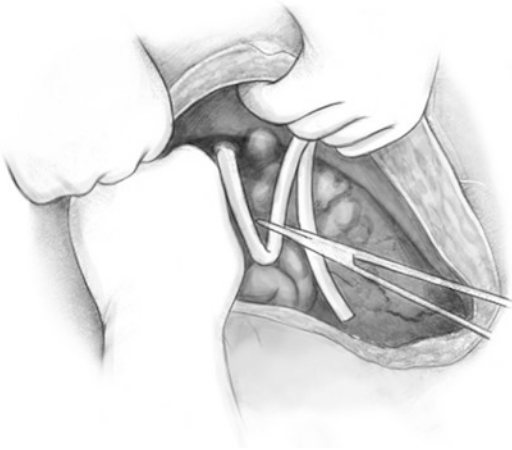

Fig. 11.21 Place the drainage tube in the wound

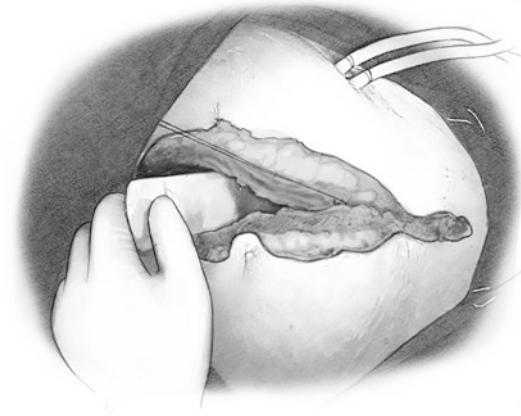

Fig. 11.23 Close the incision

Sometimes, tumor tissue that spreads into the space between muscle bundles needs to be carefully removed.

17. After the tumor was removed, the surgical field requires an adequate wash with a large amount of normal saline (Fig. 11.20) and repeated checks for residual tumor; if appropriate, complete resection of the residual lesions will be performed successively.
18. The wound generated by RPTs surgery generally requires placement of at least two drainage tubes in the abdominal cavity, especially for larger tumors, wide wound, and combined resection of adjacent organs (Fig. 11.21).
19. Carefully count the gauze sponge and devices after operation. Omentum can generally be placed below the abdominal incision, in order to prevent potential adhesions through direct contact with the intestine and reduce the incidence of postoperative ileus (Fig. 11.22).
20. PDS-II and other powerful sutures will be used for closure of the incision, white line, or rectus sheath (Fig. 11.23); if necessary, relaxation suture will be applied to reduce tension. Subcutaneous adipose tissue and skin will be sutured carefully; ensure that no dead space will be left between the incision and the sutured layers (Fig. 11.24).

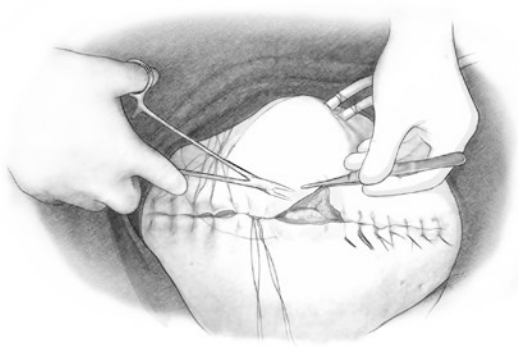

Fig. 11.24 Close layer by layer of the abdominal wall; ensure no dead space has been left

6 Postoperative Treatment

See Chap. 7 for postoperative treatment in detail. After a combined resection of organs involved in the surgery of RPTs in the lower abdomen is completed, postoperative care should be implemented appropriately. Patients, if have not undergone artificial vascular graft reconstruction during the resection of inferior vena cava, should be observed for lower limb edema and asked to lie in bed and raise their affected limbs in order to facilitate lower extremity venous return. Following abdominal aortoiliac artery myotomy and artificial vascular grafts, attention should be paid to close observation of the dorsalis pedis pulse, while systemic half-dose heparinization is performed for the purpose of thromboprophylaxis. If bowel resection and anastomosis are performed simultaneously, the vascular anastomosis must not overlap with the intestinal anastomotic site and should be completely separated by the greater omentum (Weiss and Goldblun 2002).

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Surgery for Retroperitoneal Tumors in the Pelvis

12

Cheng-Hua Luo and Weida Chen

The retroperitoneal tumors (RPTs) in the pelvis, also known as presacral tumors, are derived from the retroperitoneum, mostly or wholly located in the pelvic cavity, whereas excluding tumors that originate from internal organs such as the bladder, prostate, adnexa of uterus, colon, and rectum. Due to the presence of wide spaces between the pelvic peritoneum and presacral space, pelvic side walls, and pelvic diaphragm, soft tissue tumors originating from these spaces may be located posteriorly, laterally, inferiorly, or even anteriorly to peritoneum. All tumors are mostly or wholly located within true pelvis between the pelvic inlet (encircled by pubic joint, iliopubic line, and the sacral promontory) and pelvic outlet (comprised of coccyx, ischial tuberosity, and pubic arch). The tumor may partially spread to the lower abdomen and bilateral iliac fossa and even to the buttocks and perineum. 9.1% of patients with pelvic RPTs develop diffusion and metastasis, including peritoneal implantation, lymph node metastasis, and liver metastasis.

Pathological classification of RPTs in the pelvis is complex. The most common histological types of RPTs in the pelvis are teratoma and schwannoma followed by neurofibromatosis, primitive neuroectodermal tumor, malignant fibrous histiocytoma, malignant stromal tumor, angiosarcoma and skin cell tumor, liposarcoma, invasive fibroma and desmoid tumor, malignant lymphoma, leiomyosarcoma, Castleman's disease, leiomyoma, rhabdomyosarcoma, fibroleiomyoma, fibroma, fibromatosis, fibrosarcoma, malignant paraganglioma, ependymoma, endodermal sinus tumor, osteosarcoma, synovial sarcoma, mesothelioma, hemangioma, cystic lymphangioma, pelvic cysts, metastatic clear-cell sarcoma, unspecified muscle-derived tumors, unspecified spindle cell sarcoma, and unspecified malignancies.

1 Clinical Features

The incidence of RPTs in the pelvis is about equal between men and women. The mean age of onset is 38.3 years (range, 3–74 years), with an average duration of 37.2 months.

Due to musculoskeletal-constituted pelvic wall as a barrier, the positions of pelvic organs are relatively fixed. These organs are vulnerable to invasion of RPTs. Furthermore, based on structural varieties, all the organs in the pelvis may be involved, so the clinical presentation of RPTs in the pelvis is complex and diverse, involving digestive system, urinary system, reproductive system, surrounding pelvis, and lower limbs.

According to the author's statistics, clinical manifestations of RPTs in the pelvis include:

a. Pain: including lower abdominal pain, lower back pain, lower limb pain, sacral pain,

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buttock pain, penis and scrotum pain, hip pain, anal pain, body pain, as well as radiating pain in the genitals and lower extremity. Pain is mostly attributed to invasion of pelvic nerves by tumors, including lumbar plexus, sacral plexus, pelvic plexus, sciatic nerve, femoral nerve, and its branches.

b. Abdominal distension, anal pendant expansion, waist soreness, swollen perineum, and buttock and sacral inflation, reflecting compression or obstruction of rectum, ureter, and pelvic floor caused by tumor invasion.
c. Dyschezia (difficult defecation), deformed or narrow/thin stool, constipation, black (bloody) stools, diarrhea, and tenesmus.
d. Tumor compression and invasion-induced dysuria, weak urinary stream, frequent urination, post-micturition dribbling or inability to urinate, hematuria, urinary urgency, and urinary incontinence.
e. Lower limb syndrome: lower extremity edema, numbness or decreased sensation of hip and lower extremity, claudication, movement disorders, low body temperature, and muscle atrophy.
f. Other presentations: fever, weight loss, nausea, vomiting, perianal fistula, exudates, anemia, endless menstrual bleeding, vaginal bleeding, anorexia, and fatigue.
g. Palpable masses mostly in the abdomen or in the pelvis by digital rectal examination (DRE) and rarely in the buttock. Among these presentations, pain, dysuria, difficult defecation, and masses in abdomen, pelvis, or buttocks are initial symptoms.

2 Diagnosis

B ultrasound, CT, and MRI scans are primary imaging modalities for RPTs in the pelvis (Foshager et al. 1996). In our hospital the tumor detection rate of B ultrasound, CT, and MRI was 97%, 100%, and 91%, respectively. The imaging system with high accuracy in the localization of RPTs in the pelvis can achieve a diagnostic rate of 100% if combined with various techniques; moreover, qualification of presacral teratoma may be achieved in some cases (Hata et al. 1998). Imaging examination is also important in guiding the surgery as it can help determine the anatomic relationship of the tumor with surrounding organs, as well as secondary changes of those organs (Tingulstad et al. 1996). MRI exhibits unique advantage in the diagnosis of RPTs with involvement of nerves and skeletons. Angiography of RPTs in the pelvis before surgery may detect "hold ball" signs, as an indication for internal iliac artery embolization, which is vital to reduce blood loss intraoperatively.

3 Surgical Intervention and Approaches for Retroperitoneal Tumors in the Pelvis

For RPTs in the pelvis are always resistant to both radiotherapy and chemotherapy, surgery is the mainstay for therapy. Compared with the abdomen, the pelvis is located deeply in the body, with complex anatomical structures, thus making surgical removal of tumors more difficult in this area. Currently, lack of experience in the surgical management for pelvic RPTs is attributed to ineffective treatment compared to those in the abdomen or extremity soft tissue tumors.

It is often difficult for surgeons to determine the optimal approach for surgery, which is an important means combined with the patient's posture to improve the resection rate of RPTs in the pelvis. We believe that simple abdominal resection is suitable for the pelvic RPT whose inferior pole does not extrude into the perineum or subcutis through the pelvic diaphragm, without obvious invasion of the fourth and fifth sacral vertebrae and coccyx. Abdominal incisions include midline incision, paramedian incision, transverse incision, oblique incision, "⌟" shaped, and "⌟⌞" shaped, as well as large whole abdomen incision. If the tumor spreads through obturator into the thigh, the abdominal incision should be extended to the thigh. Simple incision via the buttock applies in (a) a tumor located in the presacral space below the level of inferior margin of the first sacral vertebrae, which is closely adhered to the lower portion of the sacrum and coccyx, with its superior

pole easily separated; (b) presacral teratoma with multiple sinuses in buttocks. Sacral incisions include transverse incision, vertical incision, "S" shaped, "⊥" shaped, "┬" shaped, "inverted ∨" shaped, "┼" shaped, and curved incision. For the tumor extending beyond the above range, combined abdominal sacral incision must be selected. The incision through buttocks or combined abdominal sacral approach is more common in reproductive embryonic tumors or fibrous tissue tumors, irrespective of benign or malignant nature. The plan for combined abdominal sacral resection is usually developed based on radiographic findings in most cases before surgery; occasionally temporary diversion of combined approach is performed according to actual requirements during surgery. An excellent command of combined approach skills is vital to increasing the removal rate and reducing unnecessary secondary injury. If the surgery is conducted via sacrococcygeal approach, the blood supply to skin flap should be protected carefully, and postoperative intensive drainage is required to prevent complications such as sacrococcygeal skin necrosis and perineal infection at pelvic floor.

4 Intraoperative Vascular Treatment and Bleeding Control in Patients with Retroperitoneal Tumors in the Pelvis

Proper care of blood vessels is a critical factor to reduce bleeding and improve the resection rate of RPTs in the pelvis. Small injuries to iliac vessels should be repaired as possible. Resection of a segment of common iliac, external iliac, or even femoral arteries can be performed when separation is impossible due to tumor invasion, followed by artificial vascular grafts. If tumor invasion-induced occlusion of common iliac and external iliac vein results in unilateral chronic venous obstruction, and collateral circulation has been established, artificial vascular grafts may not be performed after resection. If preoperative common iliac vein remains unobstructed and collateral circulation has not been established, the vein graft should be performed after the removal. The key for vascular grafts which may be autogenous saphenous vein or artificial vessels is to keep the diameter of grafts consistent with that of the body's blood vessels. The internal iliac artery is the mainstay for blood supply to RPTs in the pelvis, which usually bifurcates into obviously thickened branches and whose trunk has been invaded by large tumors. Primary care of the internal iliac vessels includes preoperative angiography and embolization of (a) internal iliac artery or tumor feeding artery; (b) internal iliac artery, which is firstly separated and then controlled with urinary catheter #8 intraoperatively. If heavy bleeding occurs, ligation may be performed. The simultaneous ligation of both internal iliac arteries will not result in secondary damage. Ligation of the internal iliac vein is also an option, but it should be noted that, firstly, ligation should be performed after separating the specific region most difficult to dissociate, to prevent high pressure of the distal vessels after ligation from exacerbating blood loss during the separation; secondly, the simultaneous ligation of internal iliac vein and ipsilateral iliac vein is not recommended in order to avoid lower extremity venous reflux disorder, as the lower extremity reflux flows into the internal iliac vein through communication branches after ligation or occlusion of external iliac vein. In our opinion, effective measures to stop bleeding during the resection of RPTs in the pelvis include:

a. For presacral bleeding, electrocoagulation and argon, suturing with triangular handheld sewing needle and pushpin into the sacrum, can be applied. Alternatively, the assistant puts his/her fingers into the rectum for backward oppression or places the gloves for injecting water to compress the presacral region.
b. If persist bleeding occurs during the separation processes, leading to difficulties in exposure of surgical field, the tumor may be resected in segments because the bleeding can be more easily stopped under good exposure.
c. The principle for dissociation of the entire tumor is starting from the most easily accessible region to the most difficult accessible region in order to reduce bleeding and to increase the rate of tumor resection.

d. If there is extensive bleeding wound after pelvic tumor resection, the bleeding may be stopped using intrauterine gauze compression for 3–5 days postoperatively until the patient's condition is generally improved and blood coagulation function recovers to normal.

5 Combined Organ Resection and Reconstruction in Patients with Pelvic Retroperitoneal Tumors

En bloc resection of RPTs in the pelvis combined with the involved organs should be conducted as possible, and part of pelvic wall muscles, nerves, and even the non-weight-bearing bones should be resected if necessary. Repair may be performed if the rectal wall is removed; however, temporary sigmoid colostomy is preferred. If the ureter is resected, ureter to bladder anastomosis and ureter end-to-end anastomosis may be performed, with a stent inserted in ureter. When the ruptured bladder is repaired, suprapubic cystostomy should be performed considering the potential major damage to pelvic plexus as a result of large volume of tumors and extensive separation area in the pelvis. If radical cystectomy is adopted, ureter may be anastomosed into sigmoid colon, or orthotopic bladder substitution ileostomy following cystectomy may be performed. Combined organ resection can improve the resection rate of RPTs in the pelvis. Notably, combined organ resection is suitable for not only high-grade malignant tumors but also low-grade malignant and benign tumors. Even benign tumors in the pelvis can grow very large, involving the surrounding organs. Surgeons should be fully familiar with the anatomy of the pelvis and techniques of combined organ resection, although combined organ resection may certainly increase the incidence of postoperative complications. The resection of sciatic nerve can cause foot drop; fortunately, clinically very few patients undergo complete resection, and most patients can walk with the aid of crutches postoperatively. Patients cannot contract quadriceps after complete resection of femoral nerve and must walk with the aid of crutches, some of whom may walk without the aid of crutches after 1–2 years of follow-up, and some will undergo flexor to extensor tendon transfer to improve dysfunction of knee extension.

6 Exenteration of Total Pelvis in Patients with Retroperitoneal Tumors in the Pelvis

Total pelvic exenteration (TPE) has been proved to be of significant importance to the treatment of advanced and recurrent colorectal cancer and achieved remarkable efficacy. However, the application of TPE in the surgical treatment of RPTs in the pelvis has not been reported previously. The author's team has performed sigmoid colostomy and internal iliac artery ligation rather than resection in two cases (one case of rhabdomyosarcoma and one case of Ewing's tumor), who presented with invasion of rectum and vagina and other organs in the early 1990s. In recent years, we treated three cases of pelvic RPTs with TPE and proved it as an effective approach for complete removal of the tumor. Attention should be paid to the following key points during TPE: (a) appropriate bypass of urinary and gastrointestinal tract, application of ureter-sigmoid anastomosis and sigmoid colostomy, as well as a good quality of life after surgery; (b) pelvic packing through sequential placement of gauze into small intestine, with no intestinal obstruction complications; and (c) perineal wound healing. After TPE, the residual pelvic cavity frequently develops infection, which can affect perineal wound healing. We have obtained the desired results using pedicled TRAM flap.

7 Multiple Surgeries for Removal of Pelvic Retroperitoneal Tumors and Resection of Multiple Recurrent Pelvic Retroperitoneal Tumors

Based on our experience, multiple times surgical procedure is indicated for patients with heavy blood loss, intolerable to continuous

surgery, or with complications such as intestinal obstruction. A high rate of recurrence occurs in patients with residual pelvic RPTs after surgical treatment. Residual tumor is common in malignant pelvic RPTs and less frequent in benign tumors. Intraoperative residual tumor is mainly attributed to the following reasons: (a) the conservation of involved pelvic organs resulting in residual tumor; (b) due to the difficulty in exposing large tumors in the pelvis intraoperatively, impossibility to separate the space between the tumor and the pelvic wall, the tumor that can be easily ruptured, or artificially partial excision or removal within the envelope; (c) a true envelope does not exist wrapping soft tissue sarcoma although it is intact. Tumors often secretly spread to distant sites along the fascia or interfiber space, so residual tumor remains in the separated surface of peritumoral tissue that looks like normal tissue. Residual tumor is the major factor contributing to the high recurrence rate of primary RPTs in the pelvis. In recent years, we have taken the following actions against residual tumor after surgery: (a) residual tumor is irradiated with a dose of 25 Gy intraoperatively, with a 6 cm collimator to separate the intestine; (b) residual lesion is marked with silver clip to guide postoperative radiotherapy; (c) brachytherapy is administered with ^{125}I radioactive particles placed into the residual lesion. Surgical resection remains the first choice for recurrent pelvic RPTs in which the complete resection rate is similar to that in naive cases. Although the complete resection rate during reoperation is low in recurrent high-grade malignant tumors, and the repeated recurrence may be accompanied by malignant transformation or an increase in malignant grade, the reoperation is of great significance to prolong the survival time of patients.

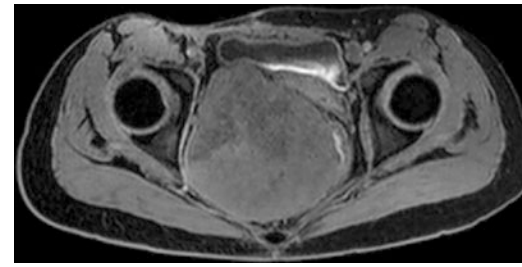

Fig. 12.1 Horizontal CT scan of a huge pelvic sarcoma

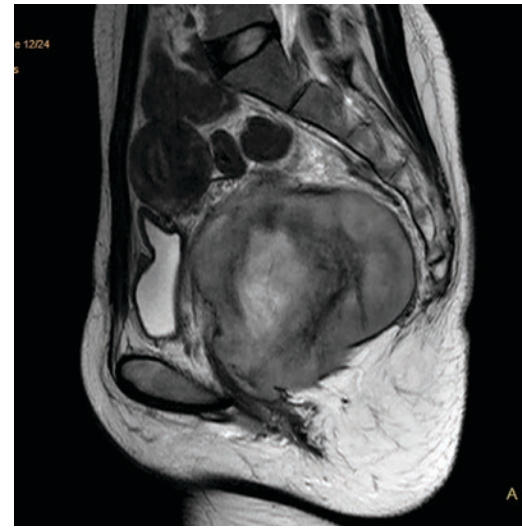

Fig. 12.2 Coronal CT scan of a pelvic tumor

8 Surgical Procedures

1. Before surgery, analyze imaging findings of RPTs in the pelvis. MRI displays pelvic RPT occupying the entire pelvis, immediately adjacent to the right pelvic wall, pushing rectum to the left whereas vaginal uterine to the left and forward (Fig. 12.1). Sagittal scan localizes the inferior pole of the tumor at the level of the apex of coccyx (Fig. 12.2). The tumor is resected based on its size and location via the sacral approach combined with transabdominal approach.
2. When the patient lies in prone jackknife position, transverse incision is made on sacrococcygeal joint level, followed by resection of sacral, buttock skin, and subcutaneous fat (Fig. 12.3).
3. The posterior fascia of coccyx and bilateral gluteus maximus encountered by the midline incision should be cut open (Fig. 12.4).
4. Further resection is performed on sacrococcygeal joint to gain access into the presacral fascia, followed by excision of the coccyx (Fig. 12.5).

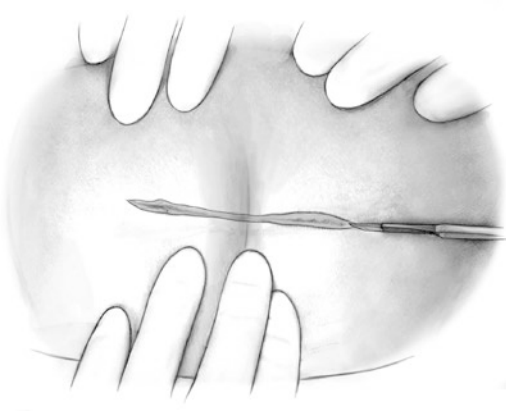

Fig. 12.3 Transverse incision at the level of the sacrococcygeal joint

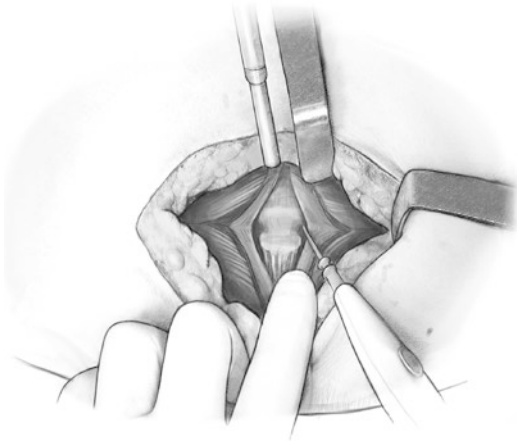

Fig. 12.4 Expose the sacrococcygeal joint

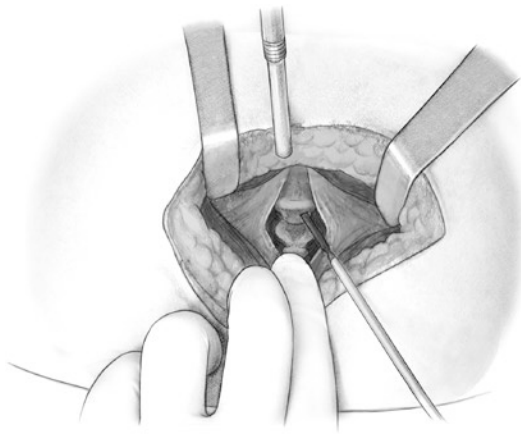

Fig. 12.5 Cut the sacrococcygeal joint

5. Dissociation of the fascia around the sacrum (Fig. 12.6) is performed by resecting the upper part of the sacrum, followed by removal of the lower part of the sacrum with rongeur forceps for the purpose of better operative field exposure (Fig. 12.7).
6. The rough edges should be rasped smooth with bone files after removal of the sacrum. Bone wax is applied to stop bleeding (Fig. 12.8).
7. Next, the presacral fascia is cut open to gain access into the presacral space (Fig. 12.9) where the lower pole of tumors may be encountered.

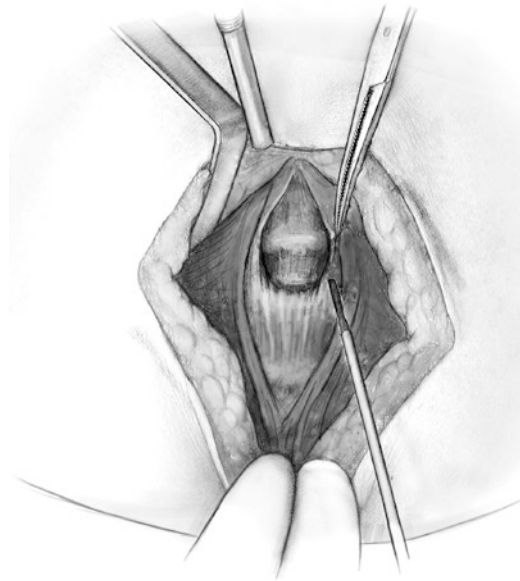

Fig. 12.6 Remove the coccyx and expose the inferior part of the sacrum

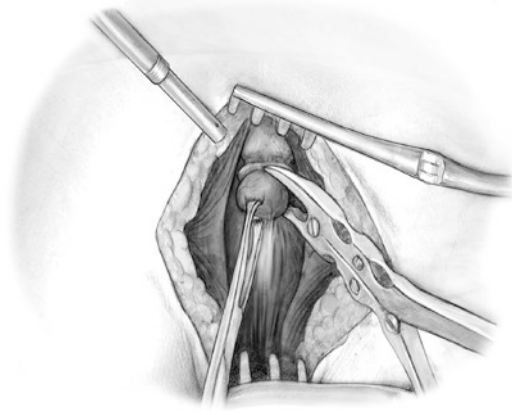

Fig. 12.7 Bite the inferior part of the sacrum

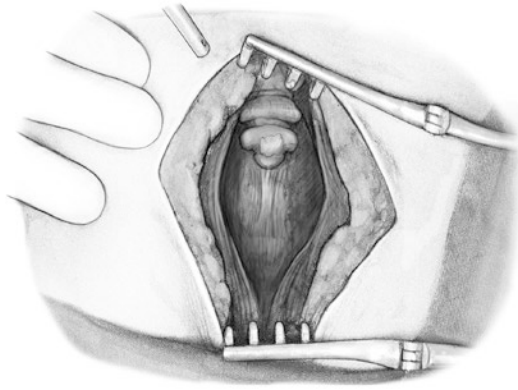

Fig. 12.8 Flat file the sacral wound and stop bleeding

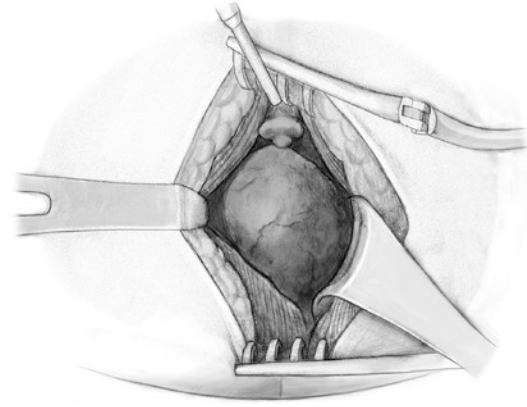

Fig. 12.10 Separate the anal side from both sides of the tumor

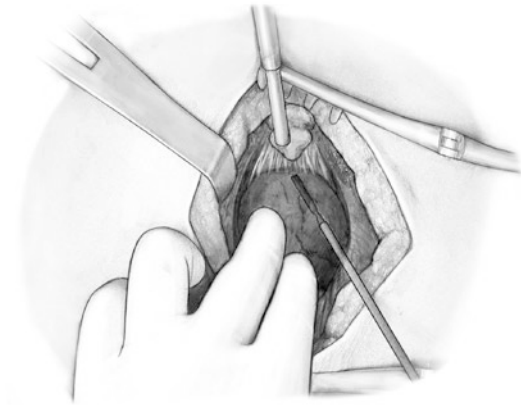

Fig. 12.9 Separate the tumor from the intra-sacral presacral space

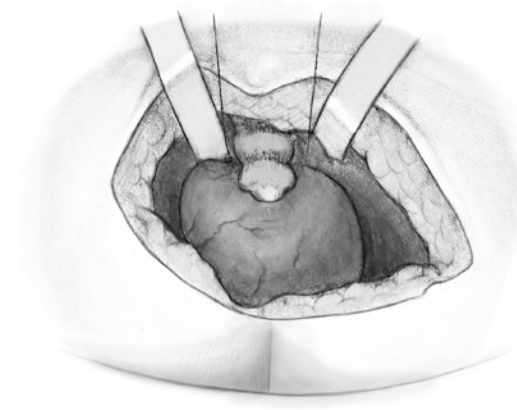

Fig. 12.11 Remove more sacrum with a coping saw as required

8. After the space around the tumor is identified, special care should be taken to dissociate the tumor (Fig. 12.10). Attention should be paid to the anal sphincter below the tumor and the rectum, which may be pushed on both sides of the tumor.
9. Dissociation in the presacral space should be as much as possible, and, if necessary, further resection of sacrum is performed. The resection of the fourth and fifth sacrum is safe without causing significant complications and achievable with fretsaw (Fig. 12.11).
10. The tumor that is adjacent to the sacrum in the rear, to pelvic wall on both sides, to rectum and vagina on the left, and to rectum anteriorly inferiorly, should be carefully separated from the sacral part until dissociation has to be discontinued (Fig. 12.12).

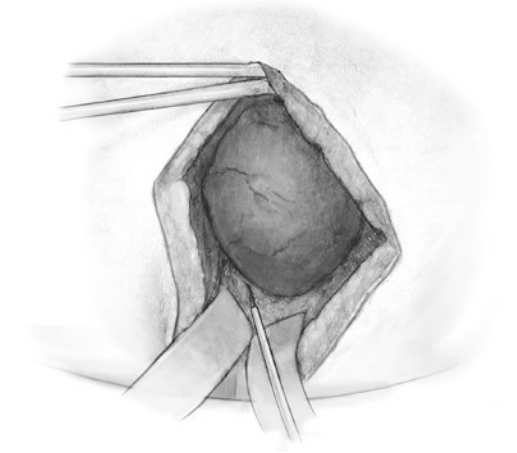

Fig. 12.12 Separate the surrounding boundary of the tumor until further access is impossible

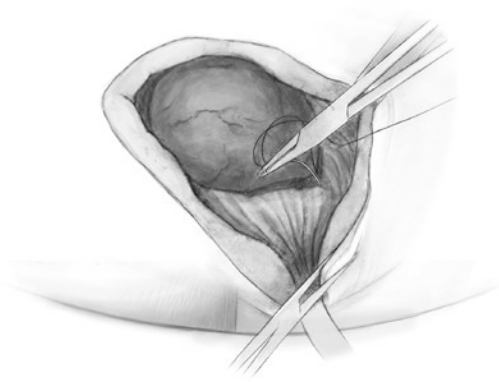

Fig. 12.13 Suture the incision in each layer at the sacrococcygeal region

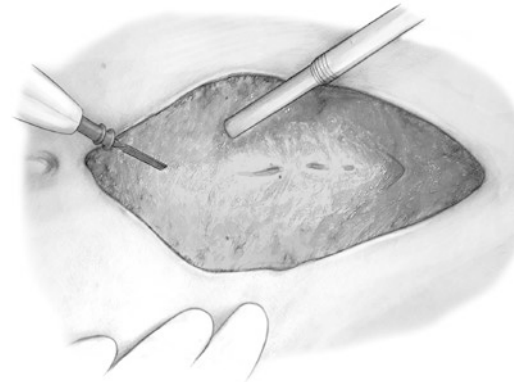

Fig. 12.15 Overturn the patient and make a longitudinal incision in the lower abdomen

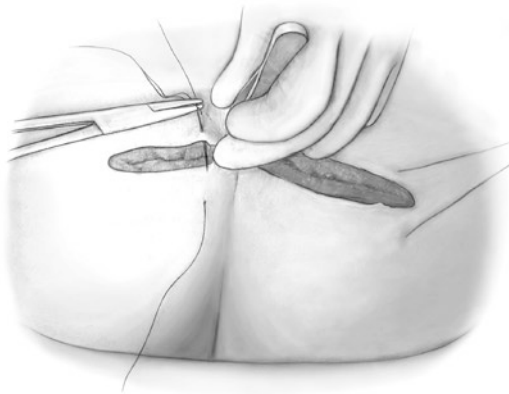

Fig. 12.14 Suture the shallow layer of the incision to avoid any dead space

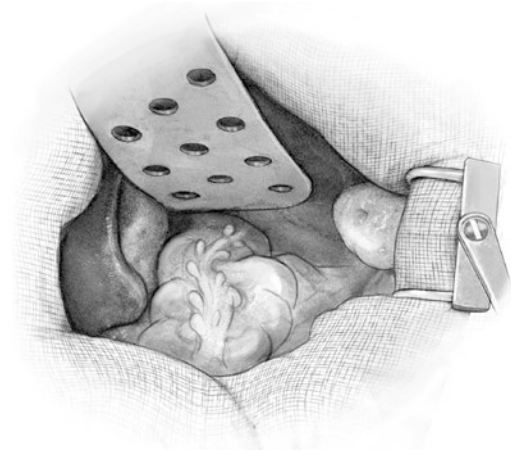

Fig. 12.16 Expose the intraperitoneal portion of the retroperitoneal tumor

11. At this point, the free surgical field of sacral wound should be compressed by gauzes and the layers of sacral incision sutured (Fig. 12.13). During the closure of subcutaneous fat and skin layers, no dead space should be left, while tissue fragments caused by burning with electric knife should be repeatedly washed (Fig. 12.14).
12. The patient is turned to supine position. A median incision is made in the lower abdomen to cut layers of the abdominal wall (Fig. 12.15).
13. The incision should be protected and then retracted by automatic retractor to expose the upper pole of the tumor that is located in the right rear of uterus (Fig. 12.16).
14. As the presacral space is tightly compressed by the tumor, the presacral venous plexus should be carefully protected during the separation (Fig. 12.17), which most easily merges into the sacral-free plane toward this direction.
15. The rectum pushed by the tumor to the left side should be carefully separated to avoid injury (Fig. 12.18).
16. Sharp separation of the uterus and vagina located anterior to the tumor should be performed. Keep in mind to avoid any damage to the abovementioned structures (Fig. 12.19).
17. Care should be taken to prevent any damage to the internal iliac artery and vein when dissociating the right-sided tumor. The ureter that is closely attached to the tumor should be repaired if it is damaged by chance in the separation process. If a segment of the ureter is removed, the end-to-end anastomosis should be performed, or, if unavailable, the end of the

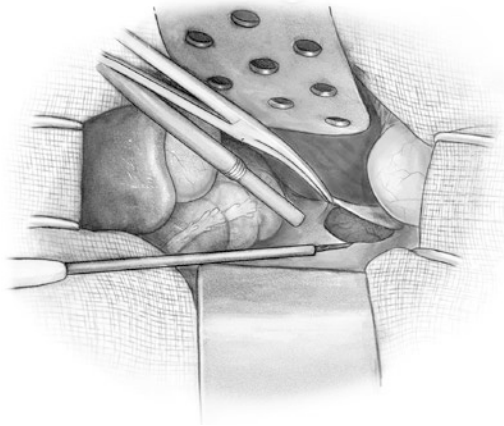

Fig. 12.17 Dissociate the presacral space superiorly

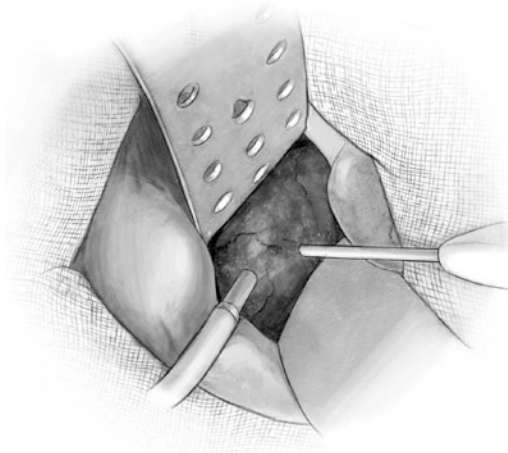

Fig. 12.18 Separate the tumor from rectal space

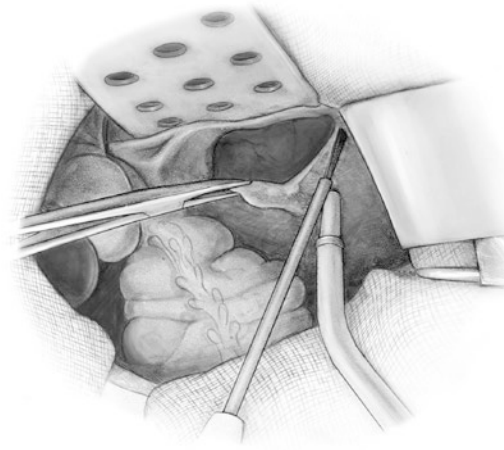

Fig. 12.19 Separate the uterus and vagina anterior to the tumor

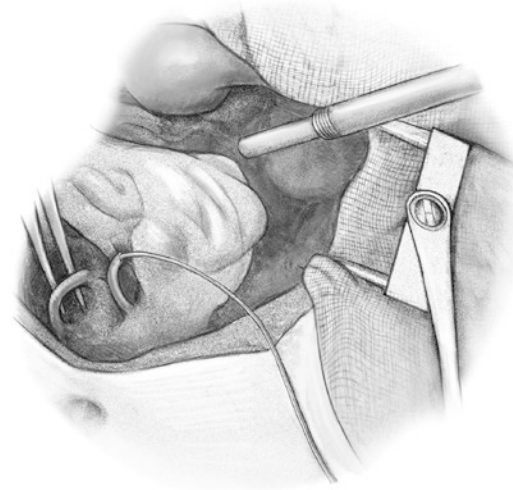

Fig. 12.20 If the ureter is removed partially, the residual end may anastomose with its contralateral counterpart

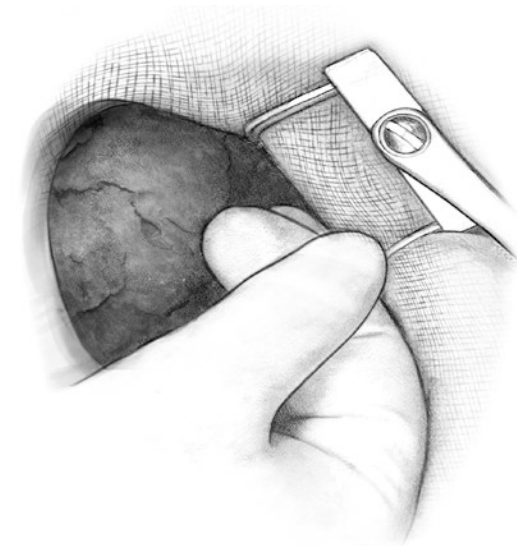

Fig. 12.21 After the separating surface of the abdominal approach is merged with the sacral approach, the tumor can be removed

ureter is anastomosed to the contralateral ureter in end-to-side fashion (Fig. 12.20). The operation should be carried out after the removal of the tumor, with placement of double "J" ureteral stents in the ureter.

18. After all-directional dissociation of the pelvic tumor, the lower abdominal incision merges into the dissociated plane of the sacral incision approach. The tumor may be pulled out when no adhesion between the tumor and surrounding structures is touched by hands (Fig. 12.21).

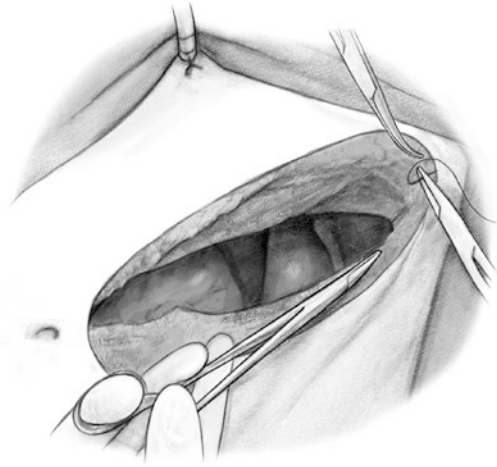

Fig. 12.22 Close and suture the abdominal incision

19. Flush the incision, accurately count the gauze, place drainage catheter in the pelvis, and then suture abdominal incision (Fig. 12.22).

9 Outcomes of Surgery on Retroperitoneal Tumors in the Pelvis

The radical resection rate of RPTs in the pelvis is 78.6%; similarly, the complete resection rate of recurrent tumors is 78%. During the surgery, bleeding loss varies from 50 to 15,000 ml with an average of 2384.5 ml, and transfusion volume varies from 0 to 9000 ml, with an average of 1897.3 ml. The operation time is ranged from 1 to 13 h with an average of 4.89 h. The incidence of postoperative complications is 7%, including deep vein thrombosis, intestinal obstruction, postoperative bleeding, avascular necrosis of skin in sacrococcygeal region, as well as pelvic and perianal abscess. The recurrence rate is 23.8% in overall pelvic RPTs whereas 50% in highly malignant tumors. The follow-up of patients with RPTs indicates that a good prognosis can be achieved with appropriate surgery. Despite longer operation time, larger intraoperative blood loss, and blood transfusion volume as compared with colorectal cancer radical surgery, the incidence of postoperative complications is low, so is perioperative mortality. For the above reasons, surgical treatment of RPTs in the pelvis should be actively pursued.

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13 Surgery for Retroperitoneal Tumors Involving Major Abdominal Vessels

Cheng-Hua Luo, Xueyan Lv, and Chengli Miao

Major retroperitoneal vessels include the abdominal aorta and its major branches, namely, the common external iliac artery, renal artery, celiac artery, and superior mesenteric artery, as well as the inferior vena cava and its main tributaries, namely, the common external iliac vein and renal vein. Retroperitoneal tumors (RPTs) often invade the major vessels by pushing, wrapping, or even growing into them. For RPTs invading major vessels, surgeons often give up complete resection as they worry about causing damage to vessels infiltrated or wrapped by tumors during the separation. Vascular injury may result in uncontrolled heavy bleeding and is regarded as a contraindication to RPT surgery. With advances in surgical techniques, combined resection of major involved vessels (with or without vascular grafts) in RPT surgery has become an increasingly common avenue to significantly improve the successful rate of tumor resection. Preoperatively comprehensive evaluation of RPTs involving major blood vessels and surrounding organs is essential to a successful operation. B-ultrasound, enhanced CT, and MRI can clearly display the location, size, shape of the tumor, and surrounding organ involvement, particularly the relationship between the tumor and major vessels (such as the abdominal aorta, inferior vena cava, renal artery, iliac artery, superior mesenteric artery, and portal veins); the displacement, compression, or wrapping of blood vessels by the tumor; as well as tumor thrombus within the blood vessels. Preoperative angiography combined with embolization can be used to determine the relationship between the tumor and blood vessels and significantly reduce blood loss intraoperatively by decreasing the blood supply to the tumor.

Indications for surgery of RPTs involving the major vessels include (a) patients who can tolerate major surgery based on general condition; (b) the tumor without distant metastasis and peritoneal implantation; (c) skilled surgeons; (d) available sufficient blood reserves; and (e) patients who are expected to survive for more than 1 year after tumor resection with high quality of life, according to pathological classification, degree of malignancy, and biological behavior characteristics.

Contraindications include (a) patients who cannot tolerate surgery due to concomitant severe cardiac and pulmonary diseases and coagulation disorders; (b) RPT that grows rapidly and occupies the whole abdomen within 6 months after previous surgery; (c) the tumors with extensively systemic metastasis; (d) limited techniques and equipment; and (e) concomitant invasion of abdominal aorta at the upper segment of the kidney or inferior vena cava at the upper segment, which must be resected.

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1 Preoperative Preparation

Preoperative preparation of retroperitoneal tumor surgery includes (a) routine preparation including intestinal preparation and prophylactic use of antibiotics; (b) reservation of sufficient red blood cells, anticoagulants, and plasma; (c) preparation of artificial blood vessels with the diameters matching to the patient's vessels; and (d) performing central venous catheterization and arterial catheterization monitoring preoperatively.

2 Surgery for Retroperitoneal Tumors Involving Major Abdominal Vessels and Branches

RPTs often involve the abdominal aorta, iliac artery, renal artery, and superior mesenteric artery and may completely enclose or seriously invade the vessels. The separation of the tumor from blood vessels will not only lead to long operation time and heavy bleeding but also tumor residues. Therefore, a correct choice is en bloc resection of the tumor together with the arteries followed by vascular grafts. Since the artery with thick wall is protected by arterial sheath, mild adhesion between RPTs and artery may be separated successfully by careful and patient surgeons with excellent dissecting techniques, while arterial sheath should be usually dissected. For RPTs extensively involving the blood vessels, combined transplantation of the abdominal aorta (and iliac artery) and inferior vena cava (and iliac vein) may be performed. Crawford and Debakey (1956) firstly reported two patients with malignant RPTs who received tumor resection and combined reconstruction of the abdominal aorta and inferior vena cava. Ito et al. have successfully performed combined resection of the abdominal aorta and inferior vena cava and Dacron graft for one patient with retroperitoneal rhabdomyosarcoma invading the bifurcation of the abdominal aorta. Over the past three decades, our team has performed combined transplantation in six patients. According to our experience, as the arterial wall is thick and easy to be separated, we firstly dissociate major blood vessels located at proximal and distal ends of the tumor, wrap #8 Foley catheter to control the bleeding, dissociate the tumor from the area without important structure or identify false capsule of the tumor, then perform the surgery within the capsule to avoid heavy bleeding, and finally separate the capsule from the surface of the blood vessels. Alternatively, sharp separation of the tumor starts from the part easy to separate and far away from major vessels to the part difficult to separate and adjacent to major vessels. The tumor with blood supply should be carefully separated and ligated. It is very difficult and important to identify whether tumor-feeding blood vessels are major retroperitoneal blood vessels, so the separation should be initiated from another direction and gradually moving toward major blood vessels. If it is necessary to resect major vessels, the tumor should be completely resected together with them after blocking their proximal and distal ends, and then the reconstruction of blood vessels is performed before repairing the integrity of reconstructed organs.

The abdominal aorta may be invaded below the level of the renal artery. If the abdominal aorta and bilateral iliac arteries are invaded, the resection of the abdominal aorta and common iliac artery, abdominal aorta anastomosis with artificial blood vessel, external iliac artery anastomosis, and bilateral internal iliac artery ligation should be performed. If the invasion is confined to the abdominal aorta, the abdominal aorta anastomosis and bilateral common iliac artery anastomosis may be performed.

When RPTs or metastatic lymph nodes involve the celiac trunk and/or common hepatic artery, resection of these vessels may be conducted without revascularization; because they are feeding the organs with rich collateral circulation, their removal won't affect the blood supply to the liver, stomach, and spleen. When the tumors or metastatic lymph nodes involve the proper hepatic artery, en bloc resection of the tumor and

metastatic lymph nodes together with proper hepatic artery may be performed without hepatic artery reconstruction; however, the gallbladder should be removed simultaneously, or otherwise ischemic gangrene of the gallbladder may occur. For either celiac artery resection or proper hepatic artery resection, once insufficient blood supply to the liver has been identified intraoperatively, the hepatic artery should be reconstructed.

For RPTs invading the superior mesenteric artery, the resection rate is extremely low. After the excision of the superior mesenteric artery, either direct anastomosis or prosthetic vascular graft or autologous vascular graft is generally considered to be a surgical contraindication, since the intestines can tolerate ischemia for a short period of time during the surgery, and the risk for postoperative thrombosis is high.

3 Surgery for Retroperitoneal Tumors Involving the Inferior Vena Cava

3.1 Surgical Treatment for Retroperitoneal Tumor Accompanied by Inferior Vena Cava Tumor Thrombus

Tumor thrombus is classified into invasive and noninvasive types, of which the invasive type accounts for approximately 12.9–28.5%. The length of the tumor thrombus has no effect on the prognosis. However, the invasion of inferior vena cava wall by tumor thrombus is associated with worse prognosis as an independent factor from lymph node and distant metastasis for overall survival of RPTs (Hardwigsen et al. 2001).

Noninvasive tumor thrombus can be removed after dissecting the inferior vena cava. By contrast, the invaded inferior vena cava or inferior vena cava wall must be removed in patients with invasive tumor thrombus. Usually, it is difficult to surgically remove the tumor thrombus which invades the inferior vena cava above the diaphragm level.

3.2 Resection and Reconstruction of Inferior Vena Cava and Renal Vein During Retroperitoneal Tumor Surgery

RPTs mostly involve the inferior vena cava by pushing, compressing, and wrapping but occasionally invade the inferior vena cava wall, or form tumor thrombus in the lumen, thus leading to chronic obstruction or stenosis. Under this circumstance, varying degrees of collateral circulation may have been established. We have previously reported four patients who underwent complete resection from the superior renal vein (below the hepatic vein) to the bifurcation of the iliac vein and resection of the right kidney. Out of them, three patients received the ligation of left renal vein and only one patient received left renal vein reconstruction (end-to-end anastomosis of the left renal vein with ovarian vein) simultaneously. All patients recovered well with normal renal function without lower limb edema and other complications, of which two patients with leiomyosarcoma in the inferior vena cava had developed complete occlusion of the inferior vena cava preoperatively. However, the ligation of the inferior vena cava below the hepatic plane and above the renal vein plane is often considered to be extremely dangerous, with the mortality rate as high as 90%. The left renal vein has seven venous collateral loops, whereas the right renal vein has only indefinite spermatic vein, ureteral vein, and renal capsular vein. Therefore, generally the venous blood disorder rarely occurs in the ligation of the left renal vein but not the right renal vein. Ligation of the inferior vena cava at the upper segment of the kidney can cause blood stasis of the right kidney which leads to renal dysfunction. If the ligation is necessary, the right nephrectomy must be performed simultaneously to reduce compensatory load of collateral circulation and to eliminate toxins produced by the right kidney with blood stagnation. If collateral circulation of the kidney is poor, one of the following methods may be employed to deal with the difficulty:

(a) direct or indirect anastomosis of the renal vein to portal vein or inferior vena cava and (b) autologous renal transplantation and anastomosis of the right renal vein with the iliac vein.

3.3 Simple Repair

Simple repair is indicated for small defect in inferior vena cava wall (typically less than one-fourth of the vascular circumference) or small cracks. Firstly, the proximal and distal ends of the inferior vena cava are blocked with forceps temporarily, and then the gap is continuously sutured and closed with 5–0 Prolene suture, without postoperative anticoagulation.

3.4 Simple Inferior Vena Cava Resection and Stump Ligation

Simple inferior vena cava resection and stump ligation apply to RPTs involving the inferior vena cava below the level of renal vein. If the inferior vena cava below the renal vein is ligated, the blood flow may return through the rich collateral circulation without reconstruction. Keep in mind that the resection of the inferior vena cava should start from the entrance of the renal vein superiorly to the bifurcation of the common iliac vein inferiorly. Simultaneously, the intersection between external iliac vein and internal iliac vein should be reserved in order to prevent pulmonary embolism caused by falling of thromboses formed in the blind-ended vessel. Alternatively, the inferior vena cava and common iliac vein may be resected, and the anastomosis of the internal iliac and external iliac vein is performed, thus allowing compensatory drainage of the lower limb blood through the internal iliac vein.

3.5 Partial Resection of the Inferior Vena Cava and Combined Right Nephrectomy

This operation is indicated for the involvement of both the inferior vena cava and right kidney or complete occlusion of inferior vena cava lumen below the level of hepatic vein. The evidence for combined right nephrectomy is supported by the presence of rich collateral circulation in left renal vein (such as left gonadal vein, left lumbar vein, left suprarenal vein, and the common trunk of left inferior phrenic vein), but not in right renal vein. In animal models, the obstruction of right renal blood flow leads to kidney congestion following ligation of hepatic vein and resection of inferior vena cava. Under this circumstance, large amounts of toxins are produced, resulting in animal death. In contrast, the removal of the right kidney not only eliminates blood stasis and toxins generated from the right kidney but also reduces the load of collateral circulation following the resection of the inferior vena cava. RPTs involving the inferior vena cava mostly lead to chronic obstruction or stenosis of the inferior vena cava, and angiography of the inferior vena cava indicates that various degrees of collateral circulation have been established. At this point, while the inferior vena cava and right kidney are removed, the ligation of the left renal vein close to the inferior vena cava and the conservation of the collateral circulation without vascular reconstruction are performed, because the left renal vein has abundant branches and constant anastomoses connected to the peripheral veins. Alternatively, left renal vein may be anastomosed with ovarian vein to strengthen left renal blood reflux and promote postoperative recovery. During the resection of the inferior vena cava and combined right nephrectomy and/or ligation of left renal vein, attention should be paid to the following points in order to prevent renal failure:

(a) Individual functional test of the left vs. the right kidney is performed preoperatively. The right kidney is removed during the surgery. Before the resection, the left renal vein should be temporarily blocked, and the urine is drained from the bladder. After the bladder is emptied and 20–40 ml of furosemide is intravenously injected, the patient is observed for about 30 min. If several tens to hundreds of milliliters of urine flows out of the bladder after the left renal vein is blocked, the left kidney will be proved to have normal urinary function via collateral venous reflux that has been previously established.

Conversely, the anastomosis of the left renal vein with the corresponding veins should be considered if no urine flows out.

(b) The inferior vena cava (above the renal vein) or the left renal vein is blocked. If no congestion or swelling occurs to the left kidney, the right kidney and involved inferior vena cava may be resected.

(c) The residual renal vein pressure is measured intraoperatively, and if greater than 56 cm H_2O, left renal vein reconstruction should be performed.

3.6 Partial Resection of the Inferior Vena Cava and Vascular Graft

The reconstruction of the inferior vena cava is required except that the collateral circulation has been established in case of thrombosis or complete occlusion of iliac vein and inferior vena cava below the level of renal vein. The reconstruction of the inferior vena cava or left renal vein must be performed under the following circumstances: (a) radical resection of tumor, with extensive resection scope in retroperitoneum and severe damage to collateral circulation; (b) preoperative patency of the inferior vena cava, regardless of the extent of collateral circulation; and (c) no urine or sudden dramatic reduction in urine output suggesting left kidney reflux disorder during the resection of the inferior vena cava and ligation of left renal vein. The surgical procedures meet the requirements of anatomy and physiology, with little effect on blood circulation, and are suitable for patients with combined inferior vena cava and bilateral renal venous reflux obstruction. An ideal graft material is autologous vein because of better graft patency without inducing foreign body reaction, but it is rarely used to replace inferior vena cava due to smaller caliber and easily collapsed under the increased abdominal pressure. At present, the commonly used graft materials are artificial blood vessels with stents, such as polytetrafluoroethylene (PTFE). However, PTFE has small elasticity coefficient and low compliance and exhibits poor histocompatibility as a foreign body, which may cause varying degrees of transplant rejection and infection. The patency of grafted vessel tends to decline over time, while long-term anticoagulant treatment may result in side effects. After the inferior vena vein is grafted, the anticoagulation and anti-aggregation treatment should be administered using the following regimen: intravenous injection of low-molecular dextran 500 ml/day for 7 days, subcutaneous injection of fraxiparine 0.4 ml/day for 5 days, and oral administration of warfarin 2.5–5 mg/day in the first 3–30 days, with dose adjustment based on weekly detection results of clotting time and prothrombin activity, as well as long-term oral administration of dipyridamole 25 mg (t.i.d.) and enteric-coated aspirin 50 mg (q.d.). To prevent the formation of thrombus in grafts following the reconstruction of the inferior vena cava, many scholars advocate the establishment of temporary arteriovenous fistula within the inguinal region in addition to appropriate anticoagulant drugs, in an attempt to increase the velocity of venous return, thereby reducing thrombosis of the graft.

3.7 Operative Steps for Combined Resection of Inferior Vena Cava, Right Nephrectomy, and Left Renal Vein Ligation

Indications for partial resection of RPTs involving inferior vena cava include (a) a tumor arising from the inferior vena cava; (b) tumor thrombus/thrombosis completely occluding the inferior vena cava; (c) a tumor tightly adhering to or wrapping inferior vena cava, thus making it extremely difficult to separate them; and (d) a tumor significantly invading inferior vena cava wall, leading to tumor residues if not removed.

Endotracheal intubation is performed under general anesthesia. During the surgery, the patient lies in supine position and is turned to the left or right when appropriate.

1. The midline incision is generally made in the upper quadrant of the abdomen, which may arise from the xiphoid superiorly to the pubic symphysis inferiorly. For patients who have previously received RPT resection, the

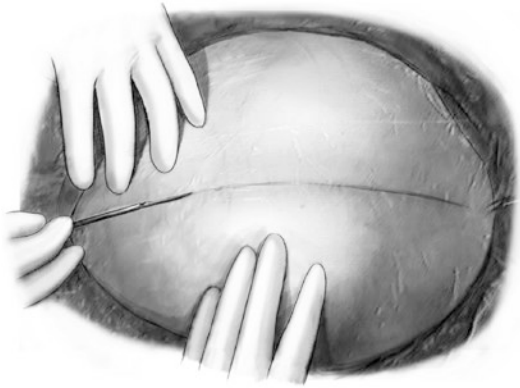

Fig. 13.1 According to the original incision into the abdominal cavity

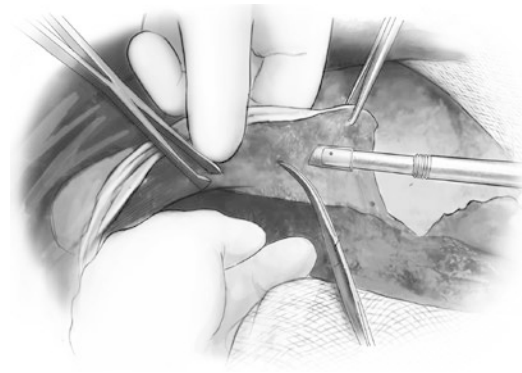

Fig. 13.3 Separate adhesion between the loop and the intestinal wall

Fig. 13.2 Add crosscutting

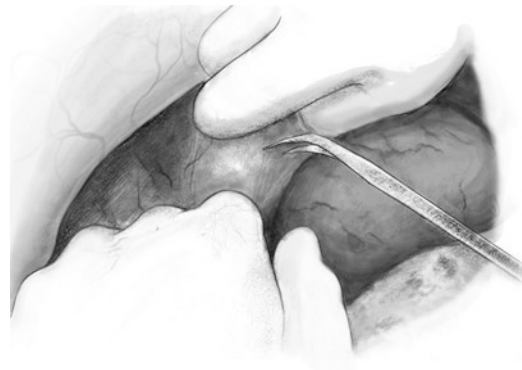

Fig. 13.4 Check if there is any injury of important intra-abdominal organs

original incision should be preferred (Fig. 13.1). If it cannot meet the needs for exposure during the surgery, the original incision may extend to both ends, or additional transverse incision may be made laterally on the basis of vertical incision (Fig. 13.2).

2. When cutting the abdomen, scars of the original incision may be encountered, which cause mutual integration of normal layers of abdominal wall, so the bleeding should be carefully controlled to identify intra-abdominal structures and avoid excessive resection of tissues. If necessary, the abdominal wall is firstly cut from the ends of the original incision without scars to gain access into the abdominal cavity, where the abdominal contents are often not adhered to the abdominal wall. Then the adhesions of the omentum, intestinal tract, or other tissues with abdominal wall below the incision should be carefully separated (Fig. 13.3).
3. The large RPTs often cause extensive adhesions, especially in cases with previous operation. Usually, the separation of adhesions is performed in the following order: anterior abdominal wall → bilateral abdominal wall → intestine → blood vessels. In the separation process, surgeons should check the presence of important structures such as major blood vessels, ureter, and nerves within the resected tissue (Fig. 13.4) by repeat palpation so as to avoid accidental injury. For tumors that have grown to large size or for a long time, the bleeding should be completely controlled in the separation process, as they extensively adhere to the inner surface of the abdominal wall, with plenty of collateral circulation.

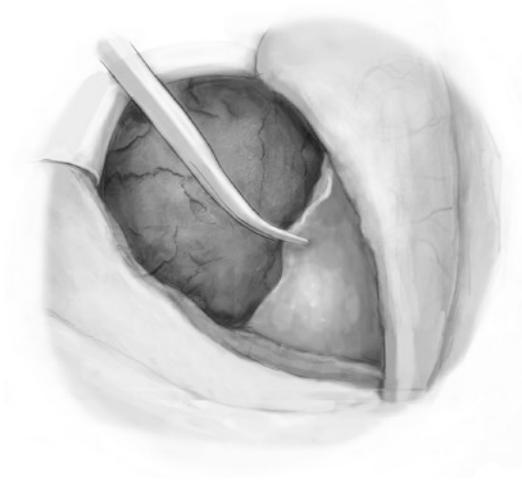

Fig. 13.5 The liver is under compression

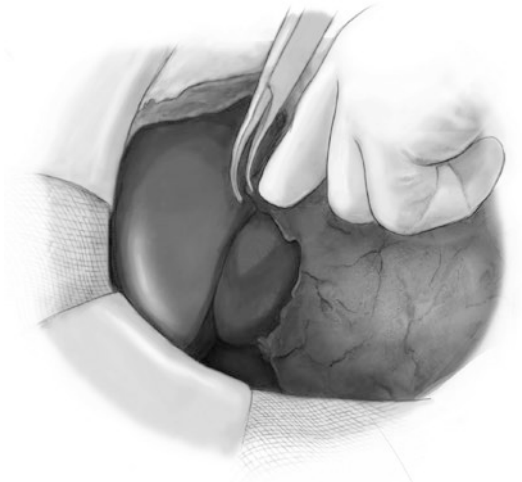

Fig. 13.6 Inferior vena cava

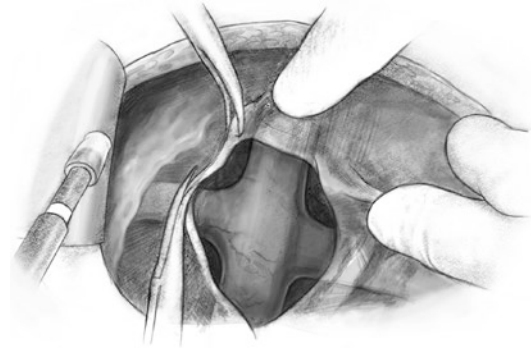

Fig. 13.7 Inferior vena cava and bilateral renal vein

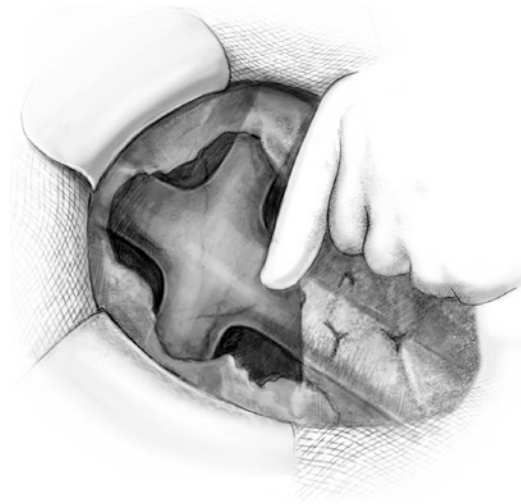

Fig. 13.8 Check the blood flow direction of the inferior vena cava

4. Large tumors themselves have extremely rich blood supply, with relatively engorged blood vessels on the surface, and can cause deformation of the abdominal organs by compressing them, e.g., making the liver deform into sheetlike pattern (Fig. 13.5).
5. When separating the adhesion between the tumor and liver, it should be noted that the liver surface at hepatic portal anteriorly and caudate lobes posteriorly can be encountered. As the inferior vena cava is located medially and posteriorly (Fig. 13.6), special attention should be paid to avoid accidental injury. The inferior vena cava and the intersection between external iliac vein and internal iliac posterior to caudate lobe should be carefully dissociated, which is "crisscross" shaped and pushed right upward by the tumor to become flattened and tightly attached to the tumor (Fig. 13.7).
6. In order to verify whether the flat structure is a blood vessel, the surgeon stretches a finger pulp to press the blood vessel and slide along the vascular direction. If the lumen is rapidly filled, the flat structure may be judged as a blood vessel. With this method, the surgeon may also check the direction of blood flow of inferior vena cava (Fig. 13.8).
7. For RPTs invading major blood vessels, dissociation of blood vessels is a major mission of the surgery. There are lots of techniques

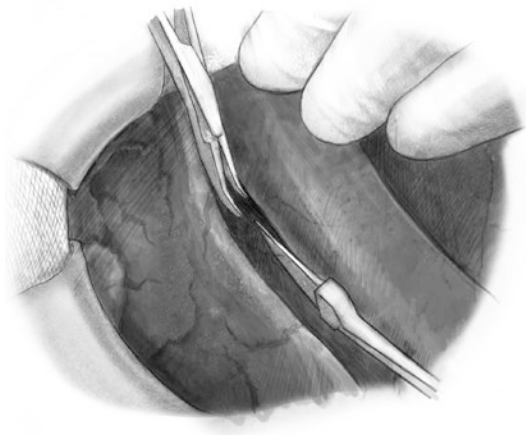

Fig. 13.9 Cut the inferior vena cava with sharpness

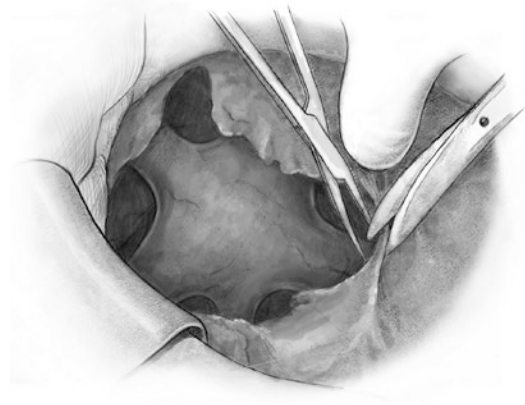

Fig. 13.11 Isolate the inferior vena cava

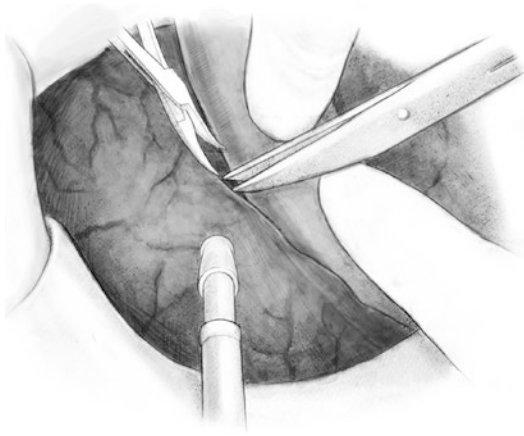

Fig. 13.10 Isolate the inferior vena cava sharply with scissors

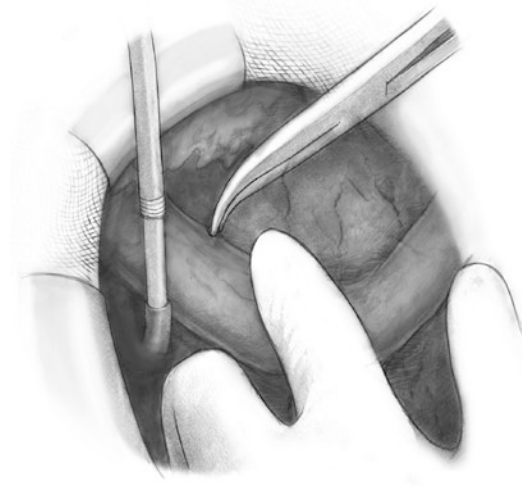

Fig. 13.12 Isolate the inferior vena cava above the tumor

suitable for separating the inferior vena cava from the tumor surface, including sharp dissection of external margin of the inferior vena cava using a blade (Fig. 13.9) or sharp separation with scissors (Fig. 13.10). The same method also applies to the separation of the medial margin of the blood vessels (Fig. 13.11).

8. When the dissociation of RPTs involving major blood vessels is completed or discontinued, the normal blood vessels with unaffected superior and inferior ends should be identified as soon as possible. Then, the inferior vena cava is wrapped by a blockage band preferably above the tumor before separation (Fig.13.12).
9. The inferior end of the involved inferior vena cava should be also dissociated with sharp dissection rather than blunt dissection, which easily causes damage to fragile vein wall (Fig. 13.13). Long-term invasion of the inferior vena cava or other major vessels by large RPTs makes it extremely difficult to identify the vessel boundaries during the surgery.
10. The dissociation should be performed posterior to the right inferior part of the tumor, equivalent to the right lower quadrant, close to the lower segment of the inferior vena cava. Then the inferior vena cava is ligated and resected, slightly above the bifurcation between the left and right common iliac

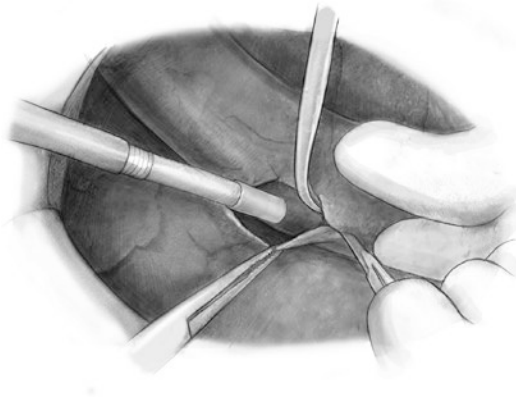

Fig. 13.13 Inferior vena cava is damaged

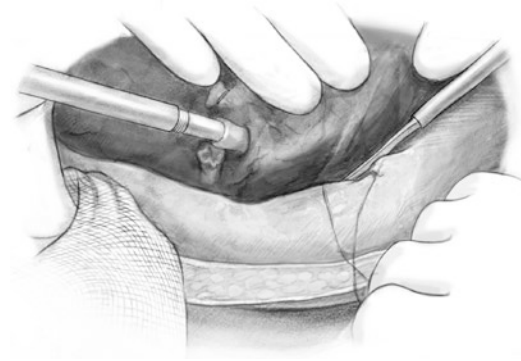

Fig. 13.15 Continue isolate inferior vena cava

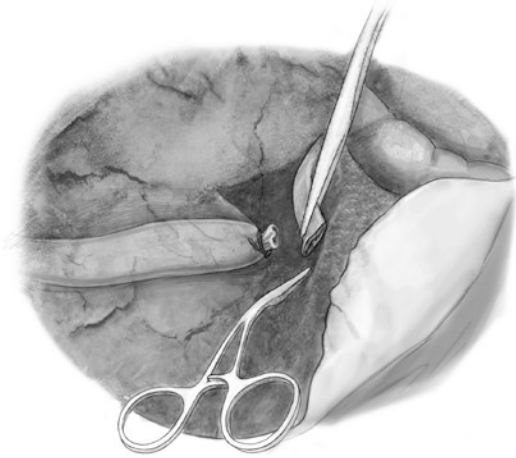

Fig. 13.14 Ligature inferior vena cava

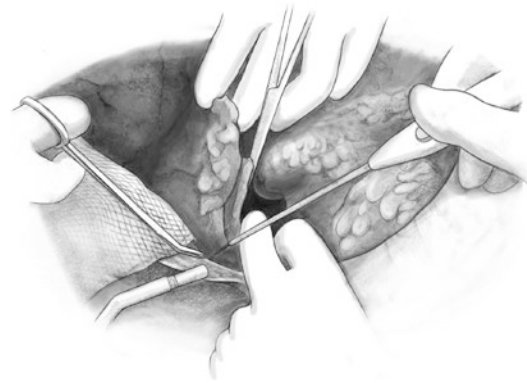

Fig. 13.16 Isolate the right renal adipose capsule

veins (Fig. 13.14). From this point, the inferior vena cava and iliac vein are gradually separating from the tumor relatively easily. The purpose of resecting the lower end of the inferior vena cava involved by the tumor as the first step is to reduce the volume of circulation at the proximal segment of the inferior vena cava, thereby facilitating the subsequent separation of the upper segment of the inferior vena cava.

11. After resection of its lower end, the inferior vena cava may be lifted up together with the tumor from the lower right side and continuously dissociated toward the cranial direction from the rear (Fig. 13.15). When the dissociation proceeds to the right superior to the tumor, the right kidney should be removed as scheduled. Specifically, inferior vena cava is tightly adhered to right renal vein branches and cannot be separated; moreover, right renal artery is also tightly adhered to and invaded by the tumor. For this reason, the dissociation direction shifts from the tumor to the external superior portion of the right kidney adipose capsule (Fig. 13.16), and then en bloc removal of the tumor and the right kidney is performed.
12. When the intersection between the renal vein and inferior vena cava is pushed by the tumor toward the right superior and closely attached to the tumor, the inferior vena cava should be cut off again and the broken ends should be sutured (Fig. 13.17). Then the residual ends of the left renal vein and inferior vena cava above the renal level become visible, together with the residual ends of the inferior vena cava connected to the right renal vein

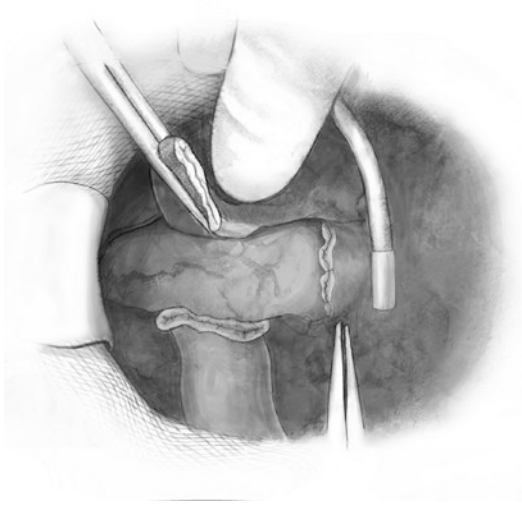

Fig. 13.17 Completely resect the inferior vena cava

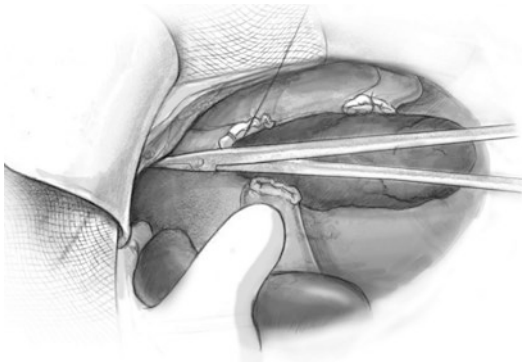

Fig. 13.18 Stitch and ligature the broken end of the inferior vena cava

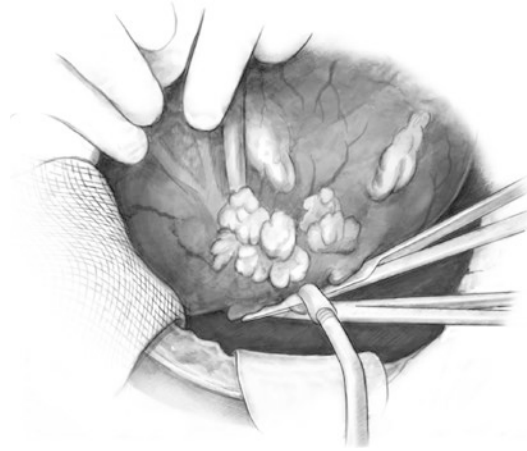

Fig. 13.19 Reveal right renal artery

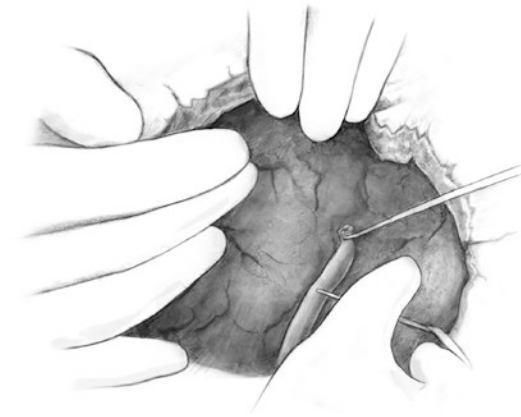

Fig. 13.20 The branch of the right renal artery

(Fig.13.18). After the left renal vein is cut, split renal function test is conducted using the method described in this chapter. If the results suggest normal function of the left kidney, the left renal vein and inferior vena cava above the renal level should be separated from the tumor.

13. After cutting the inferior vena cava, the tumor together with the right kidney may be lifted forward to expose the right renal artery at renal hilum and cut near the apex, and then the broken ends are sutured and ligated (Fig. 13.19).
14. Now, the separation shifts to the left inferior portion of the tumor. The tumor is lifted forward to carefully separate the small space between the tumor and abdominal aorta. The artery that bifurcates into small branches to provide blood supply for the tumor should be ligated (Fig. 13.20). As the exposure becomes more and more difficult when the separation continues to the posterior portion of the tumor, surgeons may place their fingers to feel the structure and perform separation and dissection with LigaSure while ensuring the safety of major blood vessels (Fig. 13.21).
15. After complete dissociation of the abdominal aorta, separate the left superior portion of the tumor. Now, the left renal vein has been dissociated, and the renal artery located pos-

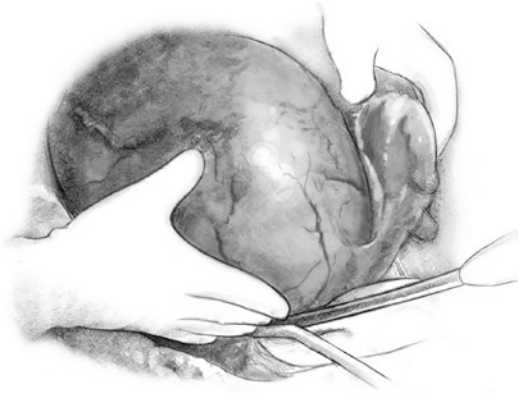

Fig. 13.21 Continue isolating the tumor

Fig. 13.23 Resect the tumor completely

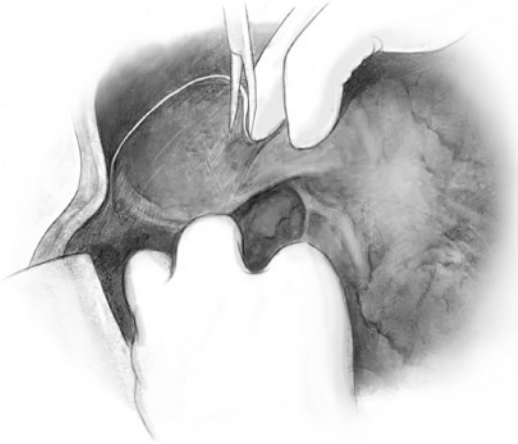

Fig. 13.22 Continue resecting the tumor

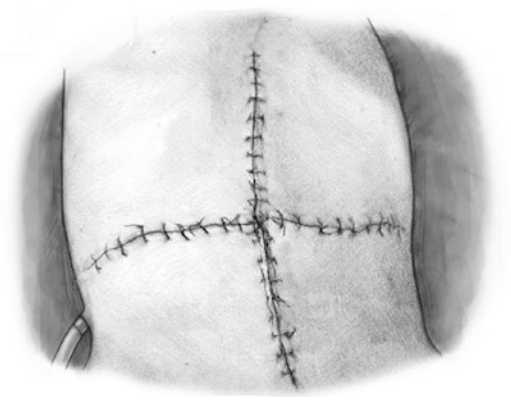

Fig. 13.24 Close the abdominal cavity

terior to the tumor should be separated from the abdominal aorta. The loose tissue within the left upper abdomen that adheres to the tumor is separated from the tumor with combined blunt and sharp dissection, and the blood vessels that are encountered in the separation process are ligated (Fig. 13.22). Finally, the tumor is completely removed after separating a little adhesion between the posterior portion of the tumor and abdominal aorta (Fig. 13.23).

16. After gaining access into the peritoneum, wound bleeding is controlled, the intestine is recovered to normal anatomic position, the device and gauze are counted accurately, the drainage catheter is placed, and the incision is sutured layer by layer (Fig. 13.24).

4 Resection and Reconstruction of Portal Vein and Superior Mesenteric Vein

Under normal circumstances, if the resected segment of the portal vein is less than 3 cm in length, end-to-end anastomosis is applicable, or if it is more than 3 cm in length, vascular grafts should be performed. In our hospital, four cases who received the resection of portal vein and three cases who received the resection of superior mesenteric vein have undergone end-to-end or end-to-side anastomosis, repair, and reconstruction. For one case of leiomyosarcoma, tumor removal failed after laparotomy in other hospitals, and the patient was referred to our hospital for a second operation. The tumor was wrapping and closely attached to the

portal vein. In the separation process, the portal vein was ruptured; the tumor was removed together with portal vein. Then end-to-side anastomosis of the proximally residual end of the portal vein with the main branches of the superior mesenteric vein is performed, followed by reconstruction of portal vein and superior mesenteric vein. The patient recovered well postoperatively with no recurrence during 1-year follow-up. It should be noted that during the resection and reconstruction of the portal vein and superior mesenteric vein, vascular occlusion period should be within 30–60 min. After vascular anastomosis, the mesenteric root should be dissociated to establish a tension-free anastomosis.

5 Postoperative Management

Patients with RPTs involving the major vessels should be closely monitored for at least 24–48 h postoperatively. Particular attention should be paid to maintain effective blood volume in order to guarantee myocardial perfusion.

Adequate oxygen is delivered and mechanical ventilation should be maintained if necessary. The blood gas should be monitored for at least 48 h. After the removal of mechanical ventilation, the patient should be urged to practice deep breathing, periodically turned over and percussed on the back, and, simultaneously, encouraged to cough and excrete sputum with the assistance of the clinician. Analgesics are administered to the patients who dare not cough due to pain.

Closely observe the occurrence of internal bleeding. Infuse low molecular dextran for 7–10 days to reduce thrombus formation. Patients in hypercoagulable state may be treated with heparin for 1–2 days. Monitor the occurrence of acidosis for timely correction. Continue administration of broad-spectrum antibiotics.

6 Postoperative Complication

Lower extremity edema is a common complication following the surgery of major retroperitoneal blood vessels, mostly of which is transient. It may occur in patients who undergo inferior vena cava ligation or vascular reconstruction. In addition to the obstruction of blood flow, extensive resection of retroperitoneal lymphatics is another factor responsible for lower extremity edema. The edema may be relieved by raising symptomatic limb, wearing elastic stockings, and administering drugs that can promote edema absorption.

Chylous fistula is relatively common in patients who undergo inferior vena cava resection, which is difficult to treat due to the following reasons: (a) the resection causes venous reflux obstruction and subsequently increased pressure inside the lymphatic vessels and (b) the damaged lymphatic vessels are not properly ligated. Caution should be taken to avoid this complication. Patients developing chylous fistula should be treated with intensive nutrition, enough water and protein, and adequate drainage. Chylous fistula may be gradually closed if it is small in size or be treated operatively if it remains open for more than 1 month (Zhan et al. 2013).

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Retroperitoneal Liposarcoma

14

Fabo Qiu, Changli Xu, and Chengli Miao

1 Introduction

Liposarcoma (LS) is a rare malignant tumor of mesenchymal origin, while retroperitoneal liposarcoma (RPLS) refers to liposarcoma arising from the abdomen and pelvic retroperitoneal adipose tissue. According to Windham and Pisters (2005), liposarcoma accounts for less than 1% of systemic malignant tumors. RPLS is the most common type (41%) of retroperitoneal soft tissue sarcoma, followed by leiomyosarcoma and malignant fibrous histiocytoma. Vijay and Ram (2015) reported that RPLS accounts for 12–40% of all systemic LS. Age of onset for RPLS is 55–75 years old. RPLS is slightly more common in men than in women, without significantly racial difference. A total of 10,782 cases of retroperitoneal tumor were reported between 1998 and 2007 in China, with a ratio of 1.3:1 for men to women, with an average age at onset of 41.8 years old, consisting of 68.3% retroperitoneal tumor and 11.6% liposarcoma (n = 1246). Among 119 cases of retroperitoneal liposarcoma, the ratio of male-to-female incidence was 1.9:1, and the median age at onset was 58 years old (range, 19–82). Retroperitoneal liposarcoma is extremely rare, with complex clinical manifestations and pathological types, thus making it very challenging to understand this disease and explore effective treatment.

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2 Etiology

The pathogenesis of retroperitoneal liposarcoma remains unclear, which is possibly associated with inheritance, genetic variation, and environmental factors.

2.1 Environmental Factors

1. Environmental carcinogens. Phenoxy acid herbicides, chlorophenols, and contaminant 2-, 3-, 7-, 8-TCDD may be related to retroperitoneal sarcomas.
2. Radiation exposure. It is commonly seen in patients undergoing radiotherapy. About 0.03–0.8% of patients who receive radiotherapy have been reported to develop retroperitoneal sarcoma.

2.2 Immunosuppressant

Both immune deficiency and immunosuppressive drugs are associated with the pathogenesis of retroperitoneal soft tissue sarcoma. It is

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reported that patients with systemic lupus erythematosus developed diffuse infiltrative retroperitoneal mucinous liposarcoma after treated with steroid hormone for 13 years, suggesting critical involvement of immunosuppressant in retroperitoneal liposarcoma.

2.3 Genetic Factors

Individuals with family history of lipoma or liposarcoma are more susceptible to developing retroperitoneal liposarcoma. Retroperitoneal liposarcoma has been reported to occur successively in two compatriots with family history of malignant fibrous histiocytoma.

2.4 Other Factors

The change in levels of insulin receptor and postreceptor in adipose tissue and decrease in biological activity of insulin may be involved in retroperitoneal liposarcoma.

3 Pathogenesis and Pathobiology

The pathogenesis of retroperitoneal liposarcoma remains unclear and may be related to the molecular mechanisms below:

3.1 Mechanism of MDM2-p53

MDM2 gene (human homologue of the murine double-minute type 2) located at 12q13-15 region shows constant amplification in well-differentiated liposarcoma (Vassilev et al. 2004). MDM2 is a p53-specific E3 ubiquitin ligase and principal cellular antagonist of p53, acting to limit the p53 growth-suppressive function in unstressed cells. In healthy body, the precise balance between p53 and MDM2 guarantees the normal proliferation and differentiation of tissue cells. If MDM2 is overamplified, p53 activity is inhibited, resulting in uncontrollable cell proliferation. This may be related to the pathogenesis of retroperitoneal liposarcoma.

3.2 Mechanism for Prune-nm23-H1

Prune, the human homologue of *Drosophila* prune gene, located in 1q21-23, encodes a protein that can bind to nm23-H1 (nucleoside diphosphate kinase) to downregulate its activity (Forus et al. 2001). The nm23-H1 may inhibit cell proliferation and tumor metastasis. The balance and precise coordination between prune and nm23-H1 expression present in healthy human bodies; in contrast, overexpression of prune gene is found in liposarcoma, with downregulation of nm23-H1 activity. This may be one of the molecular mechanisms responsible for the pathogenesis of liposarcoma.

4 Clinical Manifestation

As RPLS grows in an occult manner, most patients with RPLS in the early stage are asymptomatic. RPLS is often manifested as painless mass and has grown into a very large size before being detected. Symptoms and signs may not be obvious until the tumor has grown large and compressed adjacent organs or tissues.

4.1 Clinical Symptoms

Retroperitoneal tumors that grow in the loose connective tissue space of the retroperitoneum usually don't cause obvious symptoms when they are small. When they grow to a larger size, the tumors may result in symptoms by compressing and invading blood vessels, nerves, or other vital organs.

4.1.1 Space-Occupying Symptoms

As they are often large in size when detected, retroperitoneal liposarcomas may cause abdominal swelling, fullness, and feeling of heaviness by compressing and displacing adjacent organs.

Large retroperitoneal tumors contribute to an increased intra-abdominal pressure, which pushes outward through the weak site in the abdominal wall, resulting in abdominal or inguinal hernia.

4.1.2 Oppressive and Obstructive Symptoms

A large tumor may cause symptoms by compressing vital organs, nerves, and blood vessels in retroperitoneum. It often compresses the abdominal aorta, inferior vena cava, superior and inferior mesenteric veins, and other major blood vessels. The oppression of duodenum can cause proximal (high) or distal (low) small bowel obstruction (SBD).

1. Pain, which may be divided into abdominal pain and lower backache (lumbago). It is usually dull and occasionally sharp and colic. Approximately 40–70% of patients exhibit this symptom, resulting from the compression of surrounding tissues, organs, and nerves by the tumor. Lower backache with unilateral or bilateral radiation to the lower extremities may be caused by the oppression or violation of the lumbar plexus or sacral plexus nerve root.
2. Oppression of the gastrointestinal tract can lead to abdominal fullness after eating, anorexia, nausea, vomiting, abdominal distension, and constipation. Patients of 4–35% present with abdominal distension. Some patients develop intestinal obstruction, loss of appetite, and weight loss in advanced stage, indicating high suspicion of malignant retroperitoneal tumor. Additionally, oppression and displacement of the kidneys, ureters, or bladder can commonly occur and produce urinary tract symptoms, such as frequent urination, urgent urination, hematuria, dysuria, oliguria, and even anuria. Azotemia may occur as a result of bilateral ureteral compression.
3. Lower extremity edema and ascites. Tumor can cause obstruction of blood reflux by compressing the inferior vena cava or portal vein, thus leading to unilateral or bilateral lower extremity edema and ascites.
4. Incontinence and lower extremity paralysis. These symptoms can mainly be attributed to the compression of spinal cord as a result of invasion of intervertebral foramen.

4.1.3 Systemic Symptoms

Loss of appetite, weight loss, and fever are common. These symptoms mainly result from toxins produced by necrotic tissue, metabolites, and cachexia.

4.2 Signs

Most of these tumors can be incidentally palpable by patients. Generally, they won't consult a doctor until the mass has grown to a very large size and affected their daily lives or grown rapidly during a short period of time.

In physical examination, abdominal mass can be usually palpable with or without mild tenderness. Other signs include abdominal distension or tension, splenomegaly, lymphadenopathy, and cachexia. No specific signs have been identified. Retroperitoneal tumors generally do not move with respiration. Special attention should be paid to the mobility and hardness of the mass, which can serve as an indicator for resectability. Hard and fixed (to the abdominal wall or pelvic wall) mass is commonly suggestive of malignant tumor, teratoma, or hamartoma, whereas soft and flexible mass is commonly suggestive of lipoma or liposarcoma.

5 Diagnosis and Staging

5.1 B-Ultrasound

B-ultrasound is a noninvasive and inexpensive technique used to detect the size, number, location, cystic vs. solid nature of tumor(s), as well as relationship with adjacent organs and blood vessels. It has been widely applied in preoperative examination and postoperative follow-up. Due to its insensitivity to soft tissues, B-ultrasound can rarely identify LS. Liposarcoma presents as a large mass, in circular or irregular lobulated shape, with rough margin, and unevenly distributed moderate to strong echoes.

5.2 Examination

CT as the first choice for the diagnosis of RPLS allows precise localization and qualitative assessment. High-resolution and clear images produced by CT are able to objectively display the location and boundary of RPLS, its relationship with surrounding organs, as well as tumor-induced compression and displacement of surrounding organs and major blood vessels. CT plays a valuable role in determining the origin of retroperitoneal tumor, but an unideal role in demonstrating the extent of tumor invasion in adjacent organs. An extremely careful analysis of preoperative CT scan findings would help localize the tumor and predict the pathological nature of LS, which is vital to preoperative assessment of resectability and development of surgical strategy. CT findings vary with pathological types of retroperitoneal liposarcoma, thus providing reference to preoperative interpretation of pathogenesis.

5.2.1 Well-Differentiated Liposarcoma

CT usually depicts fat-density mass, accompanied by multiple floccules at slightly higher density and widely distributed cord-like separation, with a clear boundary between the tumor and surrounding tissue, without significant infiltration (Lahat et al. 2009). For lipoma-like liposarcoma, CT exhibits predominantly the density of adipose tissue, with thickened irregular soft tissue septa, which frequently are enhanced with soft tissue component after IV contrast administration. Sclerosing LS displays a mass of soft tissue density similar to muscle and is moderately enhanced after the injection of contrast media. Due to the lack of intratumoral fat content, sclerosing LS is easily misdiagnosed as other soft tissue sarcomas.

5.2.2 Myxoid Liposarcoma

Myxoid liposarcoma is rich in mucus matrix. Although it is a solid tumor, CT scan shows a cystic mass of uniform low-density (in-between normal fat density and muscle density), mildly progressive mesh-like or sheetlike delayed enhancement, non-enhanced cystic component, and small bifurcated vessels in cystic lesions (Singer et al. 2003).

5.2.3 Round Cell and Pleomorphic Liposarcoma

CT displays a substantially uniform solid soft tissue density inside the tumor, similar to skeletal muscle, with punctate calcification, little mature fatty component or only a small amount of mucus component inside the tumor, and frequent necrosis. Moderate to high enhancement is observed after the injection of contrast medium, with irregular necrotic tissue and non-enhanced necrotic foci. Round cell LS can only be distinguished from pleomorphic LS by histopathological findings rather than imaging.

5.2.4 Dedifferentiated Liposarcoma

Pathologically, dedifferentiated liposarcoma is characterized by the coexistence of well-differentiated and poorly differentiated liposarcoma. CT finding of well-differentiated area is similar to that of lipoma-like liposarcoma, while dedifferentiated sarcoma varies with tissue components, similar to that of primary sarcoma composed of such elements (Lahat et al. 2009). The presence of focal nodule of soft tissue density and water-like low-density area in lipoma-like tissue suggests dedifferentiated liposarcoma.

5.3 MRI Examination

With high resolution, MRI exhibits greater sensitivity than CT in distinguishing normal soft tissue from liposarcoma. Moreover, the lesion can be scanned from all directions, and the distribution and involvement of blood vessels of retroperitoneal tumor can be clearly presented by MRI without contrast medium. Overall, MRI is essential to the diagnosis of invasion of the abdominal aorta, inferior vena cava, or other structures. MRI plays critical roles in determining retroperitoneal liposarcoma subtype and clinical stage, depicting tumor's relationship with surrounding normal tissue, as well as assisting in preoperative diagnosis and development of surgical approach.

5.3.1 Well-Differentiated Liposarcoma

The fat content accounts for >75% of well-differentiated liposarcoma tissue, while the non-fat content is generally manifested as nodule or mass separated by low-intensity signals, with the septa ranging from small to large in size. Lipomatous liposarcoma shows higher intensity signal relative to fat in the abdominal cavity on T1WI. Fatty components in the tumor display low-intensity signals on fat-suppressed T1WI sequence, whereas iso- and low-intensity signals on fat-suppressed T2WI sequence. Sclerosing LS containing dense fibrous components exhibits interlaced low-intensity signals on both T1WI and T2WI (Barile et al. 2002).

5.3.2 Myxoid Liposarcoma

This type of liposarcoma that is rich in water-like components exhibits signal with an intensity similar to that of water on MRI images. As myxoid liposarcoma often contains different amount of adipose tissue, T1WI and T2WI show amorphous, cluster- or line-like high intensity signals, which are helpful for the diagnosis (Francis et al. 2005). Fibrous septa in mucus matrix show low-intensity signal on T2WI. MRI scan shows cystic lesions and progressive mesh-like enhancement of myxoid component after the injection of contrast medium, indicating the presence of solid lesion (Kim et al. 1996).

5.3.3 Round Cell Liposarcoma

Round cell liposarcoma (Song et al. 2007) exhibits slightly lower signal relative to muscle tissue on T1WI and slightly higher signal on T2WI, which is significantly enhanced after the injection of contrast medium. Due to less conspicuous myxoid matrix and capillaries compared to myxoid liposarcoma, the round cell liposarcoma displays lower-intensity signal on T2WI than myxoid liposarcoma. Intratumoral hemorrhage and necrosis most easily occur in round cell liposarcoma, with mixed signals on MRI.

5.3.4 Pleomorphic Liposarcoma

Pleomorphic liposarcoma is a rare and highly aggressive tumor. MRI exhibits aggressive margin of the lesion, whereas burr-like or halo-like change in the margin of the lesion after the injection of contrast medium. There are no characteristic signals on MRI due to the lack of fat component, so it is difficult to differentiate this tumor from other retroperitoneal soft tissue tumors (Song et al. 2007).

5.3.5 Dedifferentiated Liposarcoma

Dedifferentiated liposarcoma is characterized by coexistence of well-differentiated with poorly differentiated tumor components. It exhibits classic MRI findings, namely, a well-defined abrupt boundary between adipose and soft tissue components due to unknown reason (Tateishi et al. 2003). Lipoma-like well-differentiated liposarcoma displays signal intensity similar to other liposarcomas; in contrast, poorly differentiated tissue displays low signal relative to muscle on T1WI and heterogeneously high-intensity signal relative to muscle on T2WI (Kim et al. 2010).

5.4 Ultrasound-Guided Percutaneous Biopsy

If the diagnosis can't be made depending on image findings, ultrasound-guided percutaneous biopsy is recommended as an alternative strategy. However, percutaneous biopsy is contraindicated in patients who have undergone surgical removal as it may cause RPLS metastasis, so the final diagnosis still relies on pathology and histology after surgery. Percutaneous biopsy is indicated for patients who intend to receive preoperative radiotherapy/chemotherapy, who can't undergo tumor resection, or who have experienced hematogenous dissemination.

5.5 Renal Dynamic Imaging

If the CT scan suggests the presence of renal invasion, renal dynamic imaging should be performed to determine the bilateral renal function, in order to assess the potential resectability of the unilaterally involved kidney.

5.6 Intravenous Urography

Intravenous urography can clearly display the shape and function of the kidneys and ureters, so it plays a role in the diagnosis of large retroperitoneal mass, especially those which compress the ureter and kidneys.

5.7 Staging of Retroperitoneal Liposarcoma

5.7.1 Clinical Staging

Currently used staging system for soft tissue sarcomas is the TNM system developed by the American Joint Committee on Cancer (AJCC) (2010, 7th Edition). In this system, clinical staging is based on histology, size, depth, lymph node, and distant metastasis.

T Staging (Primary Tumor T)

Tx Primary tumor cannot be assessed
T0 No evidence of primary tumor
T1 Tumor ≤5 cm in maximum diameter
T1a Superficial tumor
T1b Deep tumor
T2 5 cm tumor, >5 cm in maximum diameter
T2a Superficial tumor
T2b Deep tumor

(Superficial tumor is located exclusively above the superficial fascia without invasion of the fascia; while deep tumor is located in any of the following: exclusively beneath the superficial fascia, superficial to the fascia, with invasion of or through the fascia, or both superficial yet beneath the fascia. Retroperitoneal, mediastinal, and pelvic sarcomas are all classified as deep tumors.)

N Staging (Regional Lymph Nodes N)

Regional lymph nodes that cannot be assessed
No regional lymph node metastasis
Regional lymph node metastasis
M staging (distal metastasis)
M0 No distal metastasis
M1 Distal metastasis
G Histologic grade (G)
GX Grade that cannot be assessed
G1 Grade 1 well differentiated
G2 Grade 2 moderately differentiated
G3 Grade 3 poorly differentiated

5.7.2 Pathological Classification and Grading

Since 2000, liposarcoma has been classified into four categories by WHO according to immunohistochemistry (IHC) and molecular and cytogenetic characteristics based on conventional histopathological findings: (a) nonclassic liposarcoma/high-grade differentiated liposarcoma, (b) well-differentiated liposarcoma/dedifferentiated liposarcoma (WDLPS/DDLPS), (c) myxoid/round cell liposarcoma (MLPS), and (d) pleomorphic liposarcoma (PLPS).

Pathological grading of LS is currently determined by the grading system of soft tissue malignant tumor, which has been recently modified by the French Federation of Cancer Centers Sarcoma Group (FNCLCC) with a new scoring classification method. Histologic grading is calculated as the total score for three parameters, including tumor differentiation, degree of necrosis, and mitotic count in the new classification system.

Differentiation: (a) score, sarcomas closely resembling normal adult mesenchymal tissue (e.g., well-differentiated LS); (b) score 2, sarcomas with confirmed histologic typing (e.g., myxoid liposarcoma); and (c) score 3, embryonal and undifferentiated sarcomas and sarcomas of uncertain types.

Mitotic Figures

a. 0–9/10 HPF score 1
b. 10–19/10 HPF score 2
c. ≥20/10 HPF score 3

Tumor Necrosis (Under Microscopy)

a. Score 0: No necrosis
b. Score 1: ≤50% tumor necrosis
c. Score 2: >50% tumor necrosis

Grading system: grade 1, total score of 2–3 points; grade 2, total score of 4–5 points; and grade 3, total score of 6–8 points. The classification is considered more objective and scientific.

The accuracy of histologic grading directly predicts the prognosis of patients with RPLS.

Histologic Grade
Grade 1: Total score 2–3
Grade 2: Total score 4–5
Grade 3: Total score 6, 7, and 8

6 Treatment

6.1 Surgical Treatment

The mainstay therapy for RPLS is complete surgical excision. Epidemiology studies on retroperitoneal tumor in mainland China have found complete resection rate of 66%, partial resection rate of 18.2%, exploratory biopsy rate of 7.9%, and combined organ resection rate of 7.8%. High postoperative recurrence rate is the most challenging problem. To completely remove the tumor and reduce recurrence rate, the resection margin should be as far away from the accessible and visible border of the tumor as possible, without residual capsule. If there is involvement of adjacent organs and blood vessels, en bloc resection should be performed, including removal of the partial gastrointestinal tract, kidney, liver, abdominal wall, and inferior vena cava. Common surgical approaches include total resection, palliative resection, and debulking/cytoreductive surgery.

6.1.1 Gross Total Resection

Gross total resection is defined as a complete resection without any visible tumor residue, namely, R1resection. Some scholars (Strauss et al. 2010) reported no significant difference in postoperative survival rate and recurrence rate during between R0 and R1 resection in follow-up studies on patients with retroperitoneal liposarcoma. R1 resection has therefore become a major goal worth pursuing. Attention should be paid to identify the false capsule during the resection, and the tumor should be removed completely beyond the false capsule to avoid tumor residue and rupture, which is vital to reduce postoperative tumor recurrence rate and prolong recurrence interval. After the removal of the tumor, the surrounding adipose tissue should be also dissected as possible to reduce the risk of recurrence. In principle, no adipose tissue residue should be left around the surgical area.

Retroperitoneal liposarcoma is often closely related to surrounding organs. If it is impossible to separate adhesions, combined organ resection may be necessary to achieve R1 resection. Combined organ resection rate is reported to be 57–83% (Neuhaus et al. 2005). The organs most common to be jointly resected during the surgical removal of retroperitoneal liposarcoma are the kidneys, followed sequentially by the spleen, intestine, stomach, and pancreas. During surgery, if the tumor is closely attached to surrounding major blood vessels and difficult to separate, firstly the majority of the tumor body should be resected to obtain better surgical field, followed by the residual tumor tissue. Forced separation may cause tear of the major vessels, which should be avoided as possible.

6.1.2 Palliative Resection

Palliative resection is defined as visible lesion residue of less than 1 cm in size when complete removal of gross tumor is impossible. If complete resection is not indicated for an individual patient, palliative resection should be performed as possible in order to decrease the symptoms, alleviate obstruction and compression of organs, protect organ function, prolong survival time, and improve quality of life. After the palliative resection, supplementary comprehensive actions should be taken to control residual tumor in an attempt to prolong survival time and ensure quality of life. Common techniques include internal radiation generated by radioactive nuclide, sustained release of chemotherapeutic drugs, and embedment of intraperitoneal chemotherapy pump.

6.1.3 Debulking/Cytoreductive Surgery

Debulking/cytoreductive surgery is defined as large residues in the main body of the lesion with visible residue of greater than 1 cm in size. It is commonly performed in patients who have

undergone multiple recurrence reoperations, as tumor resection is challenging due to abnormal anatomic structure, critical involvement of multiple organs, or distant metastasis. During debulking (cytoreductive) surgery, wound hemostasis is a major concern. It is relatively easy to stop bleeding in low-grade malignant tumors but not in high-grade liposarcoma with abundant blood vessels. In this setting, subtotal resection should be considered. The smaller the residual wound, the better the hemostatic effect.

6.2 Radiotherapy and Chemotherapy

The effect of radiotherapy and chemotherapy in patients with RPLS remains controversial due to the fact that RPLS is insensitive to both radio- and chemotherapy. Further large-scale controlled trials are guaranteed to prove the exact role of radiotherapy and chemotherapy in improving survival rate and reducing relapse rate.

Patients with retroperitoneal liposarcoma should receive radiotherapy after partial resection. Some patients with a large-volume tumor which is challenging to directly remove may undergo preoperative radiotherapy to shrink the tumor volume and reduce the difficulty in surgery. Well-differentiated mucinous liposarcoma growing slowly is relatively sensitive to radiotherapy, whereas poorly differentiated high-grade malignant liposarcoma growing rapidly is resistant to radiotherapy.

Only a few chemotherapy drugs are currently effective against RPLS, of which anthracyclines (doxorubicin, epirubicin) and ifosfamide are the most important first-line agents. A recent phase II randomized trial (Gortzak et al. 2001) compared the therapeutic effect of doxorubicin/ifosfamide neoadjuvant chemotherapy with surgery with surgery alone in patients with soft tissue sarcoma. The 5-year disease-free survival rate was 56 and 52%, respectively; the overall survival rate was 65 and 64%, respectively; therefore, no significant improvement was observed in the prognosis of patients. A chemotherapy drug, trabectedin, has been approved by the European Agency for Evaluation of Medicinal Products (EMEA) for the treatment of patients with advanced-stage myxoid/round cell liposarcoma who do not respond to anthracycline and ifosfamide.

7 Efficacy and Prognostic Factors

Surgery is the most effective therapeutic approach for RPLS. Surgical resection rate has been reported to be 71.4–88.8% in literatures (Neuhaus et al. 2005). RPLS is characterized by a high rate of local recurrence, and the recurrence interval is gradually shortened with the increased infrequency; however, distant metastasis rarely occurs. The high recurrence rate of RPLS may be attributed to the following factors (Hassan et al. 2004):

a. Large-volume tumor with complex surrounding anatomic structure, as well as invasion of the surrounding vital organs and blood vessels, making it very challenging to perform a complete resection
b. Multifocal tumors with tiny foci that are easily ignored by surgeons during surgery
c. Tumor implantation metastasis caused by surgical procedures
d. Positive pathological findings of tumor margin that is considered “completely resected” by surgeons with the naked eyes.

Although the complete surgical resection rate has been greatly improved in recent years, there is no significant reduction in the postoperative recurrence rate, which maintains at 41–71% (Porter et al. 2006).

The prognosis of RPLS closely correlates with histologic type and involvement of adjacent organs, namely, the lower the degree of differentiation, the worse the prognosis. For LS, the 5-year overall survival rate was 40–60%, and the 3-year survival rate was 73% and 43%, respectively, in those who received complete vs. incomplete surgical resection. The presence of residual tumor cells on the endoscopic resection margin (whether R0 or not) has no effect on

overall survival; however, whether or not all visible (with the naked eyes) tumors have been removed (whether R1 or not) has significant effect on overall survival of patients. In order to achieve R0 resection and reduce local recurrence rate, combined organ resection should be performed.

Myxoid and round cell liposarcoma most commonly occur in 40–50 years, with metastasis in more than one third of patients (Blair et al. 1998). These tumors often metastasize to the retroperitoneal cavity, trunk, limbs, bones, and other regions where fat is distributed (Antonescu et al. 2000), with a 3-year survival rate of 100% and 33%, respectively (Schwab et al. 2007). Pleomorphic LS is an invasive high-grade tumor, which occurs at the median age of 55–65 years old with equal female-to-male incidence (Gebhard et al. 2002). Metastasis to the lungs (90%), bone (8%), and liver (1%) can be observed in 30–50% of patients with pleomorphic liposarcoma. Most patients die quickly of metastatic disease, with an overall mortality rate of 40–50%, whereas a 5-year survival rate of 25–60% (Zagars et al. 1996). Although tumor invasion is also common in dedifferentiated liposarcoma, its overall course is longer than that of pleomorphic liposarcoma. Well-differentiated and myxoid liposarcomas are considered to have a favorable prognosis, with 3-year survival rate of about 90% (Hornick et al. 2004).

Postoperative patients should be actively followed up. For example, CT or B-ultrasound examination once every 6 months for 3 years is recommended for early detection of tumor recurrence.

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Retroperitoneal Leiomyosarcoma 15

Fuzhen Chen and Wengang Li

1 Introduction

Leiomyosarcoma is a soft tissue sarcoma arising from the uterus, gastrointestinal tract, and soft tissue smooth muscle cells, accounting for 5–10% of all soft tissue sarcomas (Gustafson et al. 1992). It is the third most common soft tissue sarcomas following liposarcoma and malignant fibrous histiocytoma. Nowadays, leiomyosarcoma is generally classified into three categories: (a) leiomyosarcoma in the retroperitoneum or peritoneal cavity, which is the most common type, of which 1/2 to 2/3 occurs in the retroperitoneum (Felix et al. 1981); (b) skin and subcutaneous leiomyosarcoma, with the best prognosis among all the three; and (c) prototype vascular smooth muscle sarcoma, which is the rarest type. Primary retroperitoneal leiomyosarcoma, accounting for 11% of all malignant retroperitoneal tumors, can occur at any age, is mostly seen in people aged 40–70 years, and is more prevalent in women than in men (ratio of 2:1). Most of the tumors grow invasively and are difficult to treat, with dismal prognosis and the lowest survival rate among all soft tissue sarcomas (Mankin et al, 2004).

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2 Etiology

The exact etiology of retroperitoneal leiomyosarcoma remains unknown, which requires further investigation. Several common factors may contribute to the development of leiomyosarcoma including loss of chromosomes 13q14 and q21, EB virus, radiation, and chorionic gonadotropin (β-HCG) (Shvarts et al, 2004).

3 Pathogenesis and Pathobiology

Retroperitoneal leiomyosarcoma may occur anywhere in retroperitoneum and outside of pelvic retroperitoneum, originating from retroperitoneal smooth muscle tissue, such as blood vessels, spermatic cord, embryonic mesonephric duct, and paramesonephric duct remnant, all of which are potential cellular origin of such tumors. Leiomyosarcoma was considered to be malignantly transformed from benign smooth muscle tumor. Nowadays, histologically most of these tumors directly arise from endothelia smooth muscle cells lining small blood vessels. As retroperitoneal leiomyosarcomas are mostly very large in size, clinically it is challenging to determine their actual cellular origin.

Retroperitoneal leiomyosarcoma usually presents gray color and fish-meat-like appearance, with focal hemorrhage, necrosis, or calcifications. The section is gray and wheel shaped, just like

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retroperitoneal leiomyoma. It is easily misdiagnosed as cystic schwannoma when cystic degeneration is obvious. Tumor body is often lobular and wrapped by false capsule composed of tumor cells in the outer layer. Pathological manifestations are as follows: (a) the majority of tumor body is typically composed of pure spindle single cells that are arranged in intersecting fascicles, with centered nucleus, in cigar shape, with little secondary changes (hemorrhage and cystic degeneration); (b) interstitial collagen may be found in some cases in which foamy cells and lymphoid tissue aggregate focally. Tumor cells are characterized by strong eosinophilic, fibrillary, or clear (watery) cytoplasm. Modifications in morphology and structural arrangement are occasionally seen. For example, most or part of the tumor body is composed of epithelial cells, being arranged in diffused sheets or trabecular pattern, or even fence-like pattern that is commonly seen in schwannoma (Paal and Miettinen 2001). Another major feature is the presence of longitudinal filaments within tumor cells. The better the differentiation, the more typical the longitudinal filaments; the poorer the differentiation, the more easily lost the characteristics, leading to disordered cell arrangement.

Morphological character is the most important basis for the diagnosis of leiomyosarcoma, which can be assisted by immunohistochemical staining and electron microscope examination. Well-differentiated smooth muscle cells exhibit Masson trichrome (+) (myofiber) and PAS (+) (glycogen in cytoplasm). Reticular fiber staining shows interfibrillar fine mesh structure. The cells are positive for vimentin and actin. Seventy percent of patients are desmin (+), mostly multifocal, but desmin is negative in high-grade tumors. The cells are generally positive for pan-muscle action (HHF-35). Thirty to forty percent of patients are positive for cytokeratin and S100. Under the electron microscope, parallel-arranged actin filaments, adhesion spots, and endocytic vesicle in cytoplasm are displayed, with dense plaques and complete/incomplete basement membrane around the cells. Leiomyosarcoma generally lacks specific cytogenetic manifestation.

Leiomyosarcoma mainly arises from the retroperitoneal vascular smooth muscle tissue. Retroperitoneal leiomyosarcoma exhibits three major growth patterns: (a) completely extravascular (extraluminal) (62%), (b) completely intravascular (intraluminal) (5%), and (c) both extra- and intraluminal (33%). Tumors located in wide retroperitoneal space can grow very large without significant resistance, thus causing displacement or even invasion of the surrounding organs. They can invade the ovary, kidney, pancreas, spine, and other structures besides the inferior vena cava. A majority of retroperitoneal leiomyosarcoma metastasizes through hematogenous dissemination, more frequently than gastrointestinal leiomyosarcoma. The most common sites of metastases are the liver and lungs, followed by the skin, soft tissue, bone, and brain. Autopsy findings suggest metastatic involvement of the lung (80%), bone (40%), liver (39%), peritoneum (19%), and brain (16%). These tumors can occasionally involve regional lymph nodes.

4 Clinical Manifestations

Retroperitoneal leiomyosarcoma grows very rapidly but only causes clinical symptoms in advanced stage. Due to the lack of specific manifestations, the tumor won't be identified until it has grown huge in advanced stage. Abdominal mass as the primary symptom in 70% of patients is mostly seen in patients who present with upper abdominal discomfort.

Retroperitoneal leiomyosarcoma in the upper abdomen may compress digestive organs, thereby causing symptoms such as abdominal bloating, abdominal pain, abdominal discomfort, anorexia, nausea, and vomiting. Of them, abdominal bloating is the most common symptom, which is aggravated after meals and even progresses to obstruction. Retroperitoneal leiomyosarcoma in the pelvis can cause difficulty urinating or rectal irritation if it compresses the posterior urethra and rectum or cause pain sensation if it compresses sacral nerve tissue. Clinical manifestations of leiomyosarcoma arising from the inferior vena cava depend on the tumor location within the vessel. For example, a tumor arising from the upper 1/3 segment of inferior vena cava or the upper segment of hepatic veins can cause Budd-Chiari syndrome, characterized by hepatomegaly,

liver failure, jaundice with massive ascites, nausea, vomiting, and lower extremity edema. A tumor originated from the middle segment of the inferior vena cava between hepatic and renal veins may cause right upper quadrant pain and tenderness, as well as renal vein thrombosis, which leads to renal dysfunction, increased BUN levels, or even nephrotic syndrome. Moreover, a tumor originated from the inferior vena cava below the renal vein may cause lower limb edema. Advanced tumor may metastasize to distant sites, resulting in systemic sera symptoms such as cachexia, anemia, and fever.

5 Examination and Staging

It is difficult to diagnose primary retroperitoneal leiomyosarcoma in early stage due to insidious onset, which is mainly detected by physical examination and imaging system. Currently, CT is the most important imaging method for evaluating tumor features and invasion of surrounding structures. Cross-sectional imaging can display tumor size and range, as well as invasion of surrounding organs and blood vessels after injection of contrast medium. Retroperitoneal leiomyosarcoma is usually very large in size, and CT detects a large and heterogeneous mass with irregular borders and a low-density center, suggesting hemorrhage, necrosis, or cystic degeneration, without calcification. The margin of a primary or metastatic tumor may be moderately enhanced. Smaller masses are typically homogeneous. MRI has the advantage in determining involved blood vessels because of multi-axis planar imaging capacity, intrinsic difference in strength of signals, flow-air interface, and flow-enhanced technology. MRI can help accurately localize the tumor and judge the involvement of surrounding structures, which is especially valuable for evaluating tumor boundary, vascular richness, and vascular invasion (Hartman et al. 1992). Leiomyosarcoma originated from major blood vessels may be located inside, outside, or both inside and outside of the lumen, which usually exhibits signals similar to the muscle on T1-weighted images, whereas moderate to high intensity signals on T2-weighted images (De Beuckeleer and Vanhoenacker 1997). Angiography not only demonstrates leiomyosarcoma with rich blood supply but also serves as a useful tool for evaluating major vascular involvement. The diagnostic value of PET-CT remains unclear; however, it may be an alternative choice for clarifying recurrence and metastasis. As a commonly used method, ultrasound can disclose the tumor's location, size, and relationship with major blood vessels, with a certain resolution for predicting the nature of the tumor. Leiomyosarcoma presents with heterogeneous echoes; however, ultrasound is insensitive in detecting lesions located in the intestine, retroperitoneum, or mesentery. Assistance in the diagnosis of liver metastasis detected by CT can be provided by ultrasound, which guides needle biopsy for pathological diagnosis as well.

Clinical staging and determination of the nature of retroperitoneal leiomyosarcoma depend on pathological interpretation. However, it is difficult to set up standard criteria for judging benign vs. malignant nature of leiomyosarcoma. In fact, leiomyosarcoma is a series of lesions varying biologically. Leiomyosarcoma may result from malignant transformation of leiomyoma. Therefore, it is almost impossible to artificially distinguish a malignant tumor from a benign one. Histological grading can be achievable based on indicators such as tumor size, cell atypia, necrosis, and mitotic activity, of which mitotic activity is the most reliable one. A tumor with more than five mitotic/10 HP should be considered malignant, whereas with one to four mitotic/10 HP considered potentially malignant, especially when the tumor is large in size with necrosis and obviously atypical nuclei. Even with this strict criterion, this large tumor cannot be absolutely predicted to be benign.

6 Treatment

6.1 Surgical Resection

Surgical resection is currently the primary means of treating retroperitoneal leiomyosarcoma. Whether the tumor can be completely resected or not will profoundly affect tumor recurrence and patient's prognosis. Prior to the development of operative strategy, if lymphoma, PNET, or other chemotherapy-sensitive tumors cannot be ruled

out, tumor's pathological nature should be confirmed by biopsy with hollow needle under the guidance of ultrasound or CT preoperatively. For a patient who has undergone biopsy, the entire puncture pathway should be removed to avoid tumor metastasis. If complete resection of leiomyosarcoma is considered challenging preoperatively, the patient can receive neoadjuvant chemotherapy based on pathological findings and won't undergo surgery until the tumor has shrunk, in order to improve operational effectiveness.

Leiomyosarcoma located in the retroperitoneum is mostly >10 cm (maximum diameter) in size. The large tumor size and important organs/structure adjacent to the tumor make surgery extremely challenging. To achieve wide resection, combined resection of the small intestine, colon, kidney, suprarenal gland, or pancreas adjacent to the tumor is often required. Another dilemma is that retroperitoneal leiomyosarcoma directly invades major blood vessels and involves partial resection and reconstruction of the inferior vena cava and renal vein. In fact, leiomyosarcoma is usually encapsulated, growing expansively rather than directly invading the surrounding structures. During surgery, the tumor body is more easily separated from the surrounding tissue; however, it is always adherent to major blood vessels. Particular attention should be paid to the separation so as not to tear blood vessels. Some clinicians therefore emphasize that the separation of blood vessels should start from the distal end of the tumor in order to avoid sudden bleeding and to ensure complete removal of the tumor. If the tumor has invaded blood vessels, removal of the specific part of major blood vessels would be safer, and if necessary, revascularization will be performed after the removal of the tumor.

Even after complete resection of the primary tumor, 50% of patients may experience a relapse. Consequently, patients should be closely followed up by CT or ultrasound to detect potential relapse as early as possible. Re-excision is an option for patients with local recurrence. Similar to the first operation, reoperation is indicated for patients without identifiable distant metastasis. Some patients with local relapse may still obtain a long-term disease-free survival after tumor resection.

Retroperitoneal leiomyosarcoma often metastasizes to the liver. As metastatic leiomyosarcoma is resistant to chemotherapy or interventional treatment, the patient's prognosis is dismal, with shortened survival time. For patients with liver metastases, the median survival time does not exceed 14 months. Due to limited treatment options for liver metastases from leiomyosarcoma, the value for resection of metastatic lesion needs to be further explored. Lung metastases from leiomyosarcoma are often multifocal, which should be surgically removed if they are isolated lesions.

6.2 Radiotherapy

Radiotherapy plays a very limited role in the treatment of leiomyosarcoma but exerts palliative effect in some patients. Adjuvant radiotherapy may be considered after lumpectomy.

6.3 Chemotherapy

Leiomyosarcoma is relatively resistant to chemotherapy, and the role of postoperative adjuvant chemotherapy remains unclear. Currently, there is no standard treatment for patients with advanced-stage tumors who have no response to other therapies. Although it cannot cure these patients, chemotherapy may slow down tumor progression. Doxorubicin, epirubicin, liposomal doxorubicin, ifosfamide, or dacarbazine alone, as well as anthracycline-based combinatory regimen, are common palliative protocols for metastatic soft tissue sarcoma. In Phase II clinical trial of gemcitabine plus docetaxel (GT), the progression-free survival (PFS) and overall survival (OS) were 6.2 months and 17.9 months, respectively. GT yields a higher response rate and survival rate for both uterine leiomyosarcoma and non-uterine leiomyosarcoma. Recently, monoclonal antibodies targeting the mTOR signaling pathway, vascular endothelial growth factor (VEGF) receptor, and insulin-like growth factor receptor have shown a certain effect on patients with refractory leiomyosarcoma.

Molecular mechanisms of retroperitoneal soft tissue sarcoma and development of new drugs are attracting more and more attention.

7 Efficacy and Prognostic Factors

The prognosis of retroperitoneal leiomyosarcoma is poor, with postoperative 5-year survival rate of 28–40%. The main factors attributed to worse prognosis of retroperitoneal sarcoma are poor tumor differentiation, postoperative local recurrence, and incomplete removal of the primary and secondary tumor. The recurrence rate of retroperitoneal liposarcoma or leiomyosarcoma is >50%; and 5-year survival rate is only 30% for relapsed cases. The prognosis is dismal in patients who have experienced recurrence and distant metastases of leiomyosarcoma and even worse if the tumor grade index is high or vascular invasion occurs.

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Leiomyosarcoma of the Inferior Vena Cava

16

Xiang Feng, Xueyan Lv, Boyuan Zou, and Chengli Miao

The vascular system has the lowest incidence of malignant tumors in the human body. Leiomyosarcoma (LMS) is the most common malignancy arising from the vascular system. It is a rare soft tissue tumor arising from smooth muscle cells in the middle layer of the vessel wall, which grows slowly and rarely invades adjacent organs. It comprises approximately 2% of all human leiomyosarcomas and 0.5% of all soft tissue tumors. The inferior vena cava (IVC) is the area of the entire vascular system where tumor is most likely to occur. More than half of all vascular leiomyosarcomas arises from the IVC, while some extremely rare tumors originate in the superior vena cava, femoral vein, and popliteal vein.

The first case of leiomyosarcoma of the inferior vena cava was reported by Peral et al. in 1871, but thereafter only several single cases or single-center studies with small case series have been documented in the literatures up to now. The available large cohort of case report is sourced from a meta-analysis of the published literatures, *International Registry of Inferior Vena Cava Leiomyosarcoma: Analysis of a World Series on 218 Patients* published by Mingoli et al. in 1996 (Mingoli et al. 1996), where 212 cases were source-published literature. In 2005, Hilliard et al. (2005) from the University of Alabama at Birmingham performed a meta-analysis of 208 cases of leiomyosarcoma of the inferior vena cava documented in the literature since 1996, of which only 3 cases were treated in their hospital. At present, the above two meta-analyses involve the largest number of leiomyosarcoma cases of the inferior vena cava. Totally, 12 patients with leiomyosarcoma of the inferior vena cava have been treated in Changhai Hospital from 2000 to 2012. Experience described here is based on the author's clinical practice in Changhai Hospital and the abovementioned published articles.

1 Etiology and Pathology

1.1 Etiology

The etiology of this type of tumor remains unclear, which may be related to abnormalities in endocrine system. It prevails in women, with male to female ratio of 1:3 (Mingoli et al. 1996), and total number of cases male to female ratio of 1:6 (Cacoub et al. 1991; Wicky et al. 1991). The reported incidence of leiomyoma of the uterus is up to 26% in patients with primary leiomyosarcoma of the inferior vena cava, accompanied with multiple endocrine neoplasia in some cases.

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Hines et al. (1999a, b) found that most of the patients exhibit positive estrogen receptor and progesterone receptor.

1.2 Age of Onset

Leiomyosarcoma of the inferior vena cava can occur at any age but is most common in women aged 50–60. Of 113 cases reported by Cacoub et al. (1991), the age of onset was l5–83 years, with the mean age of 56 years. Kaszar Seibert et al. (1988) reported that leiomyosarcoma prevails in people aged 26–70 years, with the median age of 45 years. The University of Alabama reported that the age of onset was 24–83 years and 66% of patients were older than 50 years, with the median age of 52 years.

1.3 Site of Occurrence

Leiomyosarcoma may occur in any portion of the inferior vena cava. To describe the accurate site where leiomyosarcoma arises from, the IVC is usually divided into three anatomic segments based on the junction between hepatic vein and renal vein: level 1 is from the right atrium to the origin of hepatic vein; level 2 is from the origin of the hepatic vein to the origin of renal vein; and level 3 is the distal end of the origin of the renal vein. In the meta-analysis of 211 cases reported by the University of Alabama (Hilliard et al. 2005), 3% were located in level 1, 33% in level 2, and 8% in level 3. Thirty-seven patients (17%) presented with tumors involving more than one level of the inferior vena cava (levels 1 and 2, 8%; levels 2 and 3, 9%; and the whole IVC, 1%). Although the original site is not explicitly described in some case reports, leiomyosarcoma of the inferior vena cava is considered most likely to occur in level 2 based on public literatures and our experience.

1.4 Growth Pattern

Leiomyosarcoma of the inferior vena cava arises from the smooth muscle cells in the middle layer. It initially grows within the venous wall and extends internally, externally, or both with an increase in volume, which can be pathologically divided into three subtypes: intraluminal, extraluminal, and bidirectional. In a comprehensive review of published literatures, intramural growth was seen in 5%, intraluminal growth in 23%, extraluminal growth in 23%, and bidirectional growth in 19% of the cases. The pattern of growth was not specified in 30% of the cases. Intraluminal growth was associated with thrombosis of IVC. Of 12 cases in Changhai Hospital, tumor thrombus extended into the proximal end of IVC was seen in 1 case, whereas into the distal end of IVC, in 1 case.

In cases with intraluminal growth, the proximal end of the tumor extends along the direction of blood flow of the IVC to form thrombus within the IVC. The tumor thrombus extending into the right atrium is the most commonly seen, followed by the hepatic vein. It was reported that the tumor thrombus extended into the right ventricle in only one case, whereas it extended into the pulmonary artery or its branches in two cases.

Extramurally extending tumor usually exhibited in globular shape and compressed the surrounding organs, such as the kidney, liver, and pancreas. Local invasion into these organs was very rare. The aorta was reported to be involved in two cases, whereas the intervertebral space, duodenum, stomach, and liver were involved in one case each.

1.5 Pathological Features

The gross appearance of the tumor is a globular or irregular nodular mass (Fig. 16.1), with well-defined boundary, hard texture, and false capsule. The cross-sectional color is gray or gray red. Larger tumors are accompanied with hemorrhage, necrosis, and partially cystic degeneration. The median size of the tumor is reported to be 12 cm, greater than 10 cm in 41% of cases, 5–10 cm in 33% of cases, and less than 5 cm in 19% of cases.

Under the microscope, tumor cells are arranged in bunches and closely staggered. Tumor cells vary greatly in size, presenting as fusiform shaped, with abundant and red-stained cytoplasm. The

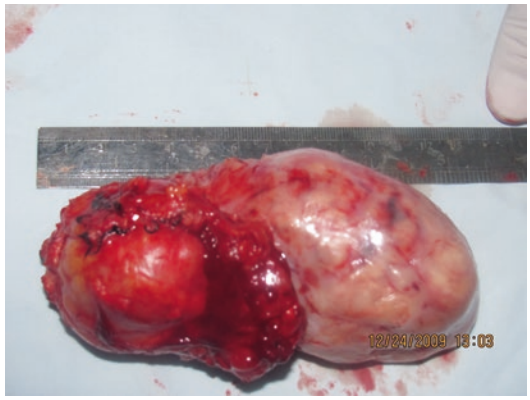

Fig. 16.1 Gross appearance of tumor is a globular or irregular nodular mass

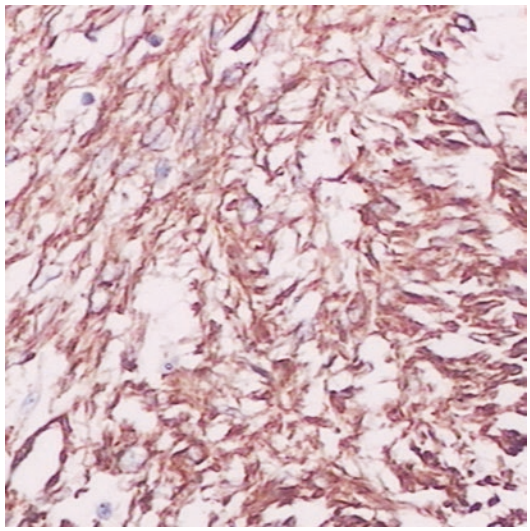

Fig. 16.2 Microscopic findings: tumor cells are arranged in bunches and closely staggered. Tumor cells vary greatly in size, presenting as fusiform shaped with abundant red-stained cytoplasm. The nuclei vary in size, presenting as spindle shaped, with dark staining, finely rounded terminus and high mitotic activity

nuclei vary in size, presenting as spindle shaped with dark staining, finely rounded terminus, and high mitotic activity (Fig. 16.2). Due to the lack of explicit standard, histological classification of retroperitoneal leiomyosarcoma of the inferior vena cava is suggested by pathologists to determine the degree of malignancy, which is established based on mitotic nuclei count. Under the microscope, more than 10 mitoses per 10 HPF (high-power fields) are considered as high-grade malignant, 5–10 mitoses per 10 HPF as intermediate-grade malignant, and 1–4 mitoses per 10 HPF as potentially malignant. However, mitotic figures were not identified in most cases documented in literatures, and these cases were instead classified into well-differentiated, intermediate-differentiated, and poorly differentiated categories.

The 117 out of 211 cases reported by the University of Alabama were histologically classified into the following categories based on mitotic index: 54 (46%) high-grade, 20 (17%) intermediate-grade, and 43 (36%) low-grade malignant.

1.6 Metastasis

The tumors grow slowly, do not invade, but are often attached to surrounding organs. Tumors metastasize mainly through blood circulation and lymphatic system. As it is more difficult to diagnose leiomyosarcoma of the inferior vena cava in early stage, the tumor does not cause symptoms until it has partially metastasized. The most common sites where the tumor disseminates include the liver, lung, brain, peritoneum, and lymph nodes, followed by the skin, soft tissue, bone, kidney, and omentum.

2 Clinical Manifestations and Diagnosis

2.1 Clinical Manifestations

Leiomyosarcoma of the inferior vena cava lacks typical manifestations, and its clinical symptoms are related to tumor size, degree of collateral circulation, and the presence or absence of secondary thrombosis; however, it is mainly determined by tumor location.

Leiomyosarcoma located in the lower segment of the inferior vena cava may cause abdominal pain, back pain, or palpable abdominal mass. A few cases may suffer from leg edema during the course. As the tumor grows slowly, mature collateral circulation has been established at the time of the inferior vena cava obstruction. The majority of patients do not develop significant

edema in lower extremity but present with superficial venous dilatation in lower extremity and abdominal wall.

Leiomyosarcoma located in the middle segment of the inferior vena cava may cause the right upper quadrant pain. When it invades the right renal vein and subsequently induces secondary renal vein thrombosis, the tumor leads to nephrotic syndrome manifested as proteinuria and kidney swelling.

Leiomyosarcoma located in the superior segment of the inferior vena cava or secondary thrombotic occlusion of hepatic vein can cause Budd-Chiari syndrome, characterized by hepatomegaly, portal hypertension, and ascites. When it spreads to the right atrium or right ventricle, the tumor may lead to heart failure, manifested as shortness of breath after exercising.

The initial symptom in 1 of 12 cases treated in Changhai Hospital was pulmonary embolism secondary to tumor thrombotic occlusion of the inferior vena cava. Some patients also experience weight loss, fever, and other nonspecific symptoms.

2.2 Imaging Findings

Ultrasound Ultrasound examination is simple, noninvasive, and economical which dynamically monitors the progress of the disease and displays the inferior vena cava and abdominal organs. Routine ultrasound may show a well-defined solid hypoechoic mass in intraperitoneal space and posterior to the liver, mostly spindle shaped with heterogeneous echo. Color Doppler flow imaging not only localizes the mass within or partially within the inferior vena cava but also displays the proximal and distal ends of the tumor in the inferior vena cava. Doppler image shows blood flow signals in the tumor mass, arterial flow in the spectrum, as well as the formation of collateral circulation around the inferior vena cava. Contrast-enhanced ultrasound (CEUS) may serve as an alternative strategy after injection of contrast agent SonoVue (Bracco UK Ltd), which can localize the mass in the inferior vena cava. In the early arterial phase, the tumor generally shows enhancement which is synchronized substantially with liver tissue and reaches the peak rapidly. At peak time, the tumor shows heterogeneous enhancement and non-enhanced flake-like zone. The contrast agent is cleared very slowly, which is synchronized substantially with the surrounding tissue. The thrombosis formed within the distal inferior vena cava appears as non-enhanced hypoechoic mass.

CT and MRI Leiomyosarcoma of the inferior vena cava has relatively homogeneous intermediate intensity signal on CT images. The tumor often adheres to or compresses surrounding tissue, displaying mild heterogeneous enhancement after injection of contrast media (Fig. 16.3).

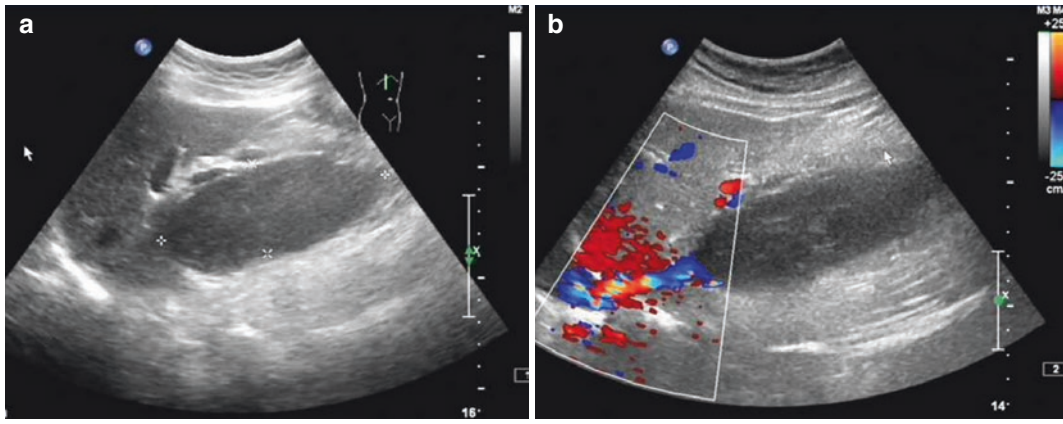

Fig. 16.3 Routine ultrasound displays a well-defined solid hypoechoic mass in intraperitoneal space and posterior tothe liver, mostly presenting as spindle-shaped with heterogeneous echoes. (**a**) and (**b**), resepctively, displays the proximal and distal end of the tumor in IVC

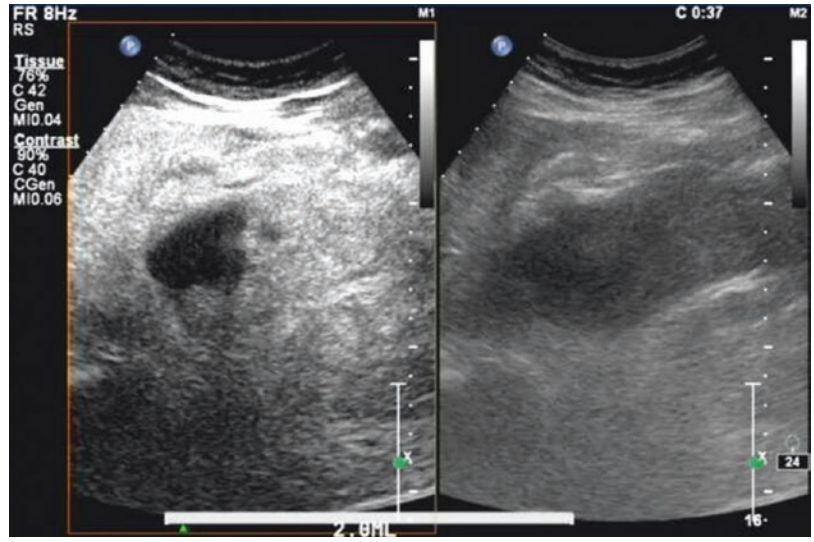

Fig. 16.4 A peak rapidly emerges after injection of contrast agent. At peak time, the tumor presents as a non-enhanced flake-like zone. The contrast agent is cleared very slowly, which is synchronized substantially with the surrounding tissue

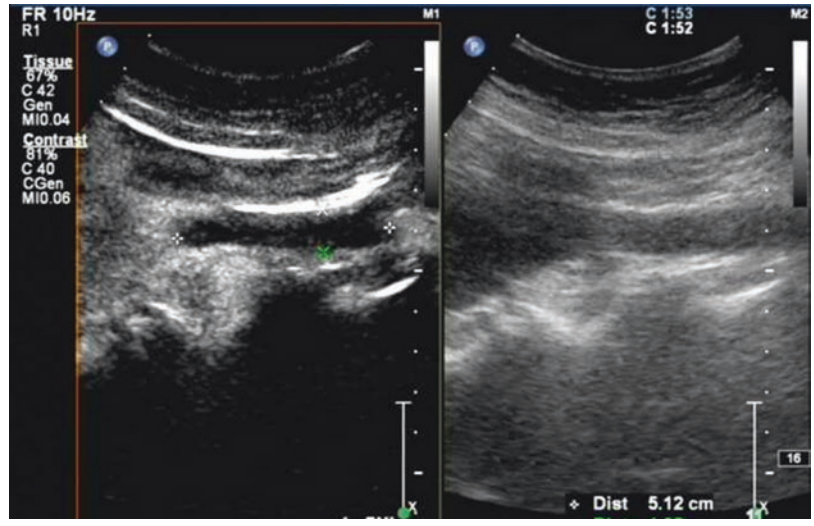

Fig. 16.5 Thrombosis formed within the distal IVC appears as a non-enhanced hypoechoic mass

Multiplanar reformation (MPR) image of multi-slice spiral CT can display tumor invasion site and the extent of compression of the surrounding tissue (Fig. 16.4). Three-dimensional reconstruction computed tomography angiography (3D-CTA) image is able to clarify the positional relationship between the tumor and the inferior vena cava, as well as the patency of the inferior vena cava and the surrounding collateral circulation.

The resolution of MRI is higher than that of CT in the detection of leiomyosarcoma of the IVC. The tumor displays equal or slightly lower intensity signal on T1W1, high mixed- intensity signal on T2W1, and homogeneous enhancement after injection of contrast media (Fig. 16.5). Similar to CTA, the MRA with three-dimensional reconstruction is able to display the complex spatial relationship among the IVC, hepatic veins, and portal vein; clearly present the panoramic view of the lesion, especially the involvement scope and extent; demonstrate longitudinally truncation signs or filling defects; and reveal the status of collateral circulation (Fig. 16.6). Three-dimensional reconstruction image can be rotated and viewed at any angle to provide more valuable information about the lesion.

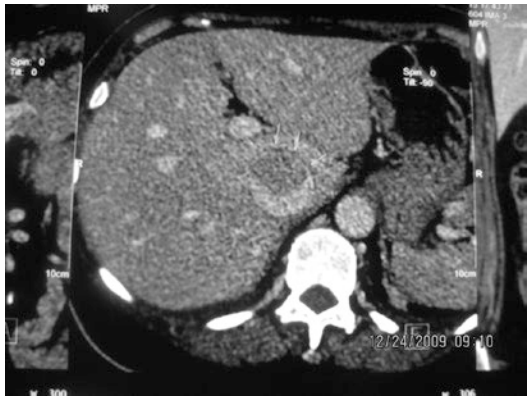

Fig. 16.6 CT plain scan of a leiomyosarcoma originated from IVC

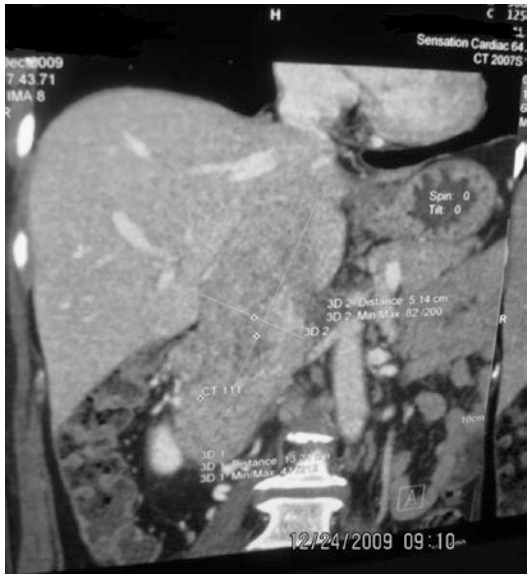

Fig. 16.7 MPR reconstructional image of a tumor on multi-slice spiral CT

Inferior Vena Cava Angiography It can directly reflect the involvement extent and patency of the IVC (Fig. 16.7). With the development of techniques, CTA or MRA images with three-dimensional reconstruction can very clearly identify the IVC and its collateral circulation. Thus, in recent years, IVC angiography has been rarely used for diagnosis of leiomyosarcoma of the IVC.

2.3 Differential Diagnosis

Based on clinical manifestations and imaging characteristics, diagnosis of leiomyosarcoma of the IVC is not difficult. Unfortunately, because of its very low incidence, it is often misdiagnosed as adrenal tumors, pancreatic cancer, malignant lymphoma, paraganglioma, or caudate lobe hepatocellular carcinoma by clinicians who are unfamiliar to this disease.

According to different imaging features, most diseases are easier to make a differential diagnosis preoperatively. Notably, primary leiomyosarcoma of the IVC should be distinguished from intravenous leiomyosarcoma. Most of the latter is derived from the ureter or uterine leiomyosarcoma, in which the tumor spreads along the draining vein into the IVC and forms tumorous thrombus. Both tumors behave differently in pathology; however, preoperative biopsy is not performed for most of the tumors, so exploratory surgery is the mainstay for discrimination. Treatment principles are also different: intravenous leiomyosarcoma requires resection of the primary tumor and removal of intravenous thrombus, while primary leiomyosarcoma of the IVC requires resection of more lesions at tumor origin of the IVC wall.

Primary leiomyosarcoma of the IVC should be differentiated from primary retroperitoneal leiomyosarcoma, and major differences between the two lie in (a) leiomyosarcoma of IVC wholly or partly grows within the IVC lumen, while retroperitoneal leiomyosarcoma usually pushes the IVC and (b) it is easy to spate the retroperitoneal leiomyosarcoma from the IVC due to a potential space; the structure of the IVC wall is complete. CT or MRI can provide differential evidence by clearly displaying the whole picture of leiomyosarcoma of the IVC as well as the structure of the IVC wall.

In addition, the leiomyosarcoma of the IVC must be differentiated from old thrombosis in the IVC, presenting as low-density signal on CT but high-intensity signal within the lumen on MRI, with a well-defined boundary between the thrombosis and the vascular wall. Meanwhile, luminal

dilation of IVC caused by the thrombosis is to a far lesser extent than that by the leiomyosarcoma of the IVC.

3 Treatment Approach

Up to now, surgical procedure remains the most effective treatment for leiomyosarcoma of the IVC. En bloc resection of the tumor combined with the involved organs is essential to ensure negative surgical margin and reduce the recurrent rate. The difficulty in resection of leiomyosarcoma of the IVC varies from tumor location as well as the extent of invasion into the IVC and surrounding organs. Successful surgery usually depends on multidisciplinary cooperation of surgeons from the department of vascular surgery, liver transplantation surgery, urologic surgery, and cardiovascular surgery, especially when the tumor invades multiple sites and organs.

3.1 Resection of Leiomyosarcoma of Level 3 Inferior Vena Cava

Leiomyosarcoma rarely occurs in the level 3 inferior vena cava (infrarenal), with the lowest incidence of 8–24%. Infrarenal IVC mainly receives the blood flow from the lower limbs and pelvis. In the course of tumor growth, the occlusion of IVC lumen leads to the formation of rich collateral circulation feeding the tumor. Surgical resection of this segment of IVC generally does not cause complications such as dysfunction of vital organs or lower limb edema. Meanwhile, even the tumor in extraluminal growth pattern rarely involves its surrounding organs. Due to the absence of important substantive organs around the infrarenal segment of IVC, it is not difficult to surgically remove the leiomyosarcoma confined to this segment.

On the premise of ensuring enough resection scope of the IVC, local excision of the tumor combined with IVC wall and subsequent patch angioplasty may be adopted based on the tumor's invasion extent and growth pattern (Fig. 16.8); or en bloc resection of the tumor and IVC may be applied without reconstruction of IVC. However, reconstruction following the resection of level 3 inferior vena cava may cause postoperative thrombosis, regardless of the type of vascular graft to be used, thus posing greater threat to patients. Therefore, the majority of vascular surgery centers performs the resection of the level 3 inferior vena cava without reconstruction.

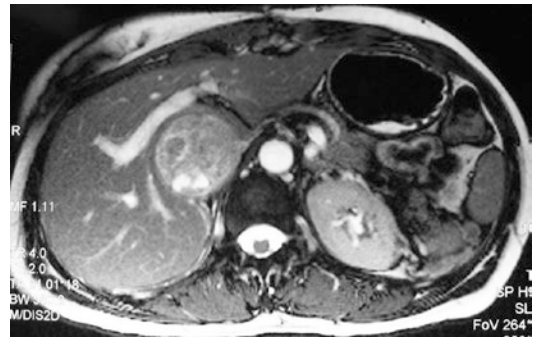

Fig. 16.8 MRI plain image of a tumor

Two key points should be noted during the resection of leiomyosarcoma of the level 3 IVC:

First, it is easier to determine the extent of involvement of the IVC by extraluminally growing leiomyosarcoma. For intraluminally or bidirectionally growing toward the direction of blood flow, the proximal end of tumor is free and similar to tumorous thrombus, which does not invade the IVC wall, although it causes dilatation of the IVC by occupying the lumen. As a result, it is unnecessary to completely remove the IVC within the range of tumor growth, and only the venous wall close to its origin needs to be resected. The extent of involvement of venous wall can be accurately determined only after dissecting the venous lumen during surgery (Fig. 16.9). If venous wall is involved to a lesser extent, partial resection plus patch angioplasty may be adopted.

Second, the excision scope of IVC should start from the inferior margin of the opening of renal vein to the confluence of the left and the right iliac veins, ensuring that the proximal and distal ends of the excised segment won't form a

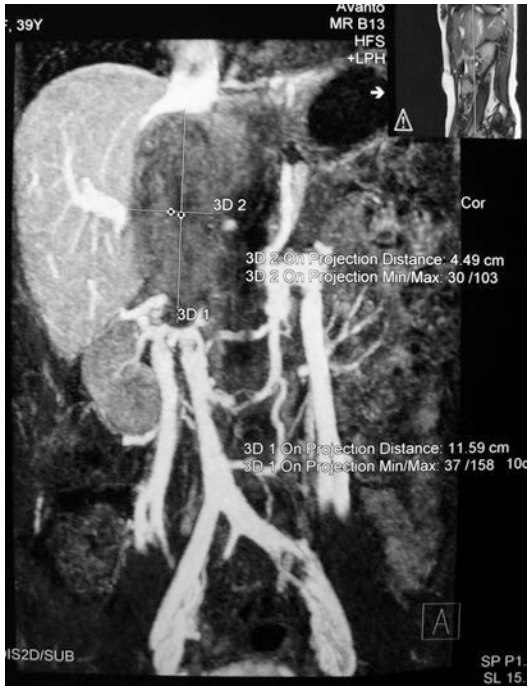

Fig. 16.9 Three-dimensional reconstruction of MRA image

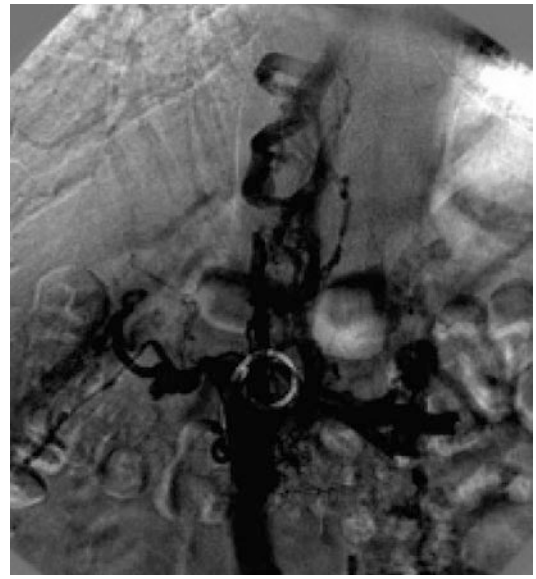

Fig. 16.10 Angiography of inferior vena cava (IVC)

blind-ended vessel (absence of blood flow), which may lead to thromboses formation in the IVC and increase the risk of pulmonary embolism.

3.2 Resection of Leiomyosarcoma of the Level 2 Inferior Vena Cava

It has been reported that leiomyosarcoma most frequently occurs in the level 2 inferior vena cava, accounting for approximately 40% of all cases (Cacoub et al. 1991). If the tumor grows extraluminally or bidirectionally, the surrounding organs will be easily involved, of which the right kidney is the most vulnerable to tumor invasion. Furthermore, this segment of the IVC is inferior to and partially located within the liver, a large-volume organ, thus making anatomical exposure, occlusion, and reconstruction more difficult than that of level 3.

Resection of leiomyosarcoma of the level 2 IVC may be completed under cardiopulmonary bypass (CPB) circuit from IVC to the right atrium (Hassan et al. 2010) or alternatively completed within the abdominal cavity without bypass circuit (Shindo et al. 2002). Both methods have their advantages and disadvantages. CPB may cause more serious injury but facilitate stable circulation, which is suitable for patients with poor cardiac functional compensation. Specific procedures of CPB are as follows: (a) cannulation of the iliac veins and right atrium is performed, and sometimes portal vein is simultaneously cannulated and (b) the blood of IVC and portal vein is drained out of the body without oxygenation to flow directly through a centrifugal pump into the right atrium.

Generally, bilateral subcostal oblique incision is usually used in liver transplantation. This approach is only adopted for specific surgery via the peritoneal access, in order to obtain a good exposure. Intraoperatively, dissociation site of IVC and occlusion method are determined by the plane where the proximal end of tumor reaches.

If the proximal end of the tumor is located below the third hepatic hilus, only the inferior hepatic segment of the IVC or the first segment of the liver needs to be dissociated, followed by ligation of short hepatic veins to expose part of intrahepatic segment of IVC (Fig. 16.10). Intraoperatively, IVC can be occluded only if the hepatic blood flow won't be affected, to complete tumor resection and reconstruction of IVC. The

specific procedure is the following: after laparotomy, the hepatocolic ligament is isolated. Then, the hepatic flexure of the colon is pushed to the lower abdomen to make a Kocher incision. The head of the pancreas and duodenum is opened toward the left side to reveal the inferior hepatic segment of the IVC. If the IVC cannot be controlled at the proximal end of the tumor, the isolation may be continued upward along the front wall of the IVC after ligating the short hepatic veins and raising the first segment of the liver, to the proximal end of the tumor.

If the proximal end of the tumor is close to the second hepatic hilus, vascular occlusion of the whole liver is required during the surgery. In this setting, organs in the right upper quadrant should be turned over to the left upper quadrant with Cattell-Braasch maneuver following the specific procedures:

1. After obtaining access to the abdomen, expose the inferior hepatic segment of the IVC, dissociate the ligamentum hepatoduodenale, and get through the occlusion band until use.
2. Dissociate 2 cm length of the superior hepatic segment of the IVC below the diaphragm, and get through the occlusion band until use.
3. Cut down the hepatic triangular ligament on the right with scissors, turn over the liver from the right to the left, and dissociate completely the intrahepatic segment of the IVC along the anterior space between the liver and the IVC (Fig. 16.11).

The tumor resection cannot be started until full segment of the IVC from the renal vein to the diaphragm is completely exposed.

The proximal end of the tumor should be resected firstly. Blood flow of the whole liver should be blocked in the following order: first, distal end of the IVC (If the distal end needs to be blocked below the level of renal vein, bilateral renal veins should be blocked simultaneously); second, ligamentum hepatoduodenale; and third, superior hepatic segment of the IVC below the diaphragm. After blocking, a longitudinal incision should be made in the proximal IVC. Tumorous thrombus usually exists freely and intraluminally in a segment of the proximal end of tumor, without adhesion to IVC wall. During the exploratory laparotomy, if the proximal end of IVC to be removed is more than 2 cm away from the opening of hepatic vein, the free proximal end of the tumor will be cut off or moved out of the lumen of IVC, and the segment of IVC below the opening of hepatic vein should be reblocked (Fig. 16.12). Then the occlusion band of hepatic hilus and the occlusion clamp of subphrenic segment of the IVC should be loosened to restore hepatic blood flow and increase venous return, thus shortening warm ischemia time for the liver and low perfusion time for the heart and other vital organs. Subsequently, the resection procedures are the same as those of the tumor located in the inferior hepatic segment of the IVC.

The proximal end of the tumor is treated firstly, aiming to shorten warm ischemia time for

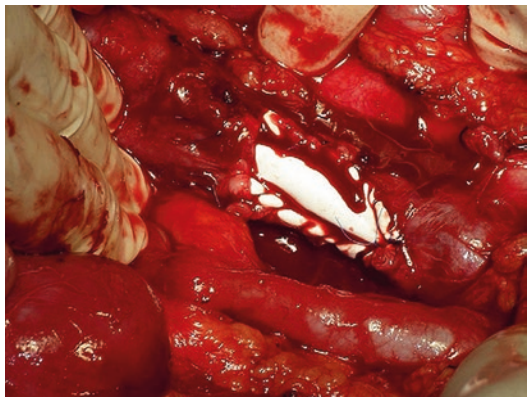

Fig. 16.11 Local excision of a tumor and IVC wall. Patch angioplasty may be adopted if necessary

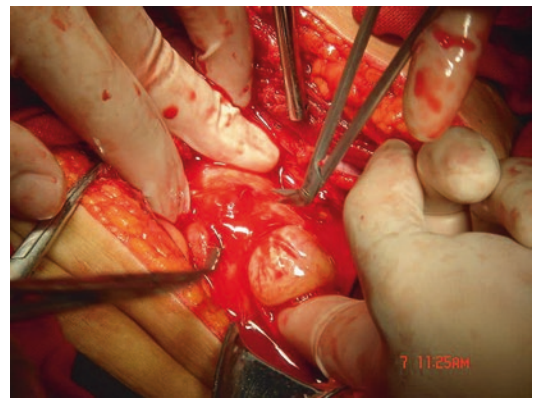

Fig. 16.12 The extent of involvement of venous wall can be accurately determined only after resecting venous lumen during surgery

the liver during tumor resection and IVC reconstruction and to improve the decreased venous return and unstable circulation attributed to the blockage of the subphrenic IVC. Using this approach, the total hepatic ischemia time is generally no more than 10 min; however, the blood pressure will be significantly reduced when the subphrenic segment of the IVC is blocked, characterized by a reduction of about 30–40 mmHg in the mean arterial pressure. Patients with poor cardiac functional compensation may even develop ventricular fibrillation. For this reason, good communication with anesthesiologist is required preoperatively and intraoperatively. If the preoperative evaluation suggests that the patient's cardiac function cannot tolerate hypoperfusion, the surgery should be performed under venous bypass.

Whether the reconstruction is necessary following the resection of the level 2 IVC remains controversial. If the distal end of the tumor does not involve the opening of renal vein, reconstruction of this segment of the IVC is usually not recommended because the blood flow of the right renal vein can return through collateral circulation formed by the branches of infrarenal IVC or the left renal vein. If reconstruction is performed, PTFE is the commonly used material, and abdominal aortic graft from corpses has been used previously, which might be able to prevent postoperative thrombosis.

If the distal end of the tumor involves the opening of renal vein, principles for the treatment of the left and right renal veins are different. The left renal vein has the left gonadal vein, left suprarenal vein, left lumbar vein, and other branches and communicates with peripheral veins such as semi-azygos vein and vertebral venous plexus. When the opening is ligated, it is easy for the left renal vein to establish abundant collateral circulation so that its blood can return via multiple branches. Based on such anatomical feature, reconstruction of the left renal vein is unnecessary.

Reconstruction of the right renal vein is determined by specific conditions. As the right renal vein is very short, the tumor involving the opening of the right renal vein has often invaded the capsule of the right kidney. In this setting, the right kidney should be removed. If the right kidney needs to be retained, reconstruction of the right renal vein should be performed. The right renal vein has only one ureteral branch, which is too small to compensate its reflow, so ligation of the right renal vein can result in renal function failure. The right renal vein can be reconstructed with artificial vessels, autologous saphenous vein, and gonadal vein (Fig. 16.13).

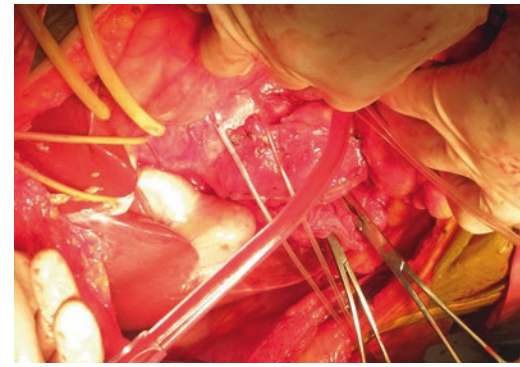

Fig. 16.13 A part of intrahepatic segment of IVC is exposed

3.3 Resection of Leiomyosarcoma of the Level 1 Inferior Vena Cava

Leiomyosarcoma located in the level 1 IVC usually causes Budd-Chiari syndrome due to the occlusion of hepatic vein. Surgical procedures should be conducted under cardiopulmonary bypass, similar to radical surgery for Budd-Chiari syndrome. The surgery is usually performed via the right intercostal abdominal incision to expose the right atrium in the thoracic cavity, superior vena cava, and ascending aorta. The exposure procedure for the IVC is the same as that for the level 2 IVC as described previously. The exposure of abdominal organs is achieved by pushing

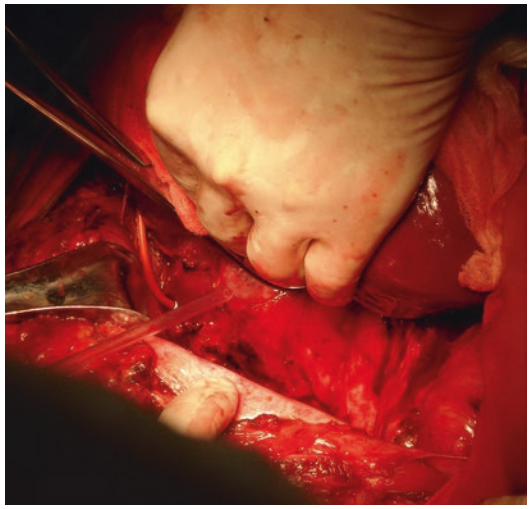

Fig. 16.14 The intrahepatic segment of IVC is dissociated completely along the space anterior to hepatic IVC

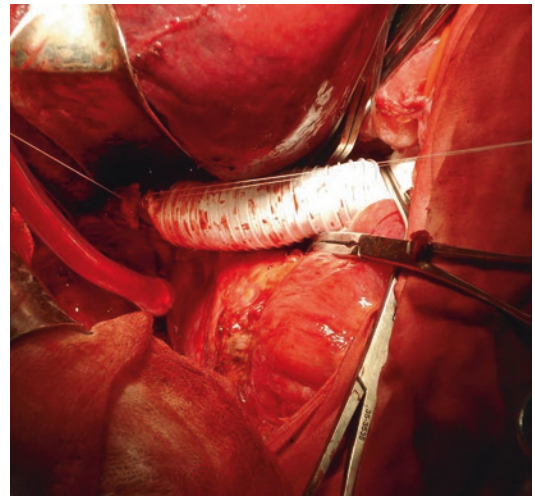

Fig. 16.15 The free proximal end of the tumor can be cut off or moved out of the lumen of IVC. The IVC segment below the opening of hepatic vein should be re-blocked

them to the left side using Cattell-Braasch maneuver, which has been used in the resection of leiomyosarcoma of the level 2 IVC to expose the IVC completely.

Cardiopulmonary bypass is established by cannulating the superior vena cava, iliac vein, and ascending aorta, respectively, after systemic heparin anticoagulation. When the right atrium is opened after occlusion of the ligamentum hepatoduodenale, the tumor extending from the IVC to the right atrium is visible, but usually it does not invade or adhere to the right atrium, which mostly arises from the level 2 IVC. Surgeon stretches a finger through the right atrium to IVC and separates along the space between the tumor and IVC to the area below the opening of hepatic vein, cuts off the tumor, and harvests its superior segment as specimen. Then the right atrium can be sutured, the IVC is occluded below the second hepatic hilus, and cardiopulmonary bypass is discontinued by releasing the occlusion of hepatic hilus in order to shorten the duration of CPB. Subsequently, surgical procedures are the same as those for the resection of leiomyosarcoma of the level 2 IVC (Figs. 16.14, 16.15, and 16.16).

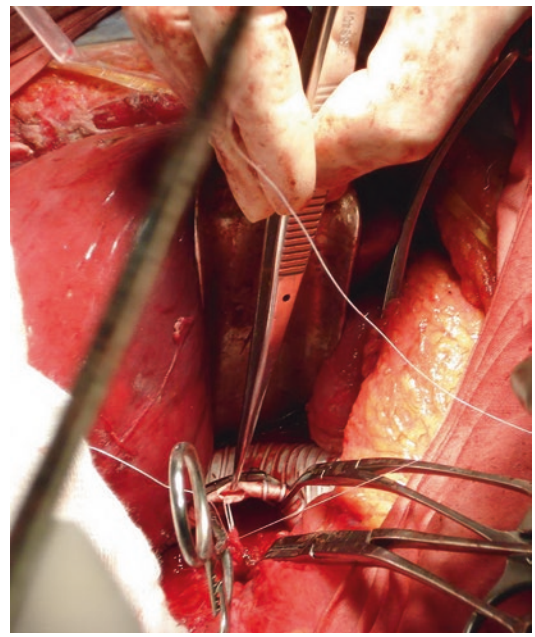

Fig. 16.16 The right renal vein may be reconstructed with artificial vessels, autologous saphenous vein or gonadal vein

4 Treatment Outcome and Prognosis

Of 12 patients treated in Changhai Hospital of Shanghai, two refused to undergo resection due to fear of the risk of surgery; and one with pulmonary embolism as the initial symptom suddenly died on the third day after admission, possibly due to recurrent pulmonary embolism. Except the above three cases who underwent diagnostic imaging, the remaining nine cases received surgery and obtained pathologic diagnosis. One of the 9 cases failed to undergo en bloc resection (this patient was admitted due to diagnosis of gynecologic tumor and was found to present with leiomyosarcoma originated in iliac vein during exploratory laparotomy and only underwent tumor biopsy due to lack of preoperative preparation), and the remaining eight cases underwent en bloc resection; among them, one case experienced combined right nephrectomy.

In a meta-analysis conducted by the University of Alabama, 151 cases (71%) underwent en bloc resection. Among them, 99 (47%) received surgical resection only and 52 (24%) underwent surgical resection combined with adjuvant radiotherapy or chemotherapy. Notably, ten (5%) cases underwent partial resection and adjuvant chemoradiation. Twenty-eight of 151 cases who underwent en bloc resection required combined multiple organ resection. The kidney is the most common organ involved. Twenty-one cases underwent combined right nephrectomy, nine underwent suprarenal joint resection, two underwent partial hepatectomy, and two underwent partial resection of the pancreatic head and duodenum.

We have carried out a detailed analysis of the cases reported by the University of Alabama from 1996 to 2005 as they basically represent the current status of treatment.

Eleven percent of patients who underwent radical resection experienced local recurrence. During a 12-month mean follow-up, 29% of patients have experienced tumor metastasis. Metastases most frequently occur in the liver (70%) and lung (20%), followed by the lymph nodes, kidneys, and omentum.

There are eight cases of perioperative deaths (4%) attributed to pulmonary embolism, hemorrhage, and pancreatitis. During a 21-month mean follow-up, 26% of patients achieved tumor-free survival, 14% experienced tumor-bearing survival, and 11% were lost to follow-up. During a 40-month mean follow-up, 42% died of tumor-related factors, and 2% died of diseases unrelated to primary tumor.

Among 151 patients who underwent en bloc resection, 128 have complete follow-up results. Of them, 51 cases achieved tumor-free survival, 19 cases experienced tumor recurrence, 34 cases died of tumor-related factors, and 7 cases died of noncancer-related diseases. Of the ten cases with partial tumor resection, four died of tumor-related factors, one died of noncancer-related illness, and five were lost to follow-up. By contrast, 50 patients who did not receive tumor resection all died of tumor-related factors during follow-up period.

Prognosis is the best in patients with tumors located in the level 2 IVC whereas the worst in those with tumors located in the level 1 IVC. Among patients with tumors located in the level 2 IVC, 42% achieved tumor-free survival after surgery, 16% experienced tumor recurrence during follow-up, and 26% died of tumor-related factors. Among those with tumors involving both levels 2 and 3 of IVC, 33% achieved disease-free survival after surgery, 33% experienced tumor recurrence, and 27% died of tumor-related factors. Among those with tumors involving the level 3 IVC, 21% achieved disease-free survival after surgery, 21% experienced tumor recurrence, and 38% died of tumor-related factors. All patients with tumors involving the level 1 IVC died of tumor-related factors during follow-up.

The survival rate is not affected by the patient's age, gender, tumor size, tumor growth pattern (intraluminal, extraluminal, and bidirectional), or regional lymph node metastasis. Correlation between tumor grade and prognosis is only mentioned in a few literatures. Currently, the most important factor associated with a favorable prognosis is en bloc resection of the tumor, suggesting that the involvement of the superior

segment of IVC and the presence of Budd-Chiari syndrome play pivotal roles in poor prognosis.

The 5-year survival rate following radical resection of leiomyosarcoma of IVC is 49–53%, lower than that of leiomyosarcoma in the stomach and small intestine, or other primary retroperitoneal sarcomas.

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Retroperitoneal Rhabdomyosarcoma

17

Chengli Miao and Cheng-Hua Luo

1 Brief Introduction

Rhabdomyosarcoma (RMS) can arise in retroperitoneum. Twenty-two cases of retroperitoneal rhabdomyosarcoma have been reported by Pack and Tabah (1954). It occurs in both children and adults. However, retroperitoneal rhabdomyosarcoma is an extremely rare tumor in general, which is occasionally reported in a large cohort of cases with retroperitoneal tumors. Of 121 cases of rhabdomyosarcoma reviewed by Stout (1946), only one case of primary retroperitoneal rhabdomyosarcoma was found.

2 Etiology

The etiology of retroperitoneal rhabdomyosarcoma is yet to be elucidated, which is seldom mentioned in the literatures.

3 Pathogenesis and Pathophysiology

Generally, rhabdomyosarcoma appears as fish meat like with varying degrees of hardness and are often encapsulated. Intra-tumoral necrosis is frequently seen, so it maybe misdiagnosed as retroperitoneal hematoma or abscess. Most of retroperitoneal rhabdomyosarcomas are fixed to or invade adjacent retroperitoneal organs or blood vessels.

Histologically, rhabdomyosarcoma can be divided into three subsets: embryonal, pleomorphic, and alveolar. Embryonal rhabdomyosarcoma (ERMS) accounts for 60% of all rhabdomyosarcoma. This subtype is the most common head and neck tumor in children and adults; however, it can occur at any age. Of the 22 cases of rhabdomyosarcoma reported by Pack and Tabah (1954), 7 cases were ERMS. Three out of four previously reported cases of retroperitoneal rhabdomyosarcoma were ERMS. ERMS often occurs in patients aged 5–10 years old, with an equal male-to-female incidence ratio. Under microscope, ERMS is characterized by spindle-shaped cells with an eosinophilic cytoplasm-rich appearance and transverse striation or longitudinal muscle fibrils. Morphology of tumor cells is similar to muscle cells of embryonic development at 7–10 weeks old.

Pleomorphic rhabdomyosarcoma comprises approximately 15–20% of RMS. It is the most common type of RMS in adults and frequently occurs in trunk and limbs. A total of 15 cases of retroperitoneal pleomorphic rhabdomyosarcoma (11 females and 4 males, with age-of-onset of 16–74 years) have been reported by MSKCC (Hawkins et al. 2001). Histologically, tumor cells vary greatly in shape, presenting spindle shaped,

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strip shaped, or ribbon shaped, abundant in cytoplasm and with transverse striation or longitudinal muscle fibrils.

Alveolar rhabdomyosarcoma accounts for 20% of all RMS; however, retroperitoneal alveolar rhabdomyosarcoma was not reported by Pack and Tabah (1954).

4 Clinical Manifestation

Retroperitoneal rhabdomyosarcoma presents nonspecific symptoms due to an insidious onset; most of the tumors can't be found until they grow to a large size. It is recently reported that embryonal rhabdomyosarcoma can cause Costello syndrome.

5 Treatment and Prognosis

The overall survival of rhabdomyosarcoma was dismal (less than 5%). With the application of adjuvant radiotherapy and chemotherapy, the survival rate in children has been increased from 14% to 76%. Even pediatric patients with residual tumors who have developed systemic metastases are also considered curable (Weiss et al. 2002).

At present, it's too early to conclude whether adjuvant radiotherapy and chemotherapy may improve the overall survival rate in adults with rhabdomyosarcoma to the same extent as in children.

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Idiopathic Retroperitoneal Fibrosis

18

Cheng-Hua Luo and Xiaobing Chen

1 Brief Introduction

Retroperitoneal fibrosis (RPF) was first reported in the literature in 1905 by a French urologist. Dr. Albarran (1905) described surgical treatment for one case of retroperitoneal extensive fibrosis with concomitant ureteral obstruction. Later this disease was occasionally reported in the French and German literatures, and not until 1948 two cases were reported by Ormond (1948) in English; it began to be widely recognized by doctors worldwide.

2 Etiology and Pathogenesis

A number of factors can induce retroperitoneal fibrosis such as bleeding, urine leakage, radiation, surgery, non-specific inflammation of the gastrointestinal tract (e.g., Crohn's disease, appendicitis, and diverticulitis), and infections (e.g., tuberculosis, histoplasmosis, syphilis, and actinomycosis). The location and presentation of fibrosis vary from these factors and distinctively differ from typical para-aortic fibrosis.

Etiology of true retroperitoneal fibrosis (also known as idiopathic retroperitoneal fibrosis) in two-thirds of patients remains mysterious. The remaining one-third is associated with administration of methysergide, cancer, and abdominal aortic aneurysm.

Retroperitoneal fibrosis may be part of systemic fibrotic diseases and correlates to four kinds of diseases: (a) fiber orbital pseudotumor, (b) Riedel's thyroiditis, (c) sclerosing cholangitis, and (d) mediastinal fibrosis. Due to the similar histological features, the above four diseases are even considered as different manifestations of the same disease at different sites. Of all patients with retroperitoneal fibrosis, 8–15% also presents with extraperitoneal fibrosis.

2.1 Idiopathic Fibrosis

In patients with idiopathic fibrosis, para-arterial fibrosis at early stage was originated from the aortic area with the severest sclerosis lesion, where atherosclerotic plaque protrudes to the outer membrane and the middle layer of aorta is obviously damaged. Inflammation in the aortic wall is consistent with or even worse than that in any serious atherosclerosis. Chronic inflammation may occur in the aortic region without para-aortic fibrosis, suggesting that further development of aortic inflammation leads to adventitial fibrosis. Inflammatory infiltration feature (e.g., infiltration of lymphocytes and plasma cells) indicates that idiopathic fibrosis is mediated by immune system.

Retroperitoneal fibrosis is associated with many immune-mediated connective tissue diseases, such

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as ankylosing spondylitis, systemic lupus erythematosus, Wegener's granulocyte cell histiocytosis, Raynaud's disease, polyarteritis nodosa, and systemic vasculitis. Accumulated evidence supports the etiology of retroperitoneal fibrosis related to immune dysfunction: firstly, the progress from active inflammation to infiltration without cell fibrosis is consistent with that of other autoimmune diseases; secondly, laboratory findings, such as increased erythrocyte sedimentation rate and γ-globulin as well as positive autoantibodies, indicate the role of immune system in retroperitoneal fibrosis; thirdly, steroids and other immunosuppressive drugs can alleviate the symptoms; and fourthly, this tumor is associated with the major histocompatibility complex HLA-B27, like many other autoimmune diseases.

Growing entities of evidence supports ceroid, a kind of multimers of oxidized fats and proteins in atherosclerotic plaque, as a potential antigen. Ceroid is deposited in atherosclerotic plaques, which cannot be recognized by lymphocytes to resultantly produce antibodies until the middle layer is destroyed. Periaortic inflammatory lymphocytes are mainly B lymphocytes, followed by T helper cells. Parums (1990) detected IgG antibodies against ceroid in patients with severe chronic periaortitis. Only when the middle layer of the aorta is damaged, accompanied by partial exarteritis, the antibody is produced against ceroid. In the absence of exarteritis, ceroid-related IgG is undetectable.

Other cells in inflammatory infiltration are the sources of matrix that can regulate the proliferation of fibroblasts, such as fibroblast growth factor secreted by macrophages, as well as fibroblast growth factor and collagen synthesis-stimulating factor produced by T cells.

2.2 Peri-aneurysmal Fibrosis

It is reported that the transudate (extravascular fluid with low-protein content and a low specific gravity) from abdominal aortic aneurysm can lead to corresponding para-aortic aneurysm fibrosis, and approximately 5–23% of abdominal aortic aneurysm is associated with fibrosis. Retroperitoneal fibrosis that lacks heme iron can be discriminated from the para-aortic aneurysm fibrosis. Para-aortic inflammatory infiltration is consistent with that of retroperitoneal fibrosis, which may share a common mechanism of pathogenesis. The only difference between retroperitoneal fibrosis and para-aortic aneurysm fibrosis lies in the degree of aortic dilatation. Up to 10% of abdominal aortic aneurysm is determined to be inflammatory and considered different from arteriosclerotic aneurysm. However, there is no histological difference between inflammatory aortic aneurysm and peri-aneurysmal fibrosis. Mitchinson therefore proposed that retroperitoneal fibrosis, peri-aneurysmal fibrosis, and inflammatory aortic aneurysm may be collectively referred as "chronic periaortitis."

2.3 Methysergide-Associated Fibrosis

In 1966, Graham (Graham 1966) described a patient who developed retroperitoneal fibrosis after receiving methysergide for treatment of migraine. The patient presented with the same clinical manifestation, gross pathological and histological features as those with idiopathic retroperitoneal fibrosis. Since then, successive cases of retroperitoneal fibrosis attributed to administration of ergot derivatives such as bromocriptine and lysergic acid diethylamide have been reported.

Methysergide is a semisynthetic derivative of ergot alkaloids. Ergot alkaloids become serotonin antagonist by acting as a competitive inhibitor at serotonin receptor sites, thus leading to elevated levels of endogenous serotonin. Although an increased level of ergot alkaloids is related to retroperitoneal fibrosis, endocardial fibrosis, and pulmonary fibrosis in carcinoid syndrome, the cause-and-effect relationship remains unclear. Methysergide may promote mast cell degranulation, which leads to serotonin release and secondary local inflammatory response. Methysergide-related fibrosis has been proven to affect the retroperitoneum as well as the heart, lungs, pleura, major vessels, and gastrointestinal tract.

The mechanism of methysergide-related retroperitoneal fibrosis involves allergic and autoimmune response induced by the drug acting as an allergen. Another notion proposes that methysergide acting as a weak vasoconstrictor may result in damage to aortic wall, as well as periaortitis or fibrosis through long-term vascular contraction or ischemia, similar to idiopathic retroperitoneal fibrosis.

Approximately 1% of the patients who receive methysergide develop retroperitoneal fibrosis, indicating a definite relationship between them, although the mechanism is unknown. After discontinuation of the drug, the symptoms can be alleviated spontaneously without further treatment.

There are also sporadic case reports about the association between retroperitoneal fibrosis and other drugs, including β-blockers and other antiallergy medicines (α-methyldopa, hydralazine, and reserpine), analgesics (aspirin, phenacetin, and codeine), and other non-related drugs (haloperidol and amphetamines); however, cause-and-effect relationship is unclear.

2.4 Malignant Fibrosis

A small number of patients develop fibrosis attributed to hyperplasia response of the connective tissue to tumor cells that metastasize to retroperitoneum. Such malignant retroperitoneal fibrosis causes medial displacement of the ureter, unlike retroperitoneal lymph node metastasis that causes lateral displacement of the ureter. The most common tumors leading to malignant fibrosis include Hodgkin's disease and other lymphomas, followed by sarcoma, carcinoid tumor, as well as breast, lung, colon, kidney, bladder, prostate, and cervical tumor.

3 Pathobiology

3.1 Gross Pathology

Generally, retroperitoneal fibrosis is a dense white fibrous plaque originated on or below the aortic bifurcation level, close to the promontory, which may spread to wrap abdominal aorta and inferior vena cava. It not only spreads along the retroperitoneum to distribute in the perivascular area but also bifurcates along the abdominal aorta in the pelvis to wrap iliac vessels or invade gonadal vessels. Occasionally, lesions spread forward along celiac artery and superior mesenteric artery. Fibrosis often spreads bilaterally and invades the ureter and psoas muscle. The fibrous envelope of ureter and resultant hydronephrosis are hallmarks of retroperitoneal fibrosis. Lesions often involve the middle one-third segment of the ureter; however, any segment of bilateral ureters may be involved (Mitchinson 1984).

Fibrosis is usually located in the retroperitoneum space between renal hilus and pelvic margin or extends to mediastinal fibrosis across the diaphragm. There is at least one case of retroperitoneal fibrosis distributed in the wide range from aortic root to its bifurcation. Retroperitoneal fibrosis can spread to small bowel mesentery, duodenum, colon, bladder, and rarely to subdural space. Benign and malignant retroperitoneal fibrosis cannot be differentiated substantially from gross appearance.

3.2 Histology

Histological features of retroperitoneal fibrosis observed by Ormond (1948) in their initial report included scarring caused by pre-existing and new-onset inflammation. They proposed that the nature of retroperitoneal fibrosis was progressive inflammation, consistent with the findings from methysergide.

Retroperitoneal fibrosis presents as active chronic inflammation. In the early stage, it is characterized by abundant infiltration of lymphocytes, plasma cells, and macrophages interspersed within fibroblasts and collagen bundle. In the advanced stage, it becomes relatively avascular and acellular with collagen bundles and scattered calcification.

Progression from active inflammation to fibrosis in patients has been demonstrated with serial biopsies. Furthermore, active inflammation and fibrosis may coexist in the same case.

Malignant retroperitoneal fibrosis can only be differentiated by the presence of scattered nests of malignant cells within the inflammatory infiltrating area, which is often misdiagnosed as primary malignancy due to sufficient differentiation of tumor cells.

In many cases, severe aortic atherosclerosis occurs below the level of the lesion. Arteriosclerotic plaques often bulge through the loose middle layer into the fibrous outer membrane, and the aortic wall presents as chronic inflammatory cell infiltration. Retroperitoneal fibrosis invades the adjacent skeletal muscle and even involves major retroperitoneal veins with fibrous intimal thickening, resulting in complete venous obstruction. Periaorta intra-tumor lymphatic vessels may be occluded. Ureter is often edematous with submucosal lymphocytes infiltration but not yet occluded due to fibrosis.

4 Clinical Manifestation

Retroperitoneal fibrosis is a rare clinical condition, with an incidence of 1/200,000 people. In general, the incidence ratio between men and women is around 2:1, which varies slightly with race. However, methysergide-related retroperitoneal fibrosis prevails in women, with female-to-male ratio of 2:1. There is no gender difference in the incidence of malignant retroperitoneal fibrosis. Retroperitoneal fibrosis occurs commonly in patients aged 50–70 years but rarely in those aged <20 years or >70 years. Several pediatric cases have been reported, including one case of stillborn fetus.

Retroperitoneal fibrosis is characterized by insidious onset and non-specific symptoms. The most common symptoms are vague and non-acute back pain, flank pain (92%), and abdominal pain. Pain is not confined to any fixed location, which may spread and distribute in zonal pattern, involving the abdomen and groin, often accompanied by gastrointestinal irritation. Pain can affect ipsilateral hip or buttocks in pediatric population, resulting in hip extension dysfunction. The cause of pain is uncertain, which may be associated with inflammation, urinary obstruction, or motility abnormalities.

Other common symptoms include weight loss, anorexia, nausea or vomiting, general malaise, and cachexia, which may be related to chronic active inflammation. Clinical signs include hypertension and fever, obstruction of the inferior vena cava, duodenal obstruction, or rectal obstruction. Patients may present with abdominal mass and lower extremity swelling. Moreover, oliguria or anuria may occur in the advanced stage.

Laboratory abnormalities are non-specific, including azotemia, anemia (in direct proportion to renal insufficiency), elevated erythrocyte sedimentation rate, and elevated neutral leukocytosis or pyuria. In recent years, alkaline phosphatase is recommended as an index of the disease, which closely correlates with elevated erythrocyte sedimentation rate. Two cases are reported to have response to the therapy, which needs to be validated by further studies.

Because of vague and non-specific symptoms, the diagnosis of retroperitoneal fibrosis is often delayed. The condition can become worse and worse due to progressive loss of renal function. The diagnosis of retroperitoneal fibrosis is more easily overlooked in young patients, even with obvious symptoms. The final diagnosis heavily depends on imaging findings.

Complications of late-stage retroperitoneal fibrosis are caused by uncontrollable development of fibrosis. Retroperitoneal fibrosis leads to renal dysfunction by wrapping the ureter, which ultimately progresses to kidney failure. The compression of inferior vena cava and retroperitoneal lymphatics or formation of thrombosis results in lower extremity edema, while gonadal vascular involvement causes scrotal edema or hydrocephalus. The duodenum, pancreas, and biliary tract may be involved occasionally. Direct involvement of duodenum contributes to small bowel obstruction. When the common bile duct is involved, the gross and histological features are similar to those of sclerosing cholangitis, and jaundice is very common. Destroyed fat layer around the pancreas misguides the diagnosis of

retroperitoneal fibrosis to pancreatic cancer. Colorectal involvement can be manifested as diarrhea, constipation, or even intestinal obstruction. Retroperitoneal fibrosis may be presented as epidural mass spreading through the neural foramen into the spinal canal, causing displacement, deformation, and atrophy of correspondingly horizontal spinal cord and subsequently leading to delayed paraplegia.

5 Examination and Staging

5.1 Excretory Urography

Retroperitoneal fibrosis-induced changes in the urinary tract are common, which is often diagnosed based on excretory urography before the discovery of CT. Urography displays blurred margin of psoas, although not always observed in all cases. Diagnosis relies on the presence of a classic triad consisting of delayed renal contrast excretion with unilateral (20%) or bilateral (68%) hydronephrosis, medial deviation of the middle third segments of bilateral ureters, and tapering of the ureteral lumen at L4–L5 vertebral levels.

The medial deviation of ureter was once considered as a character of retroperitoneal fibrosis; however, it is not presented in all patients. Further observation reveals that such medial deviation occurs in nearly 20% of healthy people. A comparative study observed no significant difference in ureteral location between 21 retroperitoneal fibrosis cases and 60 non-retroperitoneal fibrosis cases.

Interestingly, patients with retroperitoneal fibrosis have only mild ureteral obstruction, despite that they have already developed severe renal failure clinically. Thus, ureteral obstruction is hypothesized to be related to ureteral motility abnormality instead of mechanical obstruction. Histological examination identifies ureteral edema and inflammation in patients with retroperitoneal fibrosis, which is rare in ureteral fibrosis. These findings collectively support the abovementioned notion.

5.2 Retrograde Pyelography

Retrograde pyelography is indicated for the diagnosis of patients with severely impaired renal function in whom angiography is contraindicated or for further confirmation of the extent of lesion. Generally, the findings of retrograde pyelography are similar to those of excretory urography in patients with retroperitoneal fibrosis, but the former can additionally display stiffness of ureter. Interestingly, despite the widespread retroperitoneal fibrosis, thin catheter can often retrograde through ureter. Therefore, contradiction between the dilatation of renal pelvis and ureter and the ureteric patency in retrograde pyelography provides the basis for the diagnosis of this specific disease.

5.3 Lymphangiography

Lymphangiography is a complementary measure for excretory urography in the diagnosis of retroperitoneal fibrosis. Due to fine structure, retroperitoneal lymphatics are more susceptible to compression of retroperitoneal fibrosis than ureter, so lymphatic obstruction should occur ahead of compression and obstruction of ureter and major retroperitoneal vessels. Lymphangiography can clearly display retroperitoneal fibrosis before obvious changes occur in the urinary tract. No abnormal finding on lymphangiography was also reported in few patients with extensive retroperitoneal fibrosis and severe compression of ureter.

Findings on lymphangiography in patients with retroperitoneal fibrosis include (a) prolonged time of contrast agent passing through lymphatics close to aorta and iliac arteries; (b) due to obstruction of lymphatic reflux at L3–L4 level, no display of lymphatic channels above the plane of the fourth lumbar vertebrae; (c) lateral lymph node filling reflux-induced ectopic lymphatic development; and (d) small abnormal filling defects observed in para-aortic and mesenteric lymph nodes. If lymphangiography reveals no lymph node metastasis, malignant tumor may be ruled out.

5.4 CT Scan

CT scan is currently the first choice for diagnosis and follow-up of patients with retroperitoneal fibrosis. CT not only displays the progression of masses outside of the ureter but also displays retroperitoneal lesions before ureteral involvement.

On CT scans, RPF may appear as a rind of periaorta soft tissue with varying thickness, wrapping aorta, and inferior vena cava between renal hilum and sacral promontory. Laterally, RPF extends to involve ureters, causing varying degrees of hydronephrosis. The mass tends not to displace the aorta anteriorly. The fat layer between the mass and psoas muscle may be obliterated. Occasionally, the tumor presents extremely asymmetric and in abnormal position, making diagnosis very difficult. The mass in 30% of patients cannot be detected by CT, in whom fibrosis and inflammation are found to be confined to the pelvis during laparotomy.

The intensity of the mass is similar to that of muscle, displaying variable degrees of enhancement on CT, depending on the stage of the disease. In the early active vascular stage, significant enhancement is observed; in contrast, in the later avascular stage, very little enhancement is displayed. The difference between early and late stage can serve as an index for follow-up and independent factor for predicting progression vs. remission of the disease during treatment.

Retroperitoneal fibrosis should be differentiated from the following diseases by CT scanning: retroperitoneal hematoma, primary retroperitoneal sarcoma, and retroperitoneal metastases. Additionally, retroperitoneal amyloidosis mimicking retroperitoneal fibrosis has been reported in at least one case.

Morphological change in retroperitoneal structure plays a role in differential diagnosis. Most of the retroperitoneal tumor causes lateral displacement of ureter, while retroperitoneal fibrosis causes medial displacement of ureter. Although retroperitoneal fibrosis may rarely cause the anterior displacement of aorta, significant displacement of aorta often suggests malignant tumor. Unlike retroperitoneal tumor, fibrosis does not produce local bone destruction. The CT parameter and differential contrast enhancement have no significant role in distinguishing benign retroperitoneal fibrosis from malignancy. Some metastatic tumors, particularly those relating to proliferation of connective tissue, such as malignant retroperitoneal fibrosis, presenting as similar intensity to that of fibrous tissue on CT scan, cannot be differentiated from idiopathic retroperitoneal fibrosis.

5.5 Ultrasonography

RPF may be identified as a larger, well-demarcated, and smooth-bordered retroperitoneal mass on ultrasonography. Fibrosis typically centered on sacral promontory wraps aorta and inferior vena cava in a ring pattern. It spreads bilaterally to involve the ureter, and the plane between the tumor and the adjacent tissues is obliterated. The mass shows homogeneous signal and is often hypoechoic. Varying degrees of hydronephrosis and hydroureter may occur.

Doppler flow evaluation has also been assessed in the differentiation of benign from malignant RPF, with limited value. Doppler ultrasound plays a role in determining tubular structure in retroperitoneal space.

5.6 Magnetic Resonance Imaging

Thanks to its multi-axis imaging capability, MR can clearly display blood vessels without iodinated contrast agents. Taking this advantage, MRI becomes a promising tool in the diagnosis of retroperitoneal fibrosis.

MRI can better present the shape and scope of retroperitoneal fibrosis, because signal intensity and T1/T2 relaxation time of fibrosis are different from those of adjacent psoas muscle and fat tissue. Retroperitoneal fibrosis displays low-intensity signal on T1-weighted image and variable intensity signal on T2-weighted image, depending on the course of the disease. In the early stage of active inflammation, pores exist

between the epithelial connections of local capillaries in retroperitoneal fibrosis, filling with high content of fluid within the tissue, so RPF displays high-intensity signal on T2-weighted image. In advanced stage, the lesion presents characteristic low-intensity signal on T2-weighted images as avascular and acellular fibrous tissue with low content of fluid. Similarly, if steroid therapy is used to alleviate tissue edema in early stage, the lesion may exhibit low-intensity signal on T2-weighted images, and therefore MR imaging can also be used to assess the patient's response to therapy.

It is difficult to differentiate retroperitoneal fibrosis from many tumors in the early inflammatory stage, especially lymphoma with high-intensity signal on T2-weighted image. An attempt has been made to differentiate malignant from nonmalignant retroperitoneal fibrosis by MR, since heterogeneous intensity signal on T2-weighted image suggests malignant retroperitoneal fibrosis despite similar morphological presentation. However, MRI is not sensitive enough to diagnose malignant lesion, which can be only confirmed by histological biopsy.

6 Treatment

Although it is rare, retroperitoneal fibrosis, if not treated, can occlude any hollow organ with the slow progression of inflammation, especially in ureter and major blood vessels. Bilateral involvement of ureters can cause kidney failure and death; undoubtedly, more attention should be paid to this disease by clinicians. Therapeutic purposes for retroperitoneal fibrosis are to (a) establish the diagnosis and rule out the possibility of malignant tumors, (b) relieve ureteral obstruction and recover renal function, and (c) prevent the development of inflammation that can lead to further obstruction.

These patients should discontinue methysergide immediately. Once medication is withdrawn, symptoms are often alleviated and fibrosis will subside. Most patients, especially those with ureteral obstruction and mild renal dysfunction, may improve their conditions within a few days to several weeks, or otherwise they should receive further treatment, and the resumption of medication may result in the recurrence of fibrosis.

6.1 Surgical Therapy

In 1905, for the first time, Dr. Albarran described two cases of retroperitoneal fibrosis secondary to obstruction of the ureter who underwent successful ureterolysis (i.e., resected the ureter from the surrounding fibrosis). Surgery remains the fundamental approach for treatment of retroperitoneal fibrosis. Conventional surgical procedures for treatment of retroperitoneal fibrosis include laparotomy, multiple and deep biopsies of retroperitoneal mass, ureterolysis, and ureteral displacement. Especially for patients who mainly present with ureteral obstruction, ureterolysis with intraperitoneal transposition is recommended to obtain a long-term and ideal reduction in pressure on kidneys. Ureterolysis is usually easy to perform, and, if not, malignant lesions should be suspected. When severe ureteral obstruction is acute, percutaneous nephrostomy can be used to decrease the pressure on kidneys. If metabolic disorders become worse, ureterolysis must be further performed. As a small number of malignant cells are easily confused with inflammatory infiltrates, malignant retroperitoneal fibrosis is easily misdiagnosed; multiple deep biopsies are necessary. Once it is free, the ureter should be laterally shifted in the fibrous tissue, and the gap between ureter and fibrosis be filled with retroperitoneal fat. The ureter may also be wrapped with omentum, or moved into the abdominal cavity, and then sutured when it is closely anterior to the posterior peritoneum.

Many new surgical methods have been applied clinically. Gore-Tex surgical membrane can be placed between intraperitoneal ureter and retroperitoneum without closing retroperitoneum. If ureter is invaded, a segment of ureter may be resected while end-to-end anastomosis is

performed. When patients who don't respond to ureterolysis and hormone therapy or can't tolerate surgery develop persistent ureteral damage or recurrent obstruction, autologous renal transplantation in pelvis should be considered. Laparoscopic ureterolysis and intraperitoneal placement may be an alternative approach for the treatment of unilateral ureteral obstruction.

6.2 Medical Treatment

Medical treatment of retroperitoneal fibrosis aims to control chronic inflammation. Surgical treatment targets one consequence of retroperitoneal fibrosis, namely, ureteral obstruction, but can't control progressive inflammation and fibrosis that may involve other retroperitoneal structures in advanced stage. Although it has been successfully relieved by ureterolysis in approximately 90% of cases, ureteral obstruction may relapse in up to 22% of patients treated with ureterolysis alone. The relapse rate of retroperitoneal fibrosis following surgery alone is reported to be 48%; in contrast, the concomitant use of steroids with surgery can reduce the relapse rate to 10%. Large cohorts of cases demonstrate that hormone plus surgical treatment is indicated for patients with advanced renal failure, serious upper urinary tract dilatation, and urinary tract abscess.

Steroid as medical therapy for retroperitoneal fibrosis was first reported by Ross and Tinckler (1958). Through inhibiting inflammatory response and the maturity of fibrous tissue, steroid can produce desirable effect in controlling chronic inflammation of retroperitoneal fibrosis. The effective rate of steroid therapy is 100%. Patients with idiopathic retroperitoneal fibrosis who develop mild urinary obstruction without significant metabolic abnormalities or systemic symptoms can be treated with steroids alone. In the first 24 h after initiation of treatment, symptoms can be improved and renal function recovered significantly. Within 3 days, retroperitoneal soft tissue can be significantly reduced, accompanied by decreased hydronephrosis. Steroid therapy, although effective in the treatment of active inflammation of retroperitoneal fibrosis, is of little benefit to the advanced acellular fibrotic stage.

The dose of steroids is usually determined based upon the experience of clinicians. The treatment course is mostly considered to be at least 6 months. Alternatively, a long-term low-dose regimen is considered to be effective and safe. Sustained elevated ESR level generally serves as an indication for administration of steroids, while normal ESR level is an indication for discontinuation of steroids.

Interestingly, "spontaneous" improvement of retroperitoneal fibrosis followed by "spontaneous" improvement of contralateral ureteral obstruction may be observed in patients who undergo unilateral ureterolysis. Sometimes biopsy alone can produce significant improvement in clinical symptoms of the patients. These phenomena may be explained by increased endogenous steroids during the perioperative period. The level of plasma steroid hormone was reported to be increased by two times in patients with asthma and rheumatoid arthritis during surgery and remained at a higher level for 1–3 days after surgery.

The clinical use of steroid as therapy remains controversial although it has been proved to be effective in retroperitoneal fibrosis. The most significant disadvantage in the treatment of retroperitoneal fibrosis is lack of histological evidence for diagnosis and exclusion of malignant lesions. Many surgeons believe that biopsy is the most fundamental method to rule out malignant lesions. Since there is a small amount of tumor cells in rich inflammatory infiltrates, multipoint deep biopsy is needed. CT-guided fine needle aspiration or core needle biopsy plays little role or even becomes impractical because of very limited tissue specimen. It is also reported that a few cases of malignant retroperitoneal fibrosis were diagnosed properly several months later when they were initially misdiagnosed as idiopathic (nonmalignant) retroperitoneal fibrosis by biopsy.

Steroid therapy for retroperitoneal fibrosis has definite advantages as the following: firstly, patients with acute RPF can be treated with

steroids to relieve ureteral obstruction caused by edema and to improve clinical symptoms, so that they may receive elective surgery rather than emergency surgery and temporary ureteral stent placement and, secondly, steroids may serve as an adjuvant therapy after surgery to inhibit the progression of fibrosis and thus prevent further obstruction and subsequent symptoms.

Wagenknecht and Hardy (1981) reported that steroids exhibit optimal effect as adjuvant therapy following ureterolysis. However, in some cases, steroids adjuvant therapy failed to prevent the recurrence of obstruction. Third, elderly and weak patients, or those in whom the possibility of malignancy has been ruled out, can be treated with steroid alone.

Recently, immunosuppressive drugs, such as azathioprine and cyclophosphamide, are used to treat retroperitoneal fibrosis. The efficacy of these drugs provides strong support for the notion that retroperitoneal fibrosis belongs to autoimmune diseases. Tamoxifen is also effective in treating this disease, although the mechanism remains unclear, probably related to increased synthesis and secretion of an inhibitory growth factor-TGFβ.

6.3 Radiotherapy

Radiotherapy is another effective method for the treatment of idiopathic retroperitoneal fibrosis. A few cases in our hospital were treated with surgery plus postoperative radiotherapy rather than complete tumor resection alone and had achieved long-term survival.

7 Efficacy and Prognosis

The prognosis of patients with idiopathic retroperitoneal fibrosis is determined by the degree of renal dysfunction, the presence or absence of, as well as the extent of urinary tract infection, and stable or progressive disease status. Retroperitoneal fibrosis itself continues to progress after surgery; therefore, its complications, such as obstruction of inferior vena cava or duodenum, should be further observed. Patients may be regularly examined by CT. Additionally, prognostic factors such as renal function, hematocrit, and especially ESR (increased level of ESR reflects the degree of inflammation) should be followed up. Unlike those with idiopathic retroperitoneal fibrosis, patients with malignant retroperitoneal fibrosis have a poor prognosis. The majority of patients can only survive 3–6 months after the diagnosis although long-term survival has been reported in some cases.

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Retroperitoneal Fibromatosis

19

Cheng-Hua Luo and Xiaobing Chen

1 Introduction

Fibrous tumors and tumorlike lesions consist of a large group of clinical diseases with different natures and biological behaviors. Some are benign and rarely relapse, even if they are not completely removed; others are ill-defined, infiltrating the surrounding tissue, and tends to recur even if large-scale removal is performed. Some typical malignant tumors have high recurrent and metastatic rates. According to clinical and pathological features, these tumors can be classified into four categories: (a) benign fibromatosis, (b) fibromatosis, (c) fibrosarcoma, and (d) fibrosis in children and babies. Fibromatosis is divided into abdominal fibromatosis (or abdominal desmoid) and extra-abdominal fibromatosis. The former consists of abdominal wall and intra-abdominal fibromatosis. Intra-abdominal fibromatosis includes pelvic fibromatosis, mesenteric fibromatosis, and mesenteric fibromatosis in Gardner's syndrome. Strictly speaking, mesenteric fibromatosis should be classified into retroperitoneal fibromatosis. Additionally, there are some types of fibromatosis that really arise in retroperitoneum. Therefore, mesenteric and retroperitoneal fibromatosis is collectively discussed in this chapter.

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More than 1000 cases of desmoid tumor, also known as aggressive fibromatosis, have been reported since it was firstly described by Macfarlane in 1832. Muller reviewed the disease in 1938 and introduced the term "desmoid" to denominate such tumor. Desmoid tumor is very rare, for example, systemic fibromatosis accounts for less than 3% of soft tissue tumors; however, the exact incidence is difficult to estimate. It is reported that approximately two-thirds of fibromatosis occurs in the abdominal wall, followed by the neck and scapular area. It rarely occurs in retroperitoneum and pelvis, of which mesentery is relatively common. The term "desmoid" was originally used to define abdominal fibromatosis in newly pregnant women. Indeed, abdominal desmoid prevails in pregnant and post-parturient women aged at 20–35 years; however, the tumor can also occur in any part of the bodies of men and children.

2 Etiology

Up to now, the etiology of fibromatosis is poorly understood, which may be related to trauma. Similar to extra-abdominal fibromatosis, genetic, endocrine, and physical factors play important roles in the pathogenesis of intra-abdominal fibromatosis. Some tumors develop concomitantly with polyposis syndrome, which are commonly seen in the previous surgical incision sites. The fact that such tumors often occur during

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pregnancy and after childbirth provides evidence for critical involvement of endocrine factors. The disease is also reported to subside in some patients during perimenopausal period. Mardones et al. (1955) found that long-term estrogen-fed guinea pigs developed desmoid tumor, which might be prevented by administration of testosterone, progesterone, and deoxycorticosterone. Lim et al. (1986) demonstrated that one-third of patients with desmoid was estrogen receptor (ER) positive, and 79% of these cases had positive antiestrogen binding sites. The role of endocrine factors in the pathogenesis of such tumors is also supported by the suppressive effect of antiestrogen agents such as tamoxifen.

Trauma may contribute to intra-abdominal fibromatosis. Some tumors are originated in the scar areas caused by appendectomy, laparotomy, and other abdominal surgeries. Most patients with intra-abdominal fibromatosis have no history of trauma. It is speculated that small trauma such as mild muscle tear may contribute to the onset of fibromatosis in the context of hormonal and genetic background.

3 Pathology

Histologically, retroperitoneal fibromatosis lacks cytological features of malignant tumor, which consists of differentiated fibroblasts, without definite tumor cells. In the term "aggressive fibromatosis," "fibromatosis" refers to proliferation of infiltrating fibroblast without evidence of inflammation, and "aggressive" refers to its local biological characteristics of malignant behavior. Although they are not metastasized, fibromatosis lesions significantly infiltrate adjacent tissue.

Aggressive fibromatosis is indistinguishable from other fusiform-shaped fibroproliferative disorders (FPDs), such as nodular fasciitis, reactive fibrosis, low-grade malignant fibrosarcoma, malignant fibrous histiocytoma, and malignant schwannoma. Usually, aggressive fibromatosis is obviously manifested as cytologic atypia, metaplasia, active mitosis, and extensive necrosis.

4 Clinical Manifestation and Diagnosis

Aggressive retroperitoneal fibromatosis is mainly manifested as an abdominal mass which is asymptomatic or presents with mild pain accompanied by mechanical compression of adjacent organs. Weight loss is commonly seen in these patients. Clinically, it is often misdiagnosed as ovarian cancer or mesenteric cyst. Large extraperitoneal desmoid tumors may infringe on the bladder, vagina, or rectum or cause hydronephrosis, leading to oppression of iliac vessels. Clinically, desmoid tumor may be either an independent disease or a part of Gardner's syndrome, which consists of multiple familial colon polyps, tumors of ectodermal, and mesodermal origin, such as osteoma, sebaceous cysts, and fibromatosis.

5 Treatment

Wide local excision of tumor with adjacent normal tissue is currently the most effective approach for the treatment of aggressive fibromatosis. It is highly recommended that surgical margin for excision of the tumor should be 2–3 cm. Due to the infiltrating growth pattern of a tumor into the surrounding tissue, it is almost impossible to determine the tumor margin clinically. Preoperative CT and MRI can provide reliable information about anatomical localization and tumor resectability. Sometimes, complete resection is technically challenging, and substantially complete resection is accompanied by a high rate of local recurrence. Retroperitoneal location of the tumor makes it more challenging for surgeons to perform en bloc resection. The recurrence rate has been reported to be as high as 50%. In patients with Gardner's syndrome who develop aggressive retroperitoneal fibromatosis, the rate of en bloc resection is only 50%. In some studies, patients could obtain relatively long disease-free survival even when they have not undergone radical resection as indicated by pathological findings. The relapse rate of aggressive fibromatosis is comparable between complete and incomplete resection (17% vs. 25%).

Some patients with extraperitoneal desmoid were reported to achieve complete remission after receiving high-dose radiation therapy. Auxiliary external beam irradiation or intermittent irradiation at short distance may alternatively take the place of radical resection, in order to avoid or reduce serious postoperative complications (such as disability or amputation) and lower the risk of recurrence. It is recommended that patients are treated with daily fraction of 1.8–2.0 Gy to a total dose of 45–46 Gy followed by a boost of 10–15 Gy after incomplete resection. It remains unclear whether desmoid remission may be achieved by low-dose irradiation alone in patients with retroperitoneal tumor.

Although chemotherapy drugs play a limited role, some patients with desmoid in other parts of the bodies have been successfully treated with the concomitant use of vincristine, actinomycin D, and cyclophosphamide. The use of hormone therapy is also reported in the treatment of patients with desmoid. Desmoid occurs most often in pregnant women, especially in those after childbirth, indicating its hormone-dependent nature. This notion is evidenced by the successful use of tamoxifen, nonsteroidal anti-inflammatory drugs, and cholesterol cortex hormone therapy.

6 Mesenteric Fibromatosis

Mesenteric fibromatosis is the most common tumor in mesentery. Most cases occur sporadically, while some are related to Gardner's syndrome, trauma, or high estrogen status. Most commonly, these tumors are located in the small bowel mesentery (SBM); some originate from the ileocolic mesentery, gastrocolic ligament, omentum, or retroperitoneum. In the absence of history of recurrent polyps, it is difficult to distinguish mesenteric fibromatosis from other fibrosis, such as idiopathic retroperitoneal fibrosis or sclerosing mesenteritis.

Similar to pelvic fibromatosis, most mesenteric fibromatosis is manifested as asymptomatic abdominal mass, despite being accompanied by mild abdominal pain. Unusual manifestations include gastrointestinal bleeding or acute abdomen caused by intestinal perforation. Sometimes, this disease may accidentally be detected during the intestinal resection in patients with Crohn's disease. In the largest cohort study (up to now), Burke et al. (1990a, b) reported that the disease is more prevalent in men with an average age-of-onset of 41 years.

Like other retroperitoneal tumors, the maximum diameter of most mesenteric fibromatosis is 10 cm or more. Many tumors grow very rapidly in early stages and cause hydrocephalus by compressing the ureter or lead to intestinal obstruction by compressing the large and small intestine and even result in intestinal perforation and severe complications. In general, most tumors are encapsulated intact, although typical microscopic lesions are characterized by invasion to the surrounding soft tissues including the intestinal wall.

Under microscope, mesenteric fibromatosis consists of slight spindle-shaped or stellate-like cells that are uniformly accumulated in a dense collagen matrix with varying cellularity, which is almost completely replaced by dense fibrous tissue in some areas. Obvious myxoid change in matrix is observed in other areas. Collagen fibers in sporadic keloid may appear, thin-walled veins dilate significantly, and muscle cell proliferation can be seen in small arteries. Except in the cases of intestinal perforation, inflammation is usually unobvious.

It should be differentiated from the following diseases: (a) sclerosing mesenteritis, which is associated with meningitis and mesenteric lipodystrophy, characterized by fibrosis and significant chronic inflammation and bulging of the intestinal wall rather than infiltration; (b) inflammatory fibrosarcoma of the mesentery and retroperitoneum, presenting more definitive atypical cells, less fiber, and more evident inflammation compared with mesenteric fibromatosis; and (c) idiopathic retroperitoneal fibrosis, which is associated with the use of ergometrine and inflammatory abdominal aortic aneurysm. It shows denser hyaline degeneration and more obvious inflammation than fibromatosis. Likewise, fibromatosis located in this site

also shows a tendency to locally recur, although its relapse rate varies. Burke et al. (1990a, b) reported the relapse rate is 23% for idiopathic retroperitoneal fibrosis, whereas 90% and 12% in fibromatosis with and without Gardner's syndrome, respectively. Practically, patients without Gardner's syndrome did not experience multiple relapse, and no death directly caused by the disease was reported. On the contrary, most of patients with Gardner syndrome experienced more than one relapse, and four patients died of the tumor, indicating that Gardner's syndrome is a risk factor predicting the poor prognosis of mesenteric fibromatosis.

Therapeutic management for mesenteric fibromatosis is similar to that of extra-abdominal fibromatosis; however, its irregular growth and adhesion with the small intestine render surgical removal more difficult. Other treatments, including the use of antiestrogen agents and steroids, cytotoxic chemotherapy, and postoperative radiotherapy, can achieve varying degrees of efficacy.

Similar to pelvic fibromatosis, the most likely etiology is tissue damage in patients with a hereditary predisposition. Of the cases of nonpolyposis reported by Burke et al. (1990a, b), 12 (11%) had previous history of abdominal surgery before diagnosis of fibromatosis. Secondary lesion as the same as mesenteric fibromatosis was located in the scar area for abdominal incision. Individual case of mesenteric fibromatosis secondary to radiation therapy for Hodgkin's disease or testicular seminoma has also been reported (Rosoff et al. 2005). Mesenteric fibromatosis may spontaneously occur to those without polyposis or previous surgery history.

Nichols firstly found that desmoids were closely associated with familial polyposis. In 1951, Gardner reported the familial incidence of multiple intestinal polyps, osteomas, fibromatosis, and epidermal cyst or sebaceous cyst. This association with familial polyposis and osteomas was termed as "Gardner's syndrome" by Smith in 1958.

Mesenteric and retroperitoneal fibromatosis often occur in patients with Gardner's syndrome 1–2 years after the removal of intestinal lesions. Most studies found that fibromatosis occurred in approximately 10% of patients with multiple polyps.

Gurbuz et al. (1994) estimated that the absolute risk of desmoid in patients with multiple polyps was 852 times of that in healthy populations, of which 68% underwent abdominal surgery prior to tumor formation. Occasionally, the same lesion also appears in the abdominal incision scar. Not all fibromatosis was caused by trauma, which was found in a few cases before the surgery. Kawashima et al. found that Gardner-related fibromatosis had a tendency for multicenter and mesenteric onset, smaller in size, and no obvious prevalence in women compared to nonpolyposis cases.

Clinically, fibromatosis may be asymptomatic or just causes mild abdominal pain or bowel obstruction due to invasive growth of tumors into the large and small intestine. Although most tumors grow slowly, Goldblum and Fletcher (2002) reported that in a 40-year-old man, the maximal diameter of fibromatosis grows from 4 cm to 27 cm only in 1 year.

Histologically, mesenteric fibromatosis is virtually indistinguishable from that at other sites, and one cannot distinguish polyposis-related cases from sporadic cases by morphology alone. These tumors tend to have a prominent myxoid matrix, and tumor cells may be arranged in a vague storiform pattern, just like benign and malignant fibrous histiocytoma.

It is difficult to perform complete resection of nonpolyposis mesenteric fibromatosis, which often requires resection of quite long length of bowel. For tumors growing rapidly, intra-abdominal complications caused by tremendous size of the tumor should be prevented. Relapse is common, which occurs more frequently and more seriously in polyposis-related fibromatosis than sporadic counterpart. It is reported that endocrine therapy (tamoxifen and prednisolone),

noncytotoxic drugs (sulindac and indomethacin), and chemotherapy are effective for recurrent and inoperable cases.

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Retroperitoneal Fibrosarcoma

20

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It is reported that among 500 cases of fibrosarcoma located in any part of the body, only 3% occurs in the retroperitoneum (Gutierrez et al. 2007). Several cases of mesenteric fibrosarcoma are also reported. With the establishment of strict diagnostic criteria over time, fibrosarcoma is even rarely seen. Since there is an overlap with previous diagnostic criteria, the exact proportion of fibrosarcoma in retroperitoneal tumor is unclear. Of 120 cases of primary retroperitoneal tumor, only 6 were fibrosarcoma as reported by Pack and Tabah (1954a, b). Of 107 cases of retroperitoneal tumor, 5 were fibrosarcoma as reported by Frank and Velasco (2013). Two cases of fibrosarcoma out of 48 cases of retroperitoneal tumor were reported by Felix et al. (1981). A much higher proportion of retroperitoneal fibrosarcoma in primary retroperitoneal tumor was reported by Donnelly (1946) (21%) and Braasch and Mon (1967) (16%).

1 Clinical Pathological Features

Retroperitoneal fibrosarcoma is most commonly seen in people aged 50–60 years old. Due to lack of specific clinical manifestations, it is difficult to discriminate retroperitoneal fibrosarcoma from other retroperitoneal tumors before surgery. The chief complaint is a painless mass. These tumors grow slowly and eventually invade neighboring organs. The final diagnosis is only dependent on histological examination.

Generally, retroperitoneal fibrosarcoma appears as an encapsulated, uniformly firm, round, or fusiform mass. The section of retroperitoneal fibrosarcoma usually presents gray-to-white color, with hemorrhagic and/or necrotic areas. It is difficult to distinguish benign from malignant fibrous tumor cells under microscope. Benign fibrous tumor is composed of spindle cells arranged in interlacing and woven bundles, surrounded by reticular fibers and collagen fibers arranged parallel to the long axis of the cells. By contrast, fibrosarcoma contains less fiber which does not surround individual cell. There are no multinucleated giant cells in fibrosarcoma tissues; however, a single sarcoma cell may be disproportionately increased in size compared to normal cells. Additionally, microscopic examination often reveals fibrosarcoma with increased mitotic figures. Retroperitoneal fibromatosis may be differentiated from other spindle cell sarcomas based on the binding of Bcl-2 to CD34.

Metastasis in retroperitoneal fibrosarcoma is rare compared to that in other tumors of mesodermal origin. Retroperitoneal fibrosarcoma typically metastasizes through the bloodstream to the lungs. 21% of patients with fibrosarcoma

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metastasizes to the lung. Pack and Tabah (1954a, b) reported that one of six patients with retroperitoneal fibrosarcoma experienced pulmonary metastases. In a study conducted by McNamara et al. (1968), two of eight patients with retroperitoneal fibrosarcoma developed lung metastases.

2 Treatment and Prognosis

Retroperitoneal fibrosarcoma should be surgically removed once it is identified. A high rate of local recurrence is observed after surgical resection. Scout found that poorly differentiated fibrosarcoma has a higher postoperative local relapse rate (75%) compared to well-differentiated fibrosarcoma (42%). The relapse rate was reported as 56% by Pack (1954a, b) in 39 cases of somatic soft tissue fibrosarcoma.

Invasion of adjacent tissue and restriction of retroperitoneal structure make it more difficult to completely remove retroperitoneal fibrosarcoma. A 5-year survival rate of patients with retroperitoneal fibrosarcoma is 25% (van der Werf-Messing and van Unnik 1965). The overall survival rate of patients with fibrosarcoma in all parts of the body is 40–60%, which is superior to that of retroperitoneal fibrosarcoma.

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Extragastrointestinal Stromal Tumors (EGISTs)

21

Quan Jiang and Weiqi Lu

1 Introduction

Until 2002, stromal tumor has been re-recognized and correctly named, which was confused with leiomyomas for such a long time. A breakthrough has been made on stromal tumor over this short span of a decade. Especially the use of imatinib, a tyrosine kinase inhibitor (TKI), allows stromal tumor to become a model for targeted therapy. Gastrointestinal stromal tumor (GIST) is the most common gastrointestinal mesenchymal tumor, accounting for 2% of all gastrointestinal tumors. GIST often occurs in the stomach (40–70%), small intestine (20–40%), colon (5–15%), and rectum (5%). On the contrary, primary extragastrointestinal stromal tumor (EGIST) accounts only a very small percentage of all stromal tumors. EGIST occurs frequently in the mesentery, omentum, and peritoneum but rarely in the retroperitoneum. Up to now, only 59 cases have been reported. EGIST is commonly seen in young and middle-aged people, with an incidence comparable between men and women. EGIST often grows very large before it is detected incidentally, resulting in a low rate of complete resection and a high rate of recurrence (even after complete surgical resection). Although located in different primary sites, EGIST is substantially similar to GIST in terms of pathology and immune phenotype. Under microscope, tumor cells are short spindle, nest, sheet, or vesicle shaped, with translucent cytoplasm. Immunohistochemistry reveals CD117 positive, as well as actin, calponin, and S100 positive or weakly positive. C-kit gene mutation is detectable. Under electron microscope, tumor cells appear as irregular fusiform with intertwined pseudopodia of varying lengths extending toward the surrounding area and rich in original intercellular connection. CT and MRI identify "abdominal mass" in the majority of patients with EGIST, which is diagnosed based on postoperative pathology. Currently, surgery remains the most common treatment for EGISTs. Although the use of imatinib has revolutionized treatment and improved outcomes for patients with GIST, little is known with regard to its efficacy in EGIST.

2 Etiology and Pathogenesis

As noted above, genetic alteration and immunohistochemical characteristics of EGIST are substantially consistent with GIST, suggesting that both diseases may share common molecular mechanisms. Regarding the cellular origin, it is most widely accepted that GIST arises from mesenchymal progenitor cells or immature stem cells that are differentiated toward the ICC

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(interstitial cell of Cajal). ICC located intramurally are pacemaker cells to create the bioelectrical slow wave potential that leads to contraction of the smooth muscle. ICC is crucial to initiation and functional regulation of gastrointestinal motility. ICC is considered as the origin of GIST based on the following facts: (a) the activation of intestinal ICC requires the participation of C-kit; (b) the positive expression of CD117 is a classic immunophenotype of ICC; and (c) GIST cells highly resemble ICC under electron microscope.

Overwhelming amount of data have proved the close relationship between ICC and GIST; however, the cellular origin of EGIST is yet to be elucidated. From the view of anatomical position, ICC can be definitively ruled out as the cellular origin of EGIST due to their location within muscle layers of the gastrointestinal tract wall. A considerable part of EGIST cases reported in previous literatures might be originated from GIST and grow extraluminally. In the absence of visible anatomical connection to primary gastrointestinal tract, GIST is misdiagnosed as EGIST clinically. There is another possibility that EGIST may have deviated from the original site of the gastrointestinal tract in the process of tumorigenesis. It is also suggested that EGIST may originate from mesenchymal pluripotent stem cells of multiple differentiation potential. In a retrospective analysis conducted in 14 cases of EGIST, the stump of seromuscular layer is observed on the margin of tumor pseudocapsule in 8 cases after HE staining, which was further confirmed as desmin positive by immunohistochemistry. Two out of 14cases were finally diagnosed as extensive metastases of GIST into abdominal cavity. Interestingly, among them, one case was diagnosed with multiple celiac EGIST. Although the presence of GIST was ruled out, this patient had partial resection of the small intestine 5 years ago due to an abdominal mass in another hospital, and postoperatively histological findings suggested solitary fibromatosis, as mentioned in his medical history records. At that time, the diagnosis of GIST relied more on CD34, so that GIST might easily be misdiagnosed as solitary fibromatosis.

Recently a patient with large abdominal mass was admitted to Zhongshan Hospital of Fudan University. Endoscopy did not identify occupying lesions of stomach; however, CT image displayed a large mass in peritoneal cavity, indicating mesenchymal tumor of unknown origin (Fig. 21.1). Intraoperatively, a fairly large mass was found in the omentum, which was irregularly shaped, soft in nature, and easy bleeding by touch. After complete removal of the mass from the omentum, a 5-cm-long and 0.5-cm-wide (at the basal part) cord linking to the greater curvature of the stomach was identified. Postoperative pathology suggested GIST. Intraoperatively, the mass was easily detached from the cord with a little force. If the tumor was confused with the attached cord to be separated, it would be postoperatively misdiagnosed as EGIST (Fig. 21.2). This experience suggests that the incidence of EGIST may be much lower than expected. How to correctly define GIST is worthy of further discussion. In the clinical diagnosis, efforts should be taken to seek for sufficient evidence, thus providing accurate guidance for the postoperative treatment of those patients.

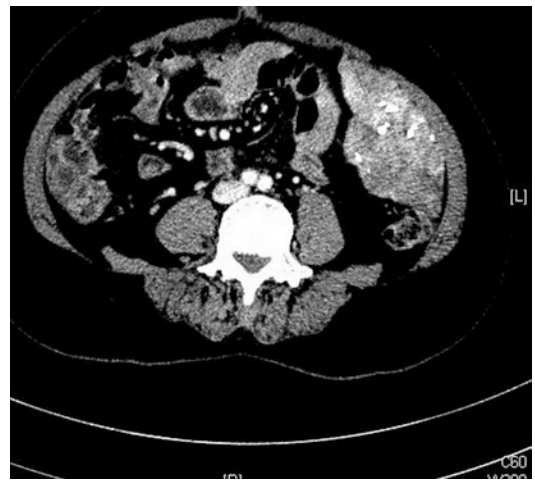

Fig. 21.1 CT image displays a huge mass, mesenchymal tumor of unknown origin in peritoneal cavity

3 Pathology

EGIST mostly appears as a solid mass in gray-pink color, surrounded by pseudo-fibrous capsule, in round or lobulated shape, with cross section in gray or reddish brown color. Unlike leiomyoma, it lacks common spiral structure, occasionally accompanied by mucus degeneration, hemorrhage, necrosis, and cystic degeneration. Calcification is sporadically observed, relatively common in large tumors but not in small ones. Under microscope, the tissue structure is complex and cell morphology varies, similar to GIST. Based on cell morphology, it can be divided into three categories: (a) spindle cell type (70%), (b) epithelial cell type (20%), and (c) mixed (10%). Immunohistochemical markers associated with GIST are the most important tool for the diagnosis. Among them, the relatively specific parameters to be detected include CD117, DOG-1, and CD34, whereas nonspecific parameters that are mainly attributable to differential diagnosis include SMA, S-100, caldesmon, desmin, vimentin, and nestin (Table 21.1).

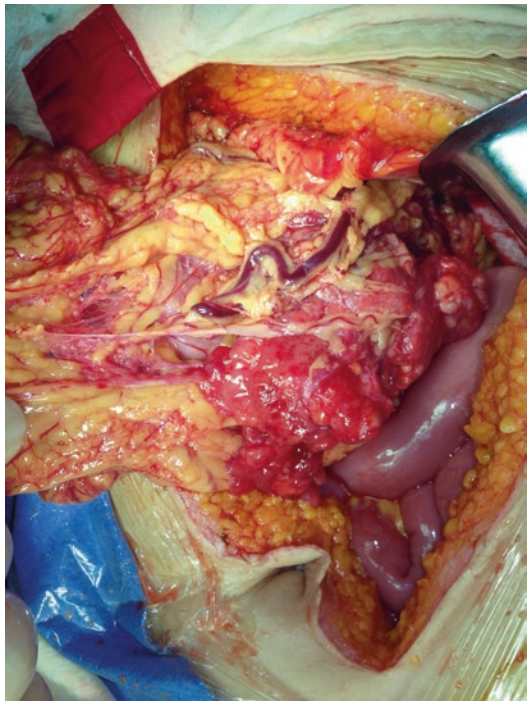

Fig. 21.2 Intraoperatively the mass is easily detached from the cord under a little force, or it is frequently confused with attached cord to be separated and misdiagnosed as EGIST postoperatively

4 Clinical Manifestation and Diagnosis

Clinical manifestations of EGIST are similar to general retroperitoneal tumors. Chief complaints include (a) abdominal mass, lower back pain, abdominal pain, and bloating; (b) difficulty in urination and defecation and lower limb pain, if it occurs in retroperitoneum and pelvis; and (c) fever, if the tumor is necrotic. Some patients feel no obvious discomfort and consult doctors only because of anemia and fatigue. Due to deep location, large space from surrounding tissue, and late presentation of clinical symptoms, the volume of retroperitoneal EGISTs often grows large, with the maximal diameter up to 32 cm at the time of diagnosis.

Table 21.1 Differential diagnosis of GIST with other tumors: immunohistochemical and molecular markers

Tumor	KIT	DOG1	CD34	SMA	CALDES	DES	S-100	Other
GIST	+	+	+	±	+	−	−	
Smooth muscle tumor	−	−	−	+	+	+	−	
Solitary fibromatosis	−	−	+	−	−	−	−	CD99, BCL-2
Inflammatory myofibroblastic tumor	−	−	−	+	−	+	−	ALK-1
Schwann cell tumor	−	−	−	−	−	−	+	
Malignant peripheral nerve sheath tumor	−	−	−	−	−	−	+	GFAP

Due to limited number of patients, the imaging data are scarce, and only a few studies on imaging features of EGIST have been reported. Preoperative imaging plays an important role in determining the origin of tumor, and the following manifestation contributes to predict the accurate location of tumor arising from the retroperitoneum: (a) the center or the maximum axis diameter of the tumor located in the retroperitoneum; (b) forward displacement of kidneys, pancreas, intestine, and other organs under compression; (c) embedded tumor pushing large abdominal vessels forward or laterally; and (d) fat space existing between the tumor and abdominal organs. Any tumor necrosis or hemorrhage, if occurs, will seriously affect the imaging manifestation of tumor. The diagnosis of EGISTs should be made based on specific imaging features combined with the general radiological characteristics of GIST through individual analysis, rather than mechanical imitation of imaging study of GIST. A case of primary retroperitoneal EGIST showed a well-defined and heterogeneous peripancreatic mass, about $16 \times 15 \times 18$ cm^3 in size, with annular calcification on CT image. Enhanced CT identified a heterogeneous mass, progressive contrast enhancement. The tumor compressed but did not invade the pancreas, stomach, or spleen. MRI showed a retroperitoneal mass with heterogeneous intensity signals on T1- and T2-weighted images and heterogeneous enhancement of the tumor on gadolinium-enhanced T1-weighted image with fat suppression. Generally, a small tumor is more homogeneous than a large one accompanied with calcification, necrosis, and other degenerative lesions. Malignant tumors are often surrounded by soft tissue, 86% of which having well-defined boundary. The density or signal strength of tumor is lower than that of enhanced liver during the same period. PET-CT may be considered for multiple EGISTs, although its clinical significance requires further investigation.

5 Risk Stratification System

Accurate assessment of the patient's condition and choosing the optimal treatment regimen for individual patient have become the focus of personalized therapy. Since stromal tumor was not recognized until 2002, clinicians (Fletcher et al. 2002a, b) reached a consensus on the criteria for classification of GIST, which is now the most commonly accepted in clinical work. GIST usually presents malignant potential, while benign GIST does not exist at all. Therefore, malignant risk of GIST is classified into minimal, minor, intermediate, and high levels. Tumor size and mitotic figure are used as the specific parameters to identify GIST. However, the biggest problem arising from the cutoff value of mitotic figures at 50/HPFs in clinics is ignoring the significant effect of tumor location and progressive rupture on the assessment. Furthermore, such parameter cannot simply apply to EGIST. For this reason, such criteria have been improved. Franquemont et al. (1992, 1995) reported that R1 resection and rupture of stromal tumor are closely related to poor prognosis. Peritoneal implantation, tumor metastasis, and invasion of adjacent organs are considered as predictors for high-degree malignancy by Fletcher et al. (2002a, b). In their opinion, EGIST with the above risk factors, regardless of tumor size and mitotic activity, is classified as high-degree malignancy. On the basis of Fletcher's opinion, Joensuu proposed new criteria including the presence of tumor rupture as a high-risk factor independent of size and mitotic count. Further modification in Joensuu's criteria reclassified non-gastric tumors in the NIH intermediate category to the high-risk group (Table 21.2). According to NIH criteria, EGIST should be classified as high-risk tumor; however, due to lack of sufficient cases of EGIST, further studies are guaranteed to verify the applicability of such criteria in evaluation of EGIST.

6 Treatment

Surgery remains the most effective treatment for EGIST. The basic principles are similar to those for general retroperitoneal tumors, namely, striving for R0 resection. To avoid tumor capsule rupture and intraperitoneal spread intraoperatively, if the tumor invades adjacent organs, the involved organs should be en bloc resected together with

the tumor. Laparotomy is a common surgical procedure for these patients. If the tumor is small (<2 to 5 cm) in size, laparoscopic surgery would be an option. Sometimes, in order to protect vital organs from being damaged, R1 resection is acceptable, but palliative surgery is not recommended. EGIST, especially retroperitoneal GIST, often grows very large and closely relates to surrounding organs and large blood vessels at diagnosis. Definite diagnosis allows patients to be treated with targeted drugs to shrink the tumor preoperatively. C-KIT exon 11 mutations have been identified in most of EGIST cases, so imatinib may be a preoperatively adjuvant therapy appropriate for them from this perspective. A patient with inoperable multiple peritoneal stromal tumors had experienced a significant reduction in tumor size after preoperatively receiving imatinib as neoadjuvant therapy and ultimately underwent R0 resection. As noted previously, the origin of EGIST remains controversial. If the tumor arises from GIST that grows extraluminally, this hypothesis would be convincible, further supporting the effectiveness of imatinib therapy. Collectively, targeted therapy can be used as an alternative strategy.

Table 21.2 NIH risk stratification system for primary GIST after resection

Classification of risk degree	Tumor size (cm)	Mitotic index (50/HPF)	Primary site
Minimal	≤2.0	≤10	Any
Minor	2.1–5.0	≤5	Any
Intermediate	2.1–5.0	>5	Stomach
	<5.0	6_10	Any
	5.1–10	≤5	Stomach
High	Any	Any	Tumor rupture
	>10	Any	Any
	Any	>10	Any
	>5.0	>5	Any
	2.1–5.0	>5	Non-primary gastric
	5.1–10	≤5	Non-primary gastric

7 Efficacy and Prognosis Factors

It is now widely accepted that CHOI or RECIST criteria for GIST targeted therapy also apply to the efficacy evaluation for EGIST. According to RECIST criteria, a decrease of more than 30% in the maximum diameter of tumor size is considered as response. Patients with GIST who respond to targeted therapy tend to present varying changes in tissues in early stage, which are characterized by necrosis, hemorrhage, cystic degeneration, and mucus. The volume of tumor may not be obviously shrunk and even becomes slightly larger because of hemorrhagic necrosis. Therefore, Choi et al. (2007) proposed a new evaluation criteria—CHOI for GISTs in combination with dynamic change rate of strengthened CT value (Table 21.3)—which may provide a reference for retroperitoneal EGIST. The prognosis of EGIST is affected by many factors such as primary tumor site, size, mitotic figures, and necrosis, all of which are considered to be important predictors of clinical outcome. EGIST originating in retina results in better prognosis than that in mesentery. It is also reported that the survival period is shorter in patients aged <50 years old than those aged ≥50 years old. Additionally, Joensuu et al. (2002, 2012) demonstrated that active mitosis,

Table 21.3 CHOI criteria for efficacy of retroperitoneal extragastrointestinal stromal tumor

Efficacy	Definition
CR	Disappearance of all lesions. No new lesions
PR	≥10% decrease in maximum diameter of tumor size and/or a ≥15% decrease in tumor density (HU). No new lesions. No obvious progression of non-measurable disease
SD	Does not meet criteria for CR, PR, or PD. No symptomatic deterioration attributed to tumor progression
PD	≥10% increase in maximum diameter of tumor size; change in HU doesn't meet PR criteria; the appearance of new lesions and intratumoral nodules or an increase in size of the existing intratumoral nodules

large tumor size, and the presence of tumor necrosis could predict poor prognosis.

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Retroperitoneal Angiofollicular Lymph Node Hyperplasia (Castleman's Disease)

22

Yunfu Cui, Pengcheng Kang, Shiwen Mei, and Chengli Miao

1 Introduction (Epidemiology)

Angiofollicular lymph node hyperplasia, also known as giant lymph node hyperplasia or Castleman's disease (CD), is a chronic lymphoproliferative disorder. It was firstly reported and named by Castleman and Towne (1954), which is one of unexplained reactive lymphadenopathy characterized by painless enlargement of giant lymph nodes. Vascular follicular lymph node hyperplasia is rarely seen with an unclear incidence. It can occur at any age, more common in people aged 10–45 years. There is no significant difference in incidence between men and women. Medical history of the patients may range from several months to decades. Castleman's disease is mainly manifested as enlargement of lymph nodes in any part of the body, most commonly seen in mediastinal lymph nodes (70%) and spreading along the bronchial and tracheobronchial tree or hilar lymph node to the neck, shoulders, armpits, groin, and vulva (20%), while rarely arises from the retroperitoneum or mesentery (7%), demonstrating an extremely low incidence of retroperitoneal Castleman's disease.

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2 Etiology

The etiology and pathogenesis of Castleman's disease is unclear, which may be associated with abnormal immune function and chronic inflammation response. Some studies indicate a close relationship between Castleman's disease and infection of human herpesvirus-8 (HHV-8) (Bacon et al. 2004) and Epstein-Barr virus (EBV) (Al-Maghrabi et al. 2006). The presence of HHV-8 in lymph nodes, peripheral blood mononuclear cell, and bone marrow has been confirmed in patients of multicentric plasmacyte subtype. HHV-8 is detected in up to 100% of infected HIV patients with Castleman's disease.

Castleman's disease is often accompanied by increased production of abnormal B-cell growth factor, such as interleukin-6 (IL-6), which mainly stimulates differentiation of lymphocytes and plasmacyte. In the presence of IL-6 gene analogs in HHV-8 genome (Kawabata et al. 2007), lymph node B-cell proliferation is induced by HHV-8 to produce large amount of IL-6. IL-6 is proposed to be involved in the pathogenesis of Castleman's disease, because it promotes upregulation of vascular endothelial growth factor (VEGF) expression and induces vascularization of germinal center in lymph nodes. Thus, immune deficiency or dysregulation may be an important factor contributing to the onset of Castleman's disease (Beck et al. 1994). Furthermore, Schulz (2000) proposed that Kaposi's sarcoma and malignant lymphoma may be associated with immune

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deficiency of angiofollicular lymph node hyperplasia. In summary, the pathogenesis of Castleman's disease results from combined effects of multiple factors, and its etiology needs to be further investigated.

3 Pathogenesis and Pathobiology

The main pathological manifestation of Castleman's disease is tumorlike proliferation of lymphoid tissue and small blood vessels, which is specifically divided into three types:

a. Hyaline vascular type (HV type), accounting for about 80–90% of all types, manifested as hyperplasia of a large amount of follicular dendritic cells, with follicular hyperplasia of varying sizes, distributed throughout the parenchyma of lymph nodes, disappearance or fibrosis of lymph sinus, and smaller germinal center. Small neoarteries with swelling endothelial cells and hyaline degeneration penetrate through the center. The mantle zone that consists of small lymphocytes arranged in a concentric ring ("onion skin") pattern is thickened surrounding germinal centers. Moreover, proliferation of interfollicular capillaries and infiltration of lymphocytes, plasma cells, immunoblasts, and eosinophils are universally presented in hyaline vascular variant.
b. Plasma cell (PC) type, accounting for about 10% of all types, manifested by significant expansion of germinal centers in lymphoid follicles and thinning of surrounding mantle zone. There is massive interfollicular infiltration of mature plasma cells, small lymphocytes, and immunoblasts with Russell bodies, without obvious capillary proliferation.
c. Mixed type, which is rarely seen and characterized by the coexistence of the histopathologic features of both variants. It commonly occurs beyond the lymph nodes.

The positive expression of CD20, CD45RO, CD45RA, and κ- and λ-light chains has been demonstrated in the lymph nodes of Castleman's disease using immunohistochemical staining. Pathological specimen of retroperitoneal Castleman's disease presents as well-encapsulated lymph nodes in oval or circular shape with enlarged volume, varying sizes, and off-white uniform cross section (Fig. 22.1). Hyaline vascular type is the most common one in pathology.

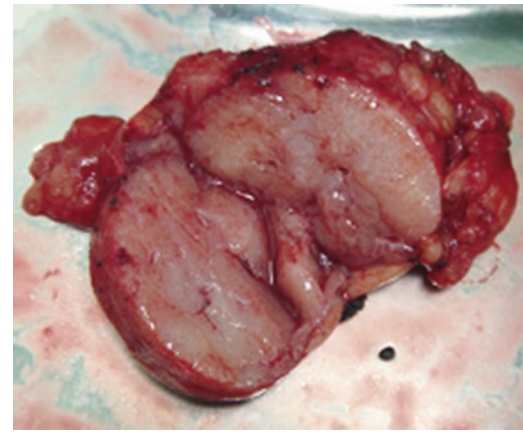

Fig. 22.1 Pathological specimen of retroperitoneal Castleman's disease

3.1 Clinical Manifestation

Castleman's disease can be divided into localized (LCD) and multicentric (MCD) types on the basis of lymph node involvement. LCD is mostly hyaline vascular type and commonly occurs in young people. It is manifested as locally enlarged painless lymph nodes without systemic symptoms in most patients. It frequently develops in the neck, followed by the mediastinum, armpit, and groin but rarely in the extranodal tissue. Compression symptom may be secondary to increased volume of the tumor or involvement of the surrounding tissue or organs.

MCD is plasma cell type dominant and commonly seen in the elderly. It is systemic diffuse lymphadenopathy, mainly manifested as multiple enlarged lymph nodes at different sites of the body, accompanied by systematic symptoms

such as chronic low-grade fever or high fever, fatigue, weight loss, accelerated erythrocyte sedimentation rate (ESR), liver and spleen enlargement, and anemia. It may be complicated by multiple system involvement, such as nephrotic syndrome, autoimmune cytopenias, Sjögren's syndrome, amyloidosis, bone marrow fibrosis, stomatitis, keratitis, paraneoplastic pemphigus (PNP), and POEMS syndrome (polyneuropathy, hepatosplenomegaly, endocrine disorders, elevated M protein levels, and skin pigmentation).

LCD is the major type of retroperitoneal Castleman's disease. It slowly grows along lymph chain in the retroperitoneum or at mesenteric roots and presents as solitary lymph node enlargement. Clinical manifestation includes waist and abdominal pain, loss of appetite, nausea, vomiting, abnormal defecation and urination, and other compression symptoms. In a few cases of retroperitoneal Castleman's disease complicated by PNP, oral mucosal erosion or pemphigoid is the first symptom. As symptoms of lung infection or bronchiolitis obliterans, such as chest tightness, suffocation, and cough, occur concurrently, these cases are easily misdiagnosed. Wang et al. (2005) reported that Castleman's disease is the most common tumor complicated with PNP in China.

3.2 Examination and Staging

Laboratory findings are often nonspecific for LCD patients. In contrast, increased ESR, thrombocytopenia, elevated γ-globulin and immune globulin, hypoalbuminemia, antinuclear antibodies, anti-double-stranded DNA antibodies, rheumatoid factor positive, and Coombs test positive are common in MCD patients.

Imaging findings of Castleman's disease are closely associated with histopathology of different types, corresponding to histopathological features of each type and varying greatly between different types. Color Doppler ultrasound, CT, MRI, and angiography are commonly applied, of which CT plays a major role in the diagnosis of Castleman's disease.

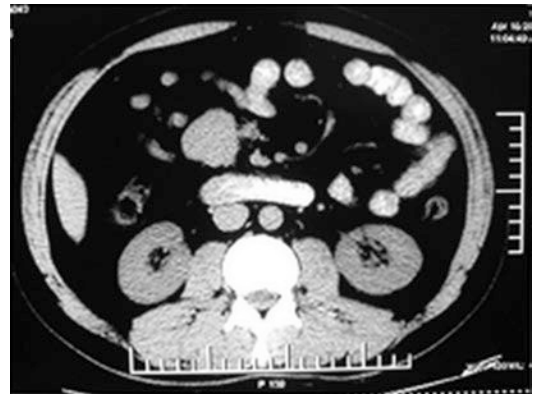

Fig. 22.2 Imaging of confined HV subtype Castleman's disease

Imaging findings of localized HV-type Castleman's disease (Figs. 22.2) include:

a. Lesions with well-defined margin, solitary soft tissue mass, round or oval in shape, uniform in density (a larger lesion with a center of relatively low density) .
b. After injection of contrast agent, the early- and mid-stage lesions exhibit enhancement to varying degrees. The early-stage significant enhancement and delayed clearance is manifested as cystic degeneration and necrosis. Dotted and striped vessels in the lesion are feeding arteries. The degree of enhancement may be affected by the number of proliferative capillaries in the lesion and the surrounding feeding arteries. In addition, injection method, dosage, and flow rate of contrast agent can also affect the degree of enhancement.
c. Dendritic calcification is the most representative feature in part of lesions and specific to HV type.

Color Doppler ultrasound mainly displays:

a. An intact capsule is clearly visible; nodular lesions and tumor margin present as clear contour, isolated hypoechoic, with normal internal structure and well-defined cortex and medulla; larger lesions are heterogeneous with hypoechoic foci.

b. Lesions with calcification exhibit high degree of echogenicity with acoustic shadowing.
c. Lesions with rich blood supply, surrounded by thickened veins and arteries.
d. Low impedance waveform is visible in diastolic phase, as one of the characteristics.

The imaging findings on PC-type angiofollicular lymph node hyperplasia are different from those on HV type and lack significant specificity. There are more enlarged lymph nodes in PC, which can be further divided into solitary and regional subtypes. Fusion of regional lymph nodes results in changes in appearance of mass-like lesions. Lesions exhibit ill-defined marginal profile and different densities in the region. Some lesions display infiltration of fat space and thickening of local fascia, with heterogeneous enhancement, accompanied by involvement of surrounding organs, such as pleural and peritoneal effusions and hepatosplenomegaly. Color Doppler ultrasound identifies multiple hypoechoic nodules with homogeneous echo pattern, normal and intact internal structure, well-defined cortex and medulla, and rare blood flow signals.

Imaging findings of mixed angiofollicular lymph node hyperplasia are more complex, as a mixture of both HV type and PC type. According to the clinical course, Castleman's disease can be classified into four categories: (a) stable, (b) chronic relapsing, (c) progressive, and (d) malignant. Stable and chronic relapsing are dominant types in LCD patients, while progressive is dominant type in MCD patients with a tendency toward lymphoma development. Four diagnostic criteria for MCD have been proposed by Frizzera (1988): (a) characteristically pathological changes of hyperplastic tissue, (b) significant lymphadenopathy and multiple peripheral lymph nodes, (c) obvious multi-system involvement, and (d) exclusion of possibly known causes.

As hyaline vascular type prevails in retroperitoneal Castleman's disease, CT has high diagnostic value. However, some retroperitoneal tumors, such as hemangioma, teratoma, and pheochromocytoma, may have similar CT findings, thus increasing the difficulty in preoperative diagnosis. Currently, the diagnosis of retroperitoneal Castleman's disease can only be established on the basis of a combination of clinical symptoms and pathological findings.

4 Treatment

As LCD is mostly benign, en bloc resection of lesions is preferred, with low recurrence rate. If there are contraindications to surgery or unresectable lesions, radiotherapy and/or glucocorticoid therapy can be effective. Chronowski et al. (2001) reported that 13/18 (72%) cases of Castleman's disease had complete or partial response to radiotherapy. For patients with retroperitoneal Castleman's disease accompanied by PNP, en bloc resection combined with postoperative adjuvant corticosteroids and anti-infection treatment would be preferred; however, most patients have poor prognosis due to complicated pulmonary damage.

MCD angiofollicular lymph node hyperplasia is potentially malignant, manifested by multiple lymph node involvement, polyserositis, and multi-organ involvement. Moreover, it is a systemic disease and should be treated with systemic regimen due to the lack of standard and specific therapy. Surgery combined with chemotherapy, radiotherapy, antiviral therapy, corticosteroids and immunomodulators, and comprehensive treatment may be considered for patients. En bloc resection is indicated for patients with small lesions; most patients with extensive disease have complete response to systemic chemotherapy with CVP (cyclophosphamide + vincristine + prednisone) or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) regimen but are predisposed to relapse. For younger patients with MCD, if conventional chemotherapy cannot effectively control the disease, autologous hematopoietic stem cell transplantation may be considered; alternatively, prednisone may be used as a single therapy. Interferon, ganciclovir, and other antiviral drugs are also effective in treatment of MCD. Targeted medicine such as anti-IL-6 antibody and anti-IL-6 receptor antibody (Nishimoto et al. 2005) (Akahane et al. 2006), anti-CD20 monoclonal antibody (rituximab) (Ide et al. 2006), and bortezomib (a protease inhibi-

tor) (Stary et al. 2008) has been developed based on the potential pathogenesis of the disease and proved effective in treating patients with MCD.

5 Efficacy and Prognostic Factors

Castleman's disease is a type of lymphoproliferative disorder that lies between benign and malignant diseases. Patients with LCD that is restricted to a particular area generally have a good prognosis after surgery; conversely, patients with MCD have relatively poor prognosis, especially those with plasma cell type. Those patients with viral infection history are particularly predisposed to severe infection and multiple organ failure due to immune dysfunction and bone marrow plasmacytosis. A small number of cases of MCD can develop into malignant lymphoma or Kaposi's sarcoma within several months to years, thus leading to a poor response to therapy.

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Retroperitoneal Lymphangioma

23

Hai Liu and Cheng-Hua Luo

1 Introduction

Lymphangioma is developed from original lymphatic sac and vessel in mesenchymal tissue. It is tumor-like malformation initiated after the original sac in some parts is isolated from lymphatic system during embryonic development. As a congenital benign hamartoma, it is divided into three subtypes: simple lymphangioma, cavernous lymphangioma, and cystic lymphangioma. 75% of these lesions occur in neck, 20% in auxiliary region, and only 5% in abdominal cavity. Retroperitoneal lymphangioma accounts for less than 1% of all lymphangiomas (Bhavsar et al. 2010). More than 90% of cases occur in people aged ≤2 years. The prevalence is similar between men and women. Localized lymphangioma has a good prognosis after surgery, with a low relapse rate. Diffuse lymphangioma is usually ill-defined, cannot be completely removed, and relapses repeatedly. Elephantiasis of limbs poorly responds to the treatment. Notably, lymphangioma will not become malignant.

2 Etiology

According to Sabin's hypothesis, lymphatic system is originated in five original sacs that are separated from venous system. In about 8 weeks of embryonic development, a sac on each side extrudes laterally from internal jugular vein, which is split to form cervical sacs; a retroperitoneal sac is bifurcated from the vein at mesenteric root; a posterior sac is fallen off from inferior gluteal vein. Then, lymphatic vessels, with the five original sacs forming a center, extending towards periphery and limbs, are connected each other to form the body's lymphatic system. Cervical sac extends forward to form subclavian sac. The thoracic duct, which is initiated by connection between left jugular sac and retroperitoneal sac, expands in the end connecting to retroperitoneal sac, thus forming chylous pool. Theoretically, blockage/isolation of the original sac leads to lymphatic cyst, while simple or cavernous lymphangioma results from hyperplasia of original local lymphatics. Lymphatic cyst is commonly seen in neck and retroperitoneum, which appears to be formed by isolated portion of residual cervical sac and retroperitoneal sac.

3 Pathogenesis and Pathobiology

Lymphangioma has been classified into three subtypes: capillary, cavernous, and cystic (Siderits et al. 2009). Some lymphangiomas

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containing vascular tissue are mixed blood-lymphatic vessel tumor, also called lymph-hemangioma. Additionally, multiple types of lymphangioma can coexist, for example, cavernous lymphangioma containing a number of capillary components, whereas cystic lymphangioma containing a lot of cavernous and capillary elements in addition to large lumens lined by endothelial cells. Lymphangioma is a benign tumor, common in children and second only to hemangioma. Similar to hemangioma, lymphangioma in nature belongs to dysplastic hamartoma, with dual features of malformation and neoplasia. Although it may grow continuously and infiltrate surrounding tissue, lymphangioma will not metastasize distantly. Under microscope, lymphangioma is lined by flat endothelial cells, with smooth muscle cells in the outer wall. Immunohistochemistry reveals flat endothelial cell factor VIII-related antigen, CD31 and CD2-40 positive, whereas calretinin, human melanoma B45 and CD117 negative. These markers can be used to identify lymphangioma from tumors of other origins.

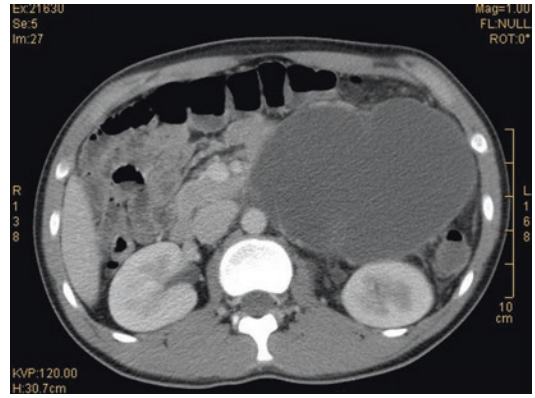

Fig. 23.1 CT image of a cystic lymphangioma displaying a mass with thin-wall, smooth surface, and uniform density

4 Clinical Manifestation

Patients with retroperitoneal lymphangioma have no obvious symptoms in early stage. When the tumor grows to large size, it presents as abdominal mass and compression symptoms. As the tumor continuously grows, clinical signs such as bleeding, infection, rupture, and twisting can occur, resulting in abdominal pain, fever, intestinal obstruction, and hydronephrosis.

5 Adjunctive Diagnostics

Doppler ultrasound, CT, and MRI are key adjunctive approaches in diagnosis of lymphangioma. Image-guided biopsy can help accurately identify retroperitoneal lymphangioma. Doppler ultrasound of retroperitoneal cavernous lymphangioma typically displays a low tension amorphous cystic mass in the form of honeycomb-like structure separated by strip-like partition. Cystic lymphangioma shows no vascular signals, however, its echo intensity varies with cystic fluid component. Calcification of cystic wall may display strong echo accompanied by acoustic shadow. CT is able to clearly display the intuitive relationship between the cysts and the surrounding organs, as well as enhanced cystic wall and partitions in cavernous lymphangioma. CT density varies with cystic elements. Cystic lymphangioma presents a thin-walled mass with smooth surface and uniform density on CT image (Fig. 23.1). MRI can clearly display the tumor size, shape, location, and relationship with the surrounding organs, which is equivalent to CT in terms of diagnostic value. If necessary, ultrasound-guided needle biopsy and drainage tests may be performed. If the liquid is serous or chylous and contains numerous lymphocytes, it would be highly suggestive of lymphangioma.

6 Differential Diagnosis

The retroperitoneal lymphangioma is mostly cystic lymphangioma, and requires to be differentiated from other retroperitoneal and peritoneal cystic lesions, including cystic teratoma, pancreatic pseudocyst, mucinous cystadenoma, cystic mesothelioma, neurogenic tumors cystic degeneration, and lymphatic cyst, urinary fistula and cyst, ovarian cysts, and omental cyst secondary to retroperitoneal sarcoma.

6.1 Cystic Teratoma

The cystic teratoma is more common in women. The tumor tissue consists of well-differentiated derivatives from at least two layers of the embryonic derm. The cystic teratoma is mostly benign, while solid teratoma may be malignant. The classic CT findings reveal that mature teratoma of the retroperitoneum is a well-circumscribed multiple-partition mass composed of a variable admixture of cystic fluid, adipose tissue, and cartilage ossification structure (Fig. 23.2).

6.2 Cystic Mesothelioma

Cystic mesothelioma is a rare benign tumor, occurring in pleural, pericardial, and peritoneal cavities and containing mesothelial cells. Cystic mesothelioma often develops on the surfaces of the pelvic viscera or less frequently in the retroperitoneum. The etiology of cystic mesothelioma is unrelated to a history of exposure to asbestos, which is different from malignant mesothelioma. This tumor occurs more frequently in women, recurs locally although almost never metastasizes. Cystic mesothelioma usually displays a unilocular or multilocular thin-walled cyst with abundant watery secretion on CT image (Sugarbaker et al. 2008). It may be radiologically indistinguishable from lymphangioma and can be diagnosed mainly depending on pathological findings, namely, the epithelium of lymphatic cyst is lined by flattened mesothelial cells.

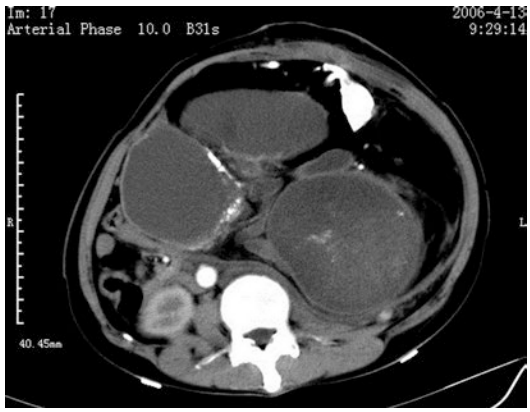

Fig. 23.2 CT image of a mature retroperitoneal teratoma

6.3 Mullerian Cyst

The Mullerian duct is embryologically called paramesonephric duct (ductus paramesonephricus). Mullerian cyst mostly occurs in the pelvis, and less frequently at any site where germ cells migrate through during embryonic development, or even in the upper abdomen. Mullerian ducts in the male degrade during embryonic development, and form prostatic utricle and epididymis accessories (Shebel et al. 2013). Incomplete degradation may result in Mullerian cyst. Mullerian cyst often occurs in the rear part of the prostate, also known as prostatic utricle cyst. Patients may develop urinary frequency, urgency, dysuria, hematuria, hematospermia, urinary tract infections, infertility, and constipation. Mullerian cyst is closely related to prostate, vas deferens, seminal vesicles, bladder, urethra, ureter, sphincter, and pelvic nerve, so attention should be paid to protect these structures during the surgery. In women, Mullerian cyst occurs commonly in adults, possibly attributed to administration of estrogen or obesity induced upregulation of endogenous estrogen. High levels of estrogen stimulate residual Mullerian duct in the retroperitoneum to develop cysts. In women, Mullerian cyst is often located in the pelvic retroperitoneum and easily misdiagnosed as ovarian cysts or fallopian tube cysts. Open surgical access including trans-abdominal, trans-perineal, and posterior trans-perirectal approach has individual advantages and disadvantages (Bullard Dunn 2010). Trans-abdominal approach is the most commonly used one and the surgeons are most familiar with it. Trans-perineal and trans-posterior perirectal approaches obtain a clear view of the surgical field, but may damage the rectal sphincter and nerve reflex arc, causing fecal incontinence. Laparoscopic resection of Mullerian cyst creates a much better exposure of the surgical field with distinguishable anatomical strata, and thus improves surgical safety compared to traditional open surgery.

6.4 Mucinous Cystadenoma

Primary retroperitoneal mucinous cystadenoma is an extremely rare retroperitoneal tumor. However, cellular origin and precursors of retroperitoneal mucinous cystadenoma are unclear, probably associated with the following tissue: (a) ectopic ovarian tissue; (b) mucus-secreting cells overgrowing in teratoma and forming single cell component; and (c) embryonic urogenital cells (Mattei et al. 2013). It is recently proposed that primary mucinous cystadenoma originates from peritoneal mesothelial cells: columnar epithelium and mucus metaplasia are developed after retraction of peritoneal mesothelial cells. Primary mucinous cystadenoma is potentially malignant. Therefore, early diagnosis and treatment are essential. CT imaging can identify this tumor as a homogeneously unilocular cystic mass (Yang et al. 2004). To delineate the nature of a cyst, aspiration is always conducted; however, cytology of the aspirated fluid cannot define the specific type of epithelial cells that lines the cyst. Thus, to accurately diagnose and radically resect the lesion, complete excision of the cyst is recommended.

6.5 Epidermoid Cyst

This is group of rare congenital lesions of ectodermal origin, affecting any site of the body from the head to the foot. The lesions originated in the presacral space are commonly seen in middle-aged women. The patients with small cysts are asymptomatic. When the tumor grows large, symptoms include constipation, anal pendant expansion, and abdominal pain. Epidermoid cysts usually display as unilocular thin-walled cystic masses on CT imaging. Histological features of these lesions are stratified squamous epithelium, mixed with cholesterol, keratin, or desquamated debris.

6.6 Tailgut Cyst

Retrorectal cystic hamartomas or tailgut cysts that are lined by different types of epithelium belong to extremely rare congenital multicystic lesions, located between the sacrum and rectum. Middle-aged women are more susceptible to tailgut cysts. The lesion displays as a well-confined multicystic mass on CT; its attenuation value varies widely (from water to soft tissue). The cyst can be infected and undergo malignant transformation.

6.7 Bronchogenic Cyst

As very rare benign congenital lesions, bronchogenic cysts are attributed to abnormal budding of tracheobronchial tree during development. They may rarely occur in the retroperitoneum despite being more commonly encountered in the mediastinum. The lesion consists of multiple components including smooth muscle, cartilage, and respiratory epithelium with bronchial glands. Patients are usually asymptomatic, unless bronchogenic cysts develop perforation or secondary infection, or compress adjacent organs. There was a case report of bronchogenic cyst transformed into adenocarcinoma in retroperitoneum. On CT imaging, bronchogenic cyst in retroperitoneum is manifested as well-circumscribed, hypo-attenuated unilocular cyst in subphrenic space.

6.8 Cystic Change in Solid Neoplasm

Neurogenic tumors such as paraganglioma and schwannomas are characterized by cystic changes (Fig. 23.3). Generally, paragangliomas occur along the aorta and have close relationship with the sympathetic chain. Clinical symptoms result from catecholamines released by the tumor. The diagnosis is confirmed with a high level of catecholamines and their metabolites in urine and blood. This tumor often presents as homogeneous attenuation of soft-tissue with low attenuation at the central area on CT imaging. Rarely, the mass demonstrates internal hemorrhage with subsequent liquefaction. Neurilemmoma originates in the neural sheath of peripheral nerves and is commonly seen in young to middle-aged adults. Retroperitoneal neurilemmoma often occurs in presacral pelvic retroperitoneum and paravertebral space. Marked cysts are secondary to

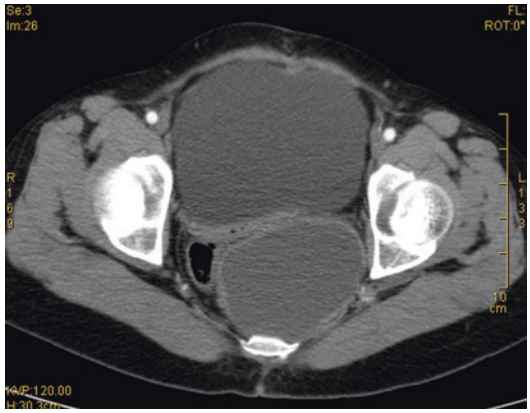

Fig. 23.3 Neurogenic tumors accompanied by cystic degeneration

degeneration due to lack of blood supply to the center. Few fast-growing retroperitoneal sarcomas can cause lymphatic obstruction, leading to secondary lymphatic cysts.

6.9 Pseudomyxoma Retroperitonei

This is a very rare disease. Due to the rupture of a mucinous mass originated in the appendix or ovary, gelatinous material is accumulated intraperitoneally. Pseudomyxomas commonly occur in the peritoneal cavity, and occasionally in the retroperitoneum. A ruptured mucinous mass in the retrocecal appendix leads to pseudomyxoma retroperitonei, which is present as a thick-walled multicystic mass on CT imaging.

6.10 Pancreatic Pseudocyst

Pancreatic pseudocyst collects pancreatic fluid, oval-/round-shaped and encapsulated. The lesion is mostly peri-pancreatic, and rarely originated in abdominal cavity, pelvis, and mediastinum. Pancreatic pseudocyst can be distinguished from other types of cystic lesions by CT scan (Chalian et al. 2011). Clinical symptoms of pancreatic pseudocyst are caused by inflammatory pancreatic diseases; and an increased level of amylase detected in the serum and urine supports its diagnosis.

6.11 Lymphocele

A lymphocele is a fluid-filled cyst without being lined by epithelium, secondary to renal transplantation or retroperitoneal/pelvic lymphadenectomy (Lee et al. 2013). Retroperitoneal lymphoceles can cause venous obstruction in the lower extremity, with subsequent thromboembolic complications.

6.12 Urinoma

Encapsulated urinomas collect chronically extravasated urine. Urinary tract obstruction, iatrogenic injury or trauma results in urinary extravasation. Urinomas usually occur in the perirenal space, and rarely in retroperitoneal or presacral space (Fig. 23.4). Hydronephrosis of varying degrees is a very common finding. Urinomas are often manifested as fluid collections with attenuation of water at unenhanced CT imaging. Notably, its intensity is progressively enhanced in response to contrast agent administered intravenously, which has entered the urinoma with the flow of urine.

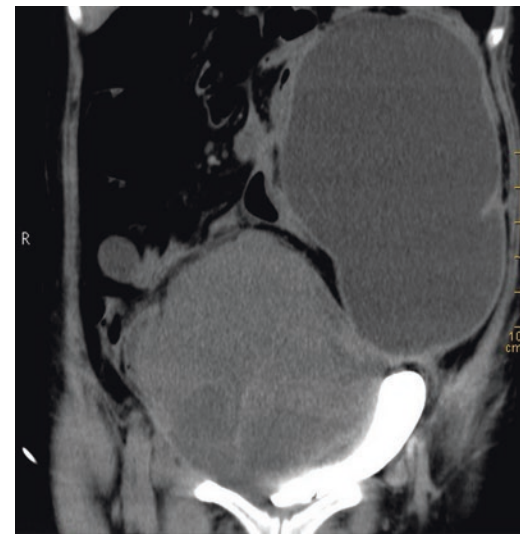

Fig. 23.4 An urinoma on CT displays a fluid collection with water attenuation, which is not enhanced

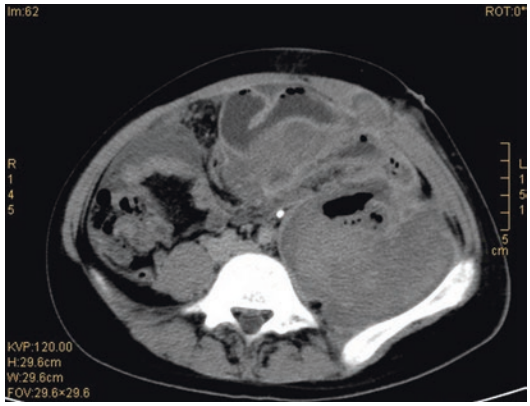

Fig. 23.5 CT image of a hematoma

6.13 Hematoma

The etiology of retroperitoneal hematoma includes hemophilia, ruptured abdominal aortic aneurysm, trauma, and anticoagulant. The time elapsed from the traumatic events to imaging examination determines different manifestations of a retroperitoneal hematoma on CT. A high attenuation value is observed for acute or subacute hematoma, while chronic phase has decreased attenuation because of the absorption of hematoma. Generally, patients have a history of trauma. It is not difficult to distinguish retroperitoneal hematoma from retroperitoneal tumor. However, patients with hemophilia can develop spontaneous retroperitoneal hemorrhage, resulting in a giant retroperitoneal hematoma that may be misdiagnosed. In one case of 13-year-old child with sudden abdominal pain who underwent resection of iliac fossa mass at a local hospital, a giant hematoma was identified during the surgery. Postoperatively, this patient was referred to our hospital due to uncontrollable bleeding, and diagnosed as deficiency of factor VIII (acquired hemophilia A). His symptoms were relieved after the infusion of factor VIII (Fig. 23.5).

7 Treatment

Retroperitoneal lymphangiomas are benign lesions, and symptomatic when growing large enough to compress surrounding organs. Intervention should be adopted for patients with obvious symptoms. For a retroperitoneal lymphangioma, surgery is the most common approach (Kasza et al. 2010), followed by cyst fluid aspiration, anticancer drugs, and sclerotherapy (Wiegand et al. 2011). Therapeutic strategy is determined by not only the size and location of the tumor, but also the complexity and risk of the surgical procedure. Both traditional and endoscopic surgeries are indicated for these patients. The latter has the advantages in diagnosis and therapy, causes less damage and thus shortens the recovery period of patients. For the lymphangiomas exhibiting invasive growth, en bloc resection is recommended according to the tumor site and involvement scope. Retroperitoneal lymphangioma surrounded by loose tissue should be separated in relatively avascular space, while the ligation of surrounding lymphatic vessels can be performed to prevent leakage and recurrence of lymphatic cysts. Usually, aspiration of cyst fluid is not the first step because it will increase the difficulty in stripping cysts. However, if the tumor is too large to be exposed, part of the cyst fluid may be aspirated in order to facilitate surgical exposure and separation. Due to invasive growth of the tumor, it is challenging for surgeons to perform en bloc resection of retroperitoneal lymphangioma, especially in cases with extensive lesions and multiple involved organs. In this setting, a combined resection of involved organs can be conducted if necessary. Paracentesis alone can temporarily relieve the oppression of the tumor on surrounding tissue or organs. As cysts are linked to lymphatics, a rapid relapse is expected. Intralesional injection of OK-432, bleomycin A5/bleomycin, or fibrin glue is used as a stand-alone treatment or in combination with surgery, which can effectively prevent the recurrence or even avoid surgery.

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Retroperitoneal Angiosarcoma

24

Hai Liu and Chengli Miao

1 Introduction

Angiosarcoma is a malignant tumor originated in the vascular or lymphatic endothelium. As described in the literature under various names, angiosarcomas were previously called vascular endothelial tumor, ductal sarcoma, angiosarcoma, malignant hemangioendothelioma, and lymphatic sarcoma. It is now known as angiosarcoma, including vascular endothelial derived hemangiosarcoma and lymphangiosarcoma. Hemangiosarcoma cannot be differentiated from lymphangiosarcoma due to lack of reliable morphologic parameters and immunohistochemical features, so they are collectively referred to as angiosarcoma. Angiosarcoma is a rare tumor, commonly seen in skin and soft tissue, accounting for approximately 1–2% of soft tissue sarcoma. Retroperitoneal angiosarcoma is extremely rare as reported in the literature. In this chapter, etiological causes, histopathological features, immunohistochemical markers, clinical manifestation, treatment strategies, therapeutic efficacy, and prognostic factors of angiosarcoma will be briefly described.

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2 Etiology

It is now widely accepted that chronic lymphedema, ionizing radiation history, chemical exposure history, trauma history, and chronic infections may contribute to the development of angiosarcoma.

Angiosarcoma is developed on the basis of long-term chronic edema, lymphatic expansion, and malignant proliferation of endothelial cells, which is originated in the following pathologic conditions: a. post-mastectomy lymphedema in the upper extremities of patients with breast cancer; b. abdominal wall of patients with penile cancer following lymphadenectomy; c. extremities of patients with congenital, idiopathic, or traumatic lymphedema; and d. filariasis lymphedema. It was first described in 1948 by Stewart and Treves (1948) in a series of 6 cases of lymphangiosarcoma after chronic post-mastectomy lymphedema, and later called Stewart–Treves syndrome, accounting for about 6% of all angiosarcoma. Since then, 14 cases of angiosarcoma resulted from chronic edema of the upper extremity secondary to mastectomy, and 2 cases induced by chronic congestion and edema of the lower extremities have been reported by Maddox and Evans (1981). Angiosarcoma has a longer latency period (range: 4–27 years; median: 10 years)

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after breast cancer treatment. Chronic lymphedema causes malnutrition of connective tissue and plays a significant role in the onset of angiosarcoma (McConnell and Haslam 1959).

Radiation tumorigenesis must meet the following three criteria: (a) tumor occurs within the radiation field; (b) pathological type of tumor is inconsistent with the primary, and (c.) the interval between the onset of two tumors is relatively longer (usually more than 10 years). Naka et al. (1996) reported that 4/5 cases of cervical cancer developed angiosarcoma in the radiation field of abdominal wall and hip following radiotherapy at an average interval of 13 years. Among18 cases of head and neck angiosarcoma, 4 met the above criteria for radiation-induced tumorigenesis (Lydiatt et al. 1994). Angiosarcoma commonly occurs in the head, face, and skin of Caucasians, related to long-term exposure to the sunlight. Mutations in the tumor suppressor genes (e.g., p53) may play a role in the pathogenesis of radiation-induced tumors.

Chemical stimulation has a major effect on the carcinogenesis of angiosarcoma. A study was carried out in America from 1964 to 1974 to investigate the pathogenesis of hepatic angiosarcoma (Falk et al. 1981). 25% of the cases had been exposed to poly vinyl chloride, thorium coagent (thoratrast), and inorganic arsenic. The high incidence of liver angiosarcoma was firstly found in workers with long-term exposure to polyvinyl chloride (PVC). Thorium is a mixture of 25% of thorium dioxide latex, which had been previously widely used as radiographic enhancer in clinical practice, and now abandoned due to non-uniform deposition in various organs of the human body (72% in liver, 12% in spleen, and 8% in bone marrow). Long-term stimulation of thorium agent can induce hepatic angiosarcoma. In recent years, arsenic compounds induced tumors in animal models have been reported.

It has been reported that patients with angiosarcoma usually have a previous history of trauma. Girard et al. (1970) found that 3/28 cases of angiosarcoma had a previous history of trauma at the occurrence site. In a study conducted by Naka et al. (1996) in Japan, 21 out of 99 cases of angiosarcoma (21%) had obvious incentives. For example, 5 patients had history of bumps, which was considered as a common risk factor, only second to chronic tuberculous pleurisy (6 cases) (Naka et al. 1996). Clinical manifestation of angiosarcoma is similar to that of bruise caused by bump, thus supporting its trauma origin.

Chronic inflammation is closely related to angiosarcoma. Chronic tuberculous pleurisy is the most common predisposing factor (Naka et al. 1996). Pleural angiosarcoma may develop in 15–40 years (median: 33 years) after the onset of pleurisy. The present study suggests that long-term inflammation is subject to angiosarcoma based on the clinical and pathological features of pleural angiosarcoma.

3 Pathogenesis and Pathobiology

Histologically, angiosarcoma can be classified as well-differentiated, moderately differentiated, and poorly differentiated subtypes. The histological findings of tumor vessels are very similar to those of normal lymphatic vessels in patients with well-differentiated angiosarcoma. Sometimes, the capillary vessels can be found in the lesion, with the lumen either void or filled with protein liquid and red blood cells.

Under the light microscope, the tumor is composed of various atypia endothelial cells in spindle-, cubic-, or irregular-shape, with obvious nuclear atypia and short stubby chromatin, and numerous mitotic figures. Irregular and mutually anastomotic lumen tubules are formed by endothelial cells. Lumen tubules of varying sizes and shapes are mutually anastomotic, so cutting of the dermis collagen results in separation of the fascia from subcutaneous fat tissue. In well-differentiated areas, luminal tubules are prominent, either slit-shaped or dilated into sinusoid-shaped, lined by flattened endothelial cells. The proliferated endothelial cells pile up in multiple layers and even block lumen or form nipples that protrude into the lumen. Nuclear atypia still exists, and mitotic figure is rare. In poorly differentiated areas, endothelial cells are arranged in a diffuse pattern to form solid nests, with inconspicuous lumen. The endo-

thelial cells are obviously atypia with a large deeply stained prominent nucleoli and numerous mitotic figures. Occasionally hyperkeratosis or parakeratosis exists, and frequently intratumoral necrosis occurs.

Under electron microscope, the tumor exhibits typical lumen in which malignant endothelial cells are arranged, accompanied by pinocytotic bubbles, intact or fragmental basement membrane, and intercellular tight junction, but lack of desmosomes. Occasionally flagellar microtubules-like bodies are visible; however, no definite Weibel–Palade bodies can be seen. Since Weibel–Palade bodies present only in endothelial cells but not in lymphatic endothelial cells, angiosarcoma cells that don't contain these bodies may have lost the ability to differentiate into the specific structure in the malignant process or arise from lymphatic endothelium.

A variety of molecular markers, such as FVIII-RA, UEA-1, CD31, cytokeratin, EMA, HMB 45, VEGF and p53, have currently been used for the diagnosis and differentiation of angiosarcoma. FVIII-RA is widely distributed in endothelial cells of the arteries, capillaries, and veins, such as lymphatic vessels and liver sinusoidal endothelium. FVIII-RA is a commonly used immunohistochemical marker of vascular endothelial cells, expressing on the surface of macrophages, platelets, mast cells as well as glomerular interstitial area. The positive rate of FVIII-RA in angiosarcoma cells reached 40–100% as reported by Poblet et al. (1996). In particular, its positive rate in vascular area was significantly higher than that in nonvascular or pancivascular area.

Both Ulex Europaeus Agglutinin 1 (UEA-1) and FVIII-RA are standard endothelial cell markers. UEA-1 is a specific lectin for a-L-fucose-containing glycocompounds, and a marker for human vascular endothelium. Among 98 cases of angiosarcoma, the UEA-1positive rate was up to 70% in angiogenesis region whereas 46% in nonvascular or pancivascular area, which was less sensitive than FVIII-RA or CD31 (Ohsawa et al. 1995).

CD31 is an adherent molecule present in the endothelial cells, monocytes, and platelet surface, also known as endothelial/platelet adhesion molecule. CD31 is positively expressed in the junction between adjacent endothelial cells. The positive rate of CD31 was reported to be higher than that of FVIII-RA in malignant vascular endothelial cells. A study (Ohsawa et al. 1995) involving 98 cases of angiosarcoma found that the positive rate of CD 31 in vascular area was 80%, lower than that of FVIII-RA (84%) but higher than that of UEA-1 (70%). Miettinen (2006) reported that 18/23 (78%) cases of angiosarcoma were positive for CD31.

Cytokeratin is a maker of epithelial origin. Al-Abbadi et al. (2007) found that cytokeratin was positive in the vascular endothelial cells. Notably, cytokeratin positive angiosarcoma is easily misdiagnosed as cancer. In another study, the positive rate was 11% in vascular area whereas 21% in non-vascular area. EMA (epithelial membrane antigen) and cytokeratin have similar positive rate and significance. Angiosarcoma with positive expression of EMA and cytokeratin is easily misdiagnosed as cancer, especially for a tumor originated in non-vascular or pancivascular area.

VEGF is a mitogen secreted by vascular endothelial cells, and plays an important role in the development of angiosarcoma. Ohsawa et al. (1995) reported that VEGF was positive in only 36% of the biopsies and 14% of cadavers. Fujimoto et al. (1998) measured VEGF concentration using ELISA assay, and found VEGF varied with tumor load. However, VEGF concentration was not deviated from the normal range (cut-off value of 18 pg/ml) throughout the clinical process. The average concentration of VEGF in angiosarcoma tissue was 108.3 pg/ml, comparable to hypervascular malignancies (such as RCC and glioblastoma multiforme) or benign angiomas. Increased mRNA level of VEGF and/or its receptor (VEGFR) was reported in angiosarcoma (Park et al. 2010; Hoshina et al. 2013). VEGF was proposed to play an important role in the pathogenesis of angiosarcoma and may serve as a vital therapeutic target (Hoshina et al.). The autocrine or paracrine mechanisms of VEGF and its receptor may contribute to the development of angiosarcoma.

Tumor suppressor gene p53 is critically involved in a variety of tumors. In murine models, loss of p53 promotes spontaneous hepatic angiosarcoma. Trivers et al. (1995) analyzed 148 serum samples from 72 patients (including 15 cases of hepatic angiosarcoma) who had been exposed to PVC, and found that loss of p53 predicted the onset of hepatic angiosarcoma. If 20% of nuclear staining positive rate serves as a cut-off value, p53 protein is positive in 20% of these cases. Mutations of p53 gene have been detected in angiosarcoma. The p53 protein plays an important role in DNA damage repair machinery.

4 Clinical Manifestation

Angiosarcoma may occur anywhere in the body, most commonly (more than 50%) in the head and facial skin and soft tissue. Angiosarcoma is roughly divided into nodular, diffuse, and ulcerated types. Among various clinical manifestations, the early appearance is a superficial lesion like bruising, petechiae, or ecchymosis, similar to bumping. The lesion is ill-defined, with slightly hard margin. The lesion grows more quickly in the advanced stage, and may bulge from the surface of the skin. It is purple in color, occasionally accompanied by ulceration. Sometimes the lesion is surrounded by small satellite nodules. Poorly differentiated type is manifested as multifocal and extensively local invasion. The focal lesions are red in color, deeply located, and locally bulged, at a rapid growth speed, vulnerable to bleeding, and in mold-like appearance with deep ulcers.

Retroperitoneal angiosarcoma is extremely rare, and its clinical manifestations are similar to other retroperitoneal tumors, such as pain and compression of local organs. The tumor size can be more than 20 cm. It mainly metastasizes through blood, and is most likely to spread to the lung, thus causing symptoms such as pleural disease, bloody pleural effusion, or pneumothorax. Other common metastatic sites include the liver, bone, soft tissue, and lymph nodes. Retroperitoneal angiosarcoma has a poor prognosis.

5 Detection and Staging

Clinically, the UICC/AJCC TNM system applies to the staging of soft tissue sarcoma. As angiosarcoma is a poorly differentiated tumor, histological classification is not considered for clinical staging.

6 Treatment

Surgery is the mainstay for treatment of angiosarcoma. Surgical procedure is the first choice. The resection margin should be 3 cm laterally from the visible basal part of the tumor, and then extend outwards 4 cm subcutaneously. Alternatively, resection margin should be determined by the pathologic findings of intraoperative frozen section. Preoperative or postoperative radiotherapy and/or chemotherapy are expected to reduce local recurrence or distant metastasis. As retroperitoneal angiosarcoma is adjacent to vital organs and blood vessels, surgical resection becomes one of the most challenging tasks and results in the worst prognosis. For giant retroperitoneal angiosarcoma, preoperative embolization of the primary feeding vessels to the tumor can reduce bleeding and surgical risk. Since patients with retroperitoneal sarcoma exhibit a high rate of postoperative relapse, Colombo et al. (2012) proposed that the scope of removal should be extended and if necessary, combined resection of multiple organs should be performed in order to reduce the recurrence rate.

Local radiotherapy can effectively control the multicentric and invasive angiosarcoma. For multicentric or ill-defined angiosarcoma, radiation of >50 Gy within a few centimeters circled the margin of gross target volume can generally achieve good results. Postoperative radiotherapy may improve local control of angiosarcoma that is multicentric and deeply infiltrated with positive margin. Preoperative radiotherapy also plays a role in inhibiting tumor growth, reducing bleeding, preventing intraoperative implantation, and increasing the resection rate.

Chemotherapy is a necessary palliative treatment for patients who have advanced non-

resectable angiosarcoma, experience a relapse, or develop a distant metastasis. Commonly used chemotherapy regimens include doxorubicin (Adriamycin/ADM)-, paclitaxel-, or gemcitabine-based protocols, of which doxorubicin-based regimen is most commonly used. Meta-analysis of randomized clinical trials found that postoperative chemotherapy with ADM-based regimen had notable efficacy in the treatment of soft tissue sarcoma (including angiosarcoma). ADM-based chemotherapy is recommended as the first-line regimen. As a new therapy for angiosarcoma, paclitaxel with anti-angiogenic effect has aroused great interest clinically. FNCLCC (French Federation of Cancer Centers Sarcoma Group) reported that 78% of patients with angiosarcoma who received two cycles of weekly paclitaxel regimen achieved tumor progression-free survival, and 3/30 achieved complete response (Penel and Lansiaux 2007). A 2-year progression-free survival was achieved in patients with primary or metastatic sarcoma after receiving docetaxel plus gemcitabine regimen (Hensley 2010).

Although the underlying molecular mechanism of angiosarcoma is yet to be elucidated, the role of anti-angiogenic molecules in the treatment of angiosarcoma has attracted great attention worldwide. Encouragingly, patients with head and facial angiosarcoma who received VEGF monoclonal antibody (bevacizumab) in combination with radiation had achieved pathologically complete response (Koontz et al. 2008). Two of three cases of progressive and recurrent angiosarcoma had complete response after receiving bevacizumab combined with docetaxel and gemcitabine (Hingorani et al. 2012). Broad-spectrum tyrosine kinase inhibitors targeting a variety of VEGF receptors have been used. In a cohort of patients who received sorafenib of 800 mg/d, 13% had response, 65% had a three-months' progression-free survival, and 31% had six-months' progression-free survival. Yoo et al. (2009) proposed that Sunitinib could effectively fight against retroperitoneal angiosarcoma that is resistant to paclitaxel and doxorubicin. Rosen et al. (2010) reported that 3 out of 26 patients who received monotherapy of bevacizumab (15 mg/kg) once every 3 weeks for 3–16 cycles had achieved partial response; and 13 out of 26 patients who received the above regimen for 3–22 cycles had achieved progression-free survival.

Biotherapy against angiosarcoma has been rarely reported. Interferon is an immune molecule with anti-angiogenic activity, which can be used as neoadjuvant therapy before surgery. Among 24 cases of soft tissue sarcomas (including angiosarcoma) who were treated with isolated limb perfusion obtained an effective rate of 84% (CR 18%; PR 64%) (Lejeune et al. 2000). In 2009, Asano et al. (2009) found that interleukin-2 alone or in combination with chemotherapy was effective in the treatment of angiosarcoma.

7 Efficacy and Prognostic Factors

Angiosarcoma denotes a higher degree of malignancy and poorer prognosis compared to other types of sarcoma. Regardless of therapeutic regimen, the risk of local recurrence and distant metastasis remains high. Local recurrence can be as high as 75%, and approximately one-third of patients may experience metastases. Most distant metastases occur within 24 months after treatment, commonly in lymph nodes, lungs, liver, bone, kidney, and suprarenal gland. Angiosarcoma has the poorest prognosis among soft tissue sarcomas. Most patients die 2–3 years after diagnosis, with a median survival time of 15–24 months and an average 5-year survival rate of about 20%. Retroperitoneal angiosarcoma is located adjacent to vital organs and blood vessels, resulting in worse prognosis than the tumor occurring in other parts of the body.

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Retroperitoneal Hemangiopericytoma

25

Cheng-Hua Luo and Xiaobing Chen

1 Introduction

Systemic hemangiopericytoma (HPC) is a rare tumor, only accounting for 5% of soft tissue sarcomas. It can arise from anywhere with capillaries in the body, commonly seen in the lower limbs, retroperitoneum, or pelvis. Nine out of 24 cases of hemangiopericytoma occurred in the trunk and retroperitoneum as reported by O'Brien and Brasfield (1965), while 41/106 (Enzinger and Smith 1976), 22/60 (McMaster et al. 1975b), or 5/20 (Felix et al. 1981) cases of hemangiopericytoma were reported to occur in the retroperitoneum.

This type of tumor was firstly described and named by Stout and Murray (1942). Although it is closely associated with vascular glomus tumors, it lacks the highly regular arrangement of the latter. Subsequent ultrastructural study had confirmed the hypothesis of vascular epithelial origin of hemangiopericytoma and indicated glomus tumor as a disease independent of hemangiopericytoma. Till 1980s, the origin of hemangiopericytoma remains controversial, which is traditionally considered that the tumor is originated in hemangiopericytes or primitive mesenchymal cells with potential of differentiation into hemangiopericytes.

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Hemangiopericytes, arranged along the outer wall of the capillaries, are confirmed a variant of vascular smooth muscle cells. The term "hemangiopericytes" was firstly described by Zimmerman in 1923. Unlike other mesenchymal cells, it is difficult to distinguish the hemangiopericyte from the endothelial cell, fibroblast, and histiocyte under the light microscope due to the lack of specific cytology characteristics, so its diagnosis should be made based on structural features of the tissue. Before the introduction of ultrastructural examination, the differentiation of hemangiopericytoma from hypervascular neoplasms had been a very tough task.

2 Pathological Features

Pathological findings reveal that retroperitoneal hemangiopericytoma is an encapsulated homogeneous tumor surrounded by dense venous plexus. Tumor size (weight) varies widely, ranging from invisible to naked eyes to more than 1 kg. It is usually gray or brown in color, hard texture, relatively confined, and up to 20–30 cm or larger in diameter. Under the microscope, the thin-walled capillary bundle branches are irregularly surrounded by closely aligned hemangiopericytes. Each hemangiopericyte is encapsulated by reticular fibers, and the tumor cells are located outside the capillary sheath. This feature can be used to identify hemangiopericytoma from hemangioendothelioma; the latter is inside the

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capillary sheath. Tumor cell nucleus is round to oval in shape, with medium and ill-defined cytoplasm. Tumor cells are separated by a mesh matrix into lobules, and vessels within the tumor vary in size ranging from capillaries to expanded sinusoid.

Hemangiopericytomas can be divided into benign, intermediate (borderline), and malignant types on the basis of histopathologic criteria. It is difficult to identify benign from malignant hemangiopericytoma. Tumor size may be related to its biological behavior. Benign tumors are often confined and encapsulated, while malignant tumors exhibit local invasion. The retroperitoneal hemangiopericytoma is characterized by larger size, higher malignant degree, and longer growing period, as well as invasion and metastasis to surrounding tissues, compared to those occurring in other parts of the body. For this reason, retroperitoneal hemangiopericytoma should be treated as an aggressive tumor.

3 Clinical Manifestations and Diagnosis

The retroperitoneal hemangiopericytoma can occur in people aged between 5 and 92 years, more common in those aged 50–60 years. There are no significant differences in race and gender. Retroperitoneal hemangiopericytomas mostly (75–95%) appearing as painless, continuously enlarging masses have locally infiltrated adjacent tissue at the time of diagnosis. Compression of adjacent organs causes urinary retention, hydroureter, and hydronephrosis and occasionally leads to constipation, abdominal swelling, vomiting, and sciatica.

Hypoglycemia is present in some cases of typically giant hemangiopericytomas in the pelvis and retroperitoneum. After complete or partial resection, all cases have returned to normal condition; however, one case has no detectable insulin level. Additionally, hypoglycemia resulting from hemangiopericytomas has been reported to correlate with masculinization in women (Howard and Davis, 1959).

This hypervascular tumor can result in the following signs and symptoms: unilateral varicose veins, nevus, palpable lesion pulsation, and auscultation of vascular murmur.

X-ray and CT findings of retroperitoneal hemangiopericytoma are nonspecific, presenting as a soft tissue mass of high density, with displacement of adjacent structures such as the bladder, colon, and ureter.

As retroperitoneal hemangiopericytoma has bleeding tendency, MRI and angiography are vital for its diagnosis. MRI shows a well-defined vascular tumor, accompanied by violation of the capsule and adjacent tissue. MRI is helpful to develop a preoperative surgical plan. Angiography can play an important role in determining the size and the extent of violation of retroperitoneal hemangiopericytoma. Compact radial-like sub-branches bifurcated from typical new vessels, feeding vessel trunk and secondary vessels on angiography can denote retroperitoneal hemangiopericytoma and provide surgeons with valuable information about tissue and vascular anatomy.

The final diagnosis depends on histopathological findings. Some histological features of hemangiopericytoma are universally observed in a series of tumors, such as neonatal muscle cell tumor, synovial sarcoma, mesenchymal chondrosarcoma, malignant schwannoma, and malignant fibrohistiocytoma. Thus, hemangiopericytoma may be identified on the basis of morphology, immunohistochemistry, and ultrastructure. Clinically, retroperitoneal hemangiopericytoma may be misdiagnosed as hemangioma or vascular malformation.

4 Treatment

Wide excision is generally recommended for primary, locally relapsed, and solitarily metastatic retroperitoneal hemangiopericytoma. As patients with hemangiopericytoma may experience bleeding during surgery or biopsy, preoperative embolization is emphasized to reduce the blood supply of the tumor, which will limit bleeding intraoperatively and help remove some nonresectable tumors in the retroperitoneum or pelvis. It has recently been reported that patients

with retroperitoneal hemangiopericytoma who developed liver metastasis and hypoglycemia postoperatively had no response to chemotherapy; however, they survived for several years following hepatic resection and transplantation, as well as subsequent correction of hypoglycemia.

The previous studies suggested that retroperitoneal hemangiopericytoma was insensitive to radiotherapy, regardless of administered as monotherapy or adjunctive therapy. However, after the mid-1970s, some studies found that a radiation dose of >4500 cGy resulted in good tumor response. With more precisely positioning and less toxicity, radiotherapy has become an effective treatment for retroperitoneal hemangiopericytoma. The destruction of a bulk tumor requires high-dose radiation therapy, which involves multiple abdominal organs in the retroperitoneum. Thus, radiotherapy is recommended as adjuvant therapy following resection of retroperitoneal hemangiopericytoma in order to reduce the rate of local recurrence. Chemotherapy administered as postoperative adjuvant therapy or as monotherapy for metastasis has always attracted great attention; however, whether retroperitoneal hemangiopericytomas is sensitive to chemotherapy remains inconclusive. Individual case with metastatic hemangiopericytomas who received doxorubicin as monotherapy or in combination with Adriamycin had partial or temporary response but did not achieve long-term survival.

5 Prognosis

Retroperitoneal hemangiopericytoma can commonly metastasize through the blood to bone, lung, and liver and rarely spread into the regional lymph nodes. Both mortality rate and relapse rate can be as high as 50%. Patients may relapse quickly or over many years following initial treatment. As a result, patients should be closely followed up after surgery. The 5-year survival rate is approximately 50% in systemic hemangiopericytoma whereas less than 50% in retroperitoneal hemangiopericytoma, which may be related to the difficulty in achieving complete resection of retroperitoneal tumors. In clinical setting, it is difficult to predict the biological behavior and prognosis of hemangiopericytoma. The malignant degree of systemic hemangiopericytoma is associated with cell proliferation, mitotic activity, atypia, necrosis, and hemorrhage. For patients with benign tumors (defined as 0–4 mitotic figures/10 HPFs), the 10-year survival rate was 77%; for those with malignant tumors (defined as >4 mitotic figures/10 HPFs), the 10-year survival rate was 29%. Occasionally the malignant degree of relapsed hemangiopericytoma is much higher than that of primary tumor.

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Retroperitoneal Neurofibroma

26

Cheng-Hua Luo, Boyuan Zou, and Chengli Miao

1 Introduction

Clinically, retroperitoneal neurofibroma is commonly seen in young people, with an incidence rate equivalent between males and females.

2 Etiology and Pathology

Similar to neurofibromatosis in other parts of the body, retroperitoneal neurofibroma originates in the nerve fiber cells. It can be divided into three types: solitary, multiple, and ganglion cells. Histologically, it is composed of nerve fibers, collagen fibers, and a small amount of Schwann cells (Chen et al., 2003).

In general, retroperitoneal neurofibroma is mostly well encapsulated and well defined, with tenacious nature and off-white cross section. Under microscope, the parenchyma of the tumor is composed of bundles of spindle-shaped cells arranged in spiral pattern, in which collagen fibers are arranged in wavy pattern accompanied by neural axons. Such tumors commonly arise from nerve-rich sites such as the mid-retroperitoneum and presacral portion. Benign neurofibromas grow in an encapsulated manner. Malignant neurofibromas show a lower malignant degree than liposarcoma and leiomyosarcoma and rarely infiltrate the retroperitoneal great vessels and abdominal organs.

3 Clinical Manifestation and Diagnosis

Retroperitoneal neurofibroma is asymptomatic in the early stage. The tumor compresses adjacent organs when it grows to a certain size and presents as a palpable abdominal mass detected by patients. Due to lack of specific findings on B-ultrasound, CT, or MRI, the preoperative diagnosis depends on a comprehensive analysis on the features of the tumor (location, boundaries, and capsule) (Kocer et al., 2003).

4 Treatment and Prognosis

Surgical resection is the mainstay for treatment of retroperitoneal neurofibroma. When the tumor grows into the intervertebral foramen, the combined neural trunk resection can result in sensory and motor dysfunction, thus making the surgery more challenging. Clinically, residual tumor within the intervertebral foramen or reserved neural trunk often leads to relapse, so postoperative radiotherapy can be considered for those patients (Nishiyama et al., 2000).

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Retroperitoneal Neurilemmoma

27

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1 Introduction

Retroperitoneal neurilemmoma is a rare benign tumor originated in the retroperitoneal spinal nerve sheath. Its malignant transformation is extremely rare. Neurilemmoma was firstly described by Verocay and also called Schwann's tumor (Stout 1946) because of Schwann's cellular origin. In recent years, some studies suggest that Schwann's cells with multiple differentiation potential can form a variety of mesenchymal cells and transform backward to the original neuroepithelial cells. Therefore, Schwann's cells are not only neurilemmoma cells but also metrocytes of soft tissue tumors. Malignant neurilemmomas usually are transformed from neurofibromas or neurofibromatosis; however, benign neurilemmoma rarely undergoes malignant transformation. Both benign and malignant neurilemmomas are very rare, commonly seen in people aged 20–50 years, with the incidence rate approximately equivalent between men and women.

2 Etiology and Pathology

Retroperitoneal neurilemmoma is commonly located on both sides of the spine, mostly solitary and slow growing with rich blood supply. A benign tumor is smaller than 5 cm in size, located in the nerve sheath, and encapsulated by epineurium. A malignant tumor is often large in size, nodular and encapsulated with a fake capsule, and wrapping the neural trunk. The cross section of both benign and malignant neurilemmomas is off-white. A giant tumor (>8 cm in diameter) exhibits intratumoral hemorrhage, cystic degeneration, and calcification. The degenerative cells are easily misdiagnosed as malignant cells.

Under the microscope, a benign neurilemmoma exhibits dense areas composed of spindle cells as well as loose mesh areas containing less cellular components. A malignant neurilemmoma presents as plump spindle-based cells and typical mitotic figures. Several important markers for neurilemmomas include S-100 and neuron-specific enolase (NSE). S-100 is positive in both benign and malignant neurilemmomas, while neuron-specific enolase (NSE) is positive only in malignant neurilemmoma (Murray et al., 1940).

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C.-H. Luo (ed.), *Retroperitoneal Tumors*, https://doi.org/10.1007/978-94-024-1167-6_27

3 Clinical Manifestations and Diagnosis

Nonspecific clinical manifestations include abdominal pain, low back pain, radiating pain in the hip or lower extremities, abdominal mass, and even difficulties in defecation and urination. Malignant tumors, although they metastasize slowly, can spread widely, 50% of which are complicated by neurofibromatosis (von Recklinghausen's disease), thus leading to pain, tenderness, and paresthesia. It is difficult to diagnose retroperitoneal neurilemmoma. The observation of retroperitoneal masses on both sides of the spine that destroy or expand the intervertebral foramen is helpful for the diagnosis.

4 Treatment

Surgery is an effective approach for treatment of benign neurilemmoma given that the nerve fibers are properly protected. The complete stripping of the tumor from the capsule represents the major task for neurilemmoma resection. As residues are common in malignant tumors, the removal of partial nerve trunk and roots is usually required. Due to lack of clear boundary between the nerve trunk and roots, the combined resection of nerves will lead to disorders of sensation and movement in the dominated areas. The dilemma is that the preservation of nerves makes it almost impossible to achieve complete resection. Therefore, the benefits against the risks should be weighed by the surgeon and the patient before surgery. Adjunctive intra- or postoperative radiotherapy may be useful in reducing the relapse rate. Postoperative chemotherapy is also effective, in which commonly used drugs are vincristine sulfate (1.5 mg/m^2, intravenous infusion, weekly for 3 months) and dactinomycin (8 μg/kg, intravenous infusion, daily for 1 week).

5 Efficacy and Prognosis

The postoperative relapse rate of malignant retroperitoneal neurilemmoma is 20–50%, and some cases may develop distant metastases.

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Retroperitoneal Nonchromaffin Paraganglioma

28

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1 Introduction

The paragangliomas, also known as chemodectoma or nonchromaffin paraganglioma tumor, belong to neuroendocrine tumors. They are generally named according to anatomical sites, such as the carotid body tumor and jugular body tumor (referring to paragangliomas located in the carotid body). Paraganglioma is common in adults aged 30–60 years, while patients with retroperitoneal paraganglioma are younger (mostly 30–40 years old) than those with head and neck paraganglioma. Malignant paraganglioma may occur at a younger age. Retroperitoneal paragangliomas are rare tumors, with the incidence equivalent between men and women. They are mostly solitary and sporadic and occasionally multiple. Patients often have a family history. Some cases are accompanied by paragangliomas in other parts of the body or complicated with gastrointestinal stromal tumor (GIST) and pulmonary chondroma as Carney's triad.

Approximately 20% of the retroperitoneal paragangliomas arise from extra-adrenal paraganglia, which are located in para-aortic region and closely related to sympathetic nerve chain. The body's largest group of paraganglia is chromaffin bodies, namely, the paired structure arranged para-abdominal aorta at the level of inferior mesenteric artery. Chromaffin bodies are highly developed in the early embryos, gradually degrade after the age of 12–18 years old, and finally leave minor residues. Although these residues have chemosensory functions in animals, their physiological functions in the human body is unclear. Most extra-adrenal paragangliomas originate from chromaffin bodies, and a small number of tumors arise from para-aorta (on other planes) and para-iliac vessel paraganglia.

2 Etiology and Pathology

Retroperitoneal paraganglioma is usually a brown clump, a few centimeters in diameter, and incompletely encapsulated. Intratumoral hemorrhage is common. Histologically, retroperitoneal paragangliomas have characteristics of branchial paragangliomas and/or pheochromocytoma, and the vast majority is very similar to pheochromocytoma.

The tumors are composed of small, polygonal, or spindle-shaped cells with eosinophilic cytoplasm and numerous deeply stained nuclei. Tumor cells are arranged into short and irregular sheet structures, with rich sinusoid in intercellular matrix, and accompanied by megakaryocytes and multinucleated giant cells. As tumor cells are always very fuzzy in appearance, the sheet

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structures are endowed with syncytial character. Eosinophilic bodies are present in the cytoplasm, varying in size (ranging from a few millimeters to the size of a nucleus). These structures appear to be the residue of dense-core granules, suggestive of benign tumors. Very few tumors are composed of the cells with melanoma-like cytoplasmic debris, and hemorrhage is common in the tumorous nests. Some retroperitoneal paragangliomas are similar to carotid body tumors, while a small number of round cells grow in small nests in retroperitoneal paragangliomas.

Pleomorphic tumor cells may be misdiagnosed as malignant cells, since they exhibit little mitotic activity that reflects the atypical changes. Ganglioma area can be rarely seen in paraganglioma. Not all of these tumors are functional; the chromaffin reaction is positive in about two-thirds of the retroperitoneal paragangliomas (Kafase and Branan). Lack et al. (1980) reported that chromaffin granules could be detected in all of the retroperitoneal paragangliomas.

The immunohistochemistry profile of retroperitoneal paraganglioma is similar to that of branchial paragangliomas, in that neuron-specific enolase (NSE), neurofilament protein, synaptophysin, and chromogranin can be identified in chief cells, which in turn are surrounded by a delicate sustentacular network outlined by the immunostaining for S-100 protein. Leu-enkephalin, an opiate-like pentapeptide comprised of β-endorphin molecules, can be identified in adrenal and extra-adrenal paragangliomas. This pentapeptide is produced by normal and hyperplastic adrenal medullary cells as well as tumor cells. Insulin-like growth factor II, a polypeptide of 67 amino acids that is homologous to the β-chain of proinsulin, has been identified in adrenal tissue, carotid body, and paraganglioma. This polypeptide can be localized in the chief cells of adrenal and extra-adrenal paragangliomas; however, its significance is unclear. To sum up, NSE, CgA, and S-100 are highly expressed in almost all of the retroperitoneal paragangliomas and can be used as reliable markers, and the sensitivity will be further improved if applied in combination with Syn.

3 Clinical Manifestation

Paragangliomas arising from sympathetic paraganglia of abdominal aorta are mainly located on both sides of the retroperitoneal spine, commonly seen in the bifurcation of abdominal aorta and connected to blood vessels. Retroperitoneal paraganglioma is asymptomatic in the early stage, while in the late stage, it is most commonly manifested by back pain and a palpable mass. Ten percent of patients firstly present metastatic tumors. About 20% of cases are incidentally identified at the autopsy. Approximately 25–60% of patients develop noradrenaline-related symptoms, such as chronic or periodic hypertension, headaches, and heart palpitations. In contrast, functional adrenal paraganglioma (chromaffin tumor) may be associated with elevated levels of epinephrine (adrenaline) and norepinephrine in the blood, and the development of definite syndromes depends on the relative levels of the two hormones. Hypertension is frequently seen in norepinephrine-secreting tumors. In contrast, hypotension, hypovolemia, heart palpitations, and rapid arrhythmia are characteristics of the adrenaline producing tumors. The difference in the secretion modes is considered to be associated with methyltransferase enzyme in adrenal pheochromocytomas. This enzyme converts norepinephrine into epinephrine and is absent in extra-adrenal paragangliomas. In very few cases of retroperitoneal paraganglioma, renal ischemia occurs due to compression of the renal vessels by the tumor, thus resulting in hypertension.

4 Examination and Diagnosis

4.1 Localization Diagnosis

Localization of the tumor prior to surgery is relatively easy. CT shows a well-circumscribed paraaortic hypervascular mass, accompanied by necrosis or calcification. MRI displays a well-defined tumor of low-intensity signal on T1-weighted image whereas significantly high intensity and enhanced signal on T2-weighted

image. With an increase in volume, the tumor is complicated by cystic degeneration and hemorrhage, resulting in heterogeneous signals. CT has been used as the primary method for localization diagnosis of functional tumors. However, I-MIBG scintigraphy can display complex tumors and detect small tumors that cannot be identified by CT. Selective arteriography is helpful in determining the location, size, and blood vessels of the tumor in order to facilitate preoperative embolization and intraoperative ligation.

4.2 Etiologic Diagnosis of Functional Paraganglioma

Retroperitoneal paraganglioma lacks pathological and cytological evidence before surgery. Few patients can be accurately diagnosed before operation. The preoperative etiological diagnosis is essential to prevent uncontrollable intraoperative bleeding as well as the risk of catecholamine-induced sudden-onset hypertension and heart failure. The catecholamines are released by paragangliomas in response to the induction of anesthesia and surgical operation. Prior to surgery, if patients with retroperitoneal tumors have complications such as hypertension and metabolic changes (an increase in basal metabolic rate or blood glucose) but do not present with hyperthyroidism or diabetes, they should be highly suspected of retroperitoneal functional chromaffin tumor or paraganglioma. Particularly, if the tumor is closely related to the adrenal gland, the diagnosis can be made based on the measurement of catecholamines and 3-methoxy-4-hydroxymandelic acid (VMA) in the blood and urine. Phentolamine inhibition test or histamine provocation test can be conducted if necessary. Paragangliomas are not necessarily located in the adrenal gland, and functional types don't always present with hypertension before surgery. In patients with preoperative hypertension, the levels of catecholamines in the blood and urine, as well as VMA in the urine, may be normal, which are possibly attributed to a stationary type and the absence of stimulation test. Using ^{131}I-labeled iodobenzoic acid (a structural analog of norepinephrine), adrenal and extra-adrenal paragangliomas can be localized. Through a similar mechanism to neurotransmitters, this agent is concentrated in adrenergic tissue and, at the minimal effective dose of 0.2 mg, enables the imaging of paragangliomas. Tiny tumors may also be localized with isotope-labeled octreotide similar to somatotropin release-inhibiting factors.

4.3 Diagnostic Criteria for Malignant Paraganglioma

Retroperitoneal paragangliomas can be divided into benign and malignant tumors. The nature of the tumor is not related to its functional status, and the degree of malignancy is not associated with its functional activity.

Based on the potential of distant metastasis and local infiltration, approximately 50% of adrenal and extra-adrenal tumors are malignant. The criteria for malignant paragangliomas have been controversial. Some studies propose that only the appearance of metastasis is the definitive evidence for malignancy. In a review of various characteristics of both benign and malignant tumors carried out by Linnoila et al. (1990), the extra-adrenal site, coarse tumor nodularity, widespread necrosis, and lack of intracellular hyaline globules were considered to be harbingers of malignant tumors. Seventy-one percent of such malignant tumors exhibited two to three of the above features, while 89% of benign tumors exhibit none or only one of the aforementioned features. They also suggested that low expression of neuropeptides in most cases is associated with malignancy and therefore can be used as adjunctive index to identify infiltrative behavior. More than five neuropeptides are found to be expressed in typically benign retroperitoneal paragangliomas, whereas only two are in malignant tumors. Clarke et al. (1998) proposed that extra-adrenal location, male gender, young age, high tumor weight, and high Ki-67 index were harbingers of malignant tumors. The correlation between the increasing rate of MIB-1 antibody and malignant

potential has also been identified in other studies. Relative values of flow cytometry have been used to assess the malignant nature of retroperitoneal paraganglioma. Although the chromosomes in a metastatic tumor are often aneuploidy or tetraploidy, it significantly overlaps with the benign tumors. Thus, ploidy cannot be used to distinguish benign from malignant tumors.

5 Treatment of Retroperitoneal Paraganglioma

Either benign or malignant retroperitoneal paraganglioma, once it is diagnosed, should be completely removed as soon as possible. The control of blood pressure, correction of arrhythmias, and improvement of potential cardiomyopathy before the surgery are essential to improve the treatment and outcome of patients who have been diagnosed with functional retroperitoneal paraganglioma preoperatively. The volume expansion and appropriate blockers can effectively prevent the risks of ultra-hypertension, heart failure, and bleeding. Usually α-receptor blocker phenoxybenzamine (20–40 mg/day) is administered preoperatively for 2 weeks to control the blood pressure. If patients who have received phenoxybenzamine present with heart rate greater than 90 bpm, additional β-blockers should be applied to control the heart rate. For a patient, whose blood pressure has not been well-controlled with α-blockers alone, the addition of calcium channel blockers or angiotensin-converting inhibitors can achieve good results.

Since retroperitoneal paragangliomas are located adjacent to blood vessels, it is challenging to perform a complete surgical resection. If necessary, a combined resection of blood vessels or organs that are adherent to or invaded by tumors, such as pancreatic body and tail, spleen, kidney, colon, or inferior vena cava, should be conducted. During the surgery, squeezing and pulling of the tumor should be avoided as possible. The separation is generally carried out outside the capsule to control blood supply to the tumor as early as possible. Modern radiotherapy techniques enable to accurately localize these tumors, so some patients may undergo laparoscopic surgery instead of laparotomy.

Whenever an unexplained dramatic increase in blood pressure with intensive fluctuations occurs during an operation under anesthesia, retroperitoneal paraganglioma or chromaffin tumor should be suspected. In this setting, the operation should be discontinued, and antihypertensive measures should be taken. The first step is to expand the blood volume and control the blood pressure with sodium nitroprusside. As an effective antihypertensive agent, sodium nitroprusside acts directly on vascular smooth muscle. As a quick-acting vasodilator, it dilates both arteries and veins, and the blood pressure can recover quickly upon discontinuation. It is considered as an ideal choice to control hypertension induced by functional paraganglioma intraoperatively. Surgeons should be aware that the tumor cannot be squeezed and the blood supply to tumors should be blocked as soon as possible. The purpose is to avoid a sudden increase in blood pressure caused by released adrenaline into the blood, as well as hypotension-induced shock after tumor resection. The close cooperation between surgeons and anesthesiologists in this setting will ensure the operation to proceed smoothly. An appropriate amount of blood transfusion can be performed at the beginning of the surgery, and the amount of fluid infusion should be increased within a short period of time before dissecting the major blood vessels. After the tumor resection, blood transfusion and fluid infusion should be administered at a constantly accelerated speed. Excessive rehydration is very effective in correcting hypotension after tumor resection. Ephedrine and norepinephrine are vasopressor agents commonly used following tumor resection. Adjuvant therapies for retroperitoneal paraganglioma include radiotherapy, chemotherapy, and iodobenzoic acids, all of which are considered palliative care.

6 Efficacy and Prognosis

Retroperitoneal paragangliomas can spread through lymphatics and blood, most often metastasizing to the regional lymph nodes, bone, liver, and lungs. In a study conducted by Clarke et al.

(1998), 10 of 66 cases of chromaffin tumor and retroperitoneal paraganglioma experienced metastasis, including four cases of extra-adrenal tumors.

Previous studies suggested that extra-adrenal paraganglioma was more invasive than adrenal paraganglioma. However, the studies conducted by MSKCC (Memorial Sloan Kettering Cancer Center, 1990) put forth opposite evidence that the 5-year survival rate was 77% in adrenal paraganglioma whereas 82% in extra-adrenal paraganglioma; and no significant differences in 5-year survival rate or tumor-free survival rate were observed between them.

The serum level of neuropeptide Y correlates with tumor relapse, which can be used as a reliable marker to detect recurrent retroperitoneal paraganglioma.

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Retroperitoneal Neuroblastoma

29

Chengli Miao and Cheng-Hua Luo

1 Introduction

Retroperitoneal neuroblastoma is a malignant tumor arising from sympathetic crest cells. Those derived from primitive neural crest cells are also known as primitive neuroblastoma tumors, including neuroblastoma, ganglion-cell-derived neuroblastoma, and ganglioneuroma-/ganglion-cell-derived neurofibromatosis subtypes. It is more common in infants and young children.

2 Etiology

Adverse environmental factors, alcohol, and hair dye are associated with the disease. Retroperitoneal neuroblastoma can be presented as familial diseases in children, accompanied by Hirschsprung's disease or neurofibromatosis.

3 Pathogenesis and Pathology

Under microscope, retroperitoneal neuroblastoma presents numerous small poorly differentiated cells in round or oval shape, with interlaced fibrovascular bundles, hemorrhage, necrosis, and calcification. There are neurosecretory granules within the tumor cells.

4 Clinical Manifestation

In clinical practice, retroperitoneal neuroblastoma causes symptoms such as abdominal pain, bloating, abdominal mass, anorexia, diarrhea, constipation, frequent urination, and fever, which are similar to those of other retroperitoneal tumors. If the tumor secretes intestinal peptide hormone, it results in intractable diarrhea, hypokalemia, and hypertension clinically.

5 Examination and Staging

Retroperitoneal neuroblastoma often distributes along the sympathetic chain on both sides of the spine. Tumor size, scope, and relationship with the surrounding organs can be determined by B ultrasound, CT, and MRI. The measurement of catecholamines or their metabolite VMA in the blood or urine is helpful for the diagnosis of retroperitoneal neuroblastoma.

The clinical staging system of retroperitoneal neuroblastoma stratifies neuroblastomas as follows: stage I, localized tumor confined to the area of origin; stage II, tumor extending in continuity beyond the organ or structure of origin, not crossing the midline, with ipsilateral regional lymph node involvement; stage III, tumor infiltrating

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across midline with bilateral regional lymph node involvement; and stage IV, dissemination of tumor to distant organs. Surgical staging system for retroperitoneal neuroblastoma is as the following: stage A, complete gross resection (with naked eyes), without metastasis; stage B, incomplete gross resection, without metastasis; stage C, regardless of complete or incomplete resection of the primary tumor, with lymph node metastasis; and stage D, dissemination of tumor to distant organs such as the liver and bones (Tokiwa et al., 2003).

6 Treatment

Retroperitoneal neuroblastoma metastasizes in early stage to the liver, skin, and bones in addition to the lymph nodes. The main treatment approach is surgery, combined with postoperative chemotherapy.

Adjuvant therapy is not necessary for patients with stage I tumor who have undergone a complete resection. Radical resection followed by postoperative chemotherapy and radiotherapy is recommended for those with stage II and III tumors. Another option is that surgical resection is conducted after patients' symptoms are controlled by chemotherapy.

Retroperitoneal neuroblastoma is relatively sensitive to chemotherapy in which CTX, DDP, VP16, VM26, VCR, and DTIC are commonly used. Patients with stage II and III tumors can receive preoperative chemotherapy, while those with stage IV tumor can receive chemotherapy-based treatment as a major choice. Patients with stage III and IV tumors can also receive preoperative radiotherapy to reduce the tumor volume as possible before surgery.

7 Efficacy and Prognosis

In pediatric retroperitoneal neuroblastoma, the children's age is the key factor in evaluation of prognosis. The age of onset >1.5 years indicates a good prognosis for patients with well-differentiated tumor (Exelby et al., 1981).

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Retroperitoneal Teratoma

30

Cheng-Hua Luo, Weida Chen, and Chengli Miao

1 Introduction

Teratoma is a rare tumor of mixed dermal structures derived from three germ layers. The majority of congenital teratoma is identifiable in the human body and usually occurs within the ovaries of young women and testes of young men. Extragonadal teratoma arises at the midline structures such as anterior mediastinum, retroperitoneal, sacrum, ischial region, and pineal gland. Primary retroperitoneal teratoma accounts for 1–11% of all teratomas. In author's database, the incidence of retroperitoneal teratoma is 7.7% in adults with retroperitoneal tumors. The age of onset exhibits double peak that appears at 6 months after birth and in early adulthood, respectively. It is observed in less than 10–20% of patients over 30 years. The incidence is higher in females than in males. Primary retroperitoneal teratoma is the third most common tumor secondary to neuroblastoma and Wilms tumor in pediatric retroperitoneal tumors, accounting for 2–5% of pediatric tumors. A total of 32 cases (15 women and 17 men; age range: 20–82 years) of adult retroperitoneal teratoma have been reported between 1937 and 1987.

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2 Etiology and Pathogenesis

Historically, teratoma has ever been linked to the devil, sexual misbehavior and abnormal fertilization. Its bizarre histological findings and gross appearance attract wide attention. Totipotent cell lines are considered to be related to the origin of teratomas. In order to explain the diversity of these cells within the tumor, various hypotheses on pluripotent cells have been proposed, of which the germ cell origin is widely accepted.

In the embryo, the primordial germ cells arise from the yolk sac and begin to migrate in the first fourth and fifth weeks. The germ cell origin hypothesis proposes that pluripotent cells can give rise to cells derived from all three embryonic germ layers—mesoderm, endoderm, and ectoderm. Mobility of germ cells may explain the anatomical types of teratomas and why most teratomas occur in the gonads and at midline sites. Embryonic cell origin hypothesis suggests that teratomas development in pluripotent embryonic tissue can escape from the impact of the primitive organizer in early embryogenesis. In extra-embryonic cell origin hypothesis, teratomas arise from ectopic visceral yolk sac and contain primordial germ cells in early development. Unified origin hypothesis is a combination of germ cell and embryonic cell origin hypotheses. Teratoma lacks vascular structures and has always been recognized as an undeveloped fetus, so-called "internal parasitic twin." Fetus in fetu is a developmental abnormality that one fetus is partially

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developed but aborted in the abdominal cavity. It is often manifested as an undeveloped lump and was once thought to be the causes of teratoma. However, fetus in fetu is currently interpreted as abnormal twin and unrelated to teratomas.

The recent studies on molecular biology and chromosomal karyotype suggest that teratomas can be divided into gonadal and extragonadal lesions. Extragonadal teratoma is originated in the primordial germ cells, while gonadal teratoma arises from germ cells produced by haploid division. Furthermore, if gonadal teratoma contains pairs of identical chromosome, it is probably haploid derivative of embryonic germ cells after haploid breeding. Wagner et al. (1997) proposed that the extragonadal teratomas were originated in pluripotent cells with diploid chromosomes.

3 Pathology

Teratoma is comprised of mixed dermal elements derived from the three germ layers, characterized by the presence of multiple tissue types. Teratomas that consist of only one or two mesodermal components are accordingly known as monodermoma or bidermoma.

3.1 Pathomorphology

Macroscopically, teratomas exist in two forms. Cystic teratomas are composed of mature components and usually benign. They contain sebum and hair. Solid teratomas are mostly malignant (with invasive growth potential) and composed of immature embryonic tissue, such as fibrous tissue, fat, cartilage, and bone. However, Davidson et al. (1989) raised an objection to such classification criteria because they found 25% cases of solid benign teratomas among 23 cases of mature teratoma. They proposed that necrosis and hemorrhage are more important hallmarks for malignant teratomas.

Under microscope, the cystic wall of teratoma is lined by a variety of epithelial cells (squamous, ciliated, and adenoid), and commonly accompanied by ossification and calcification. Benign mature cystic teratomas contain epithelium, brain and glial tissue, teeth, cartilage, peripheral nerve, smooth muscle, respiratory epithelium, connective tissue, and gastrointestinal epithelium. Mesoderm and endoderm derived tissue and ectoderm glial tissue are very common. The presence of nerve tissue is closely related to invasion and metastasis. If nephroblastoma is present, teratoma may be confused with Wilms tumor.

3.2 Chromosomal Abnormalities

The most common chromosomal abnormality in teratoma is an isochromosome of the short arm of chromosome 12. An isochromosome is an abnormal chromosome that has lost one of its arms and replaced it with an exact copy of the other arm. The identical arm chromosome (i[12p]) of isochromosome 12 can be found in gonadal and extragonadal seminomatous, nonseminomatous germ cells as well as non-seminoma cells, and considered to be a specific pathological genetic marker. It can be identified in 81% of the primary non-seminomatous germ cell tumors and almost 100% of metastases, indicating that one or more of 12p genes play an important role in malignant transformation of germ cells. In germ cell tumors without i(12p), an excess of genetic materials on 12p can be detected using chromosome G-banding technique, indicating that the excess of genetic materials on 12p is a common genetic defect in all germ-cell tumors. Additionally, i(12p) is helpful in predicting the prognosis. Bosl et al. (1989) reported that treatment failure rate was significantly higher in germ cell tumors carrying three or more copies of 12p whereas lowered in those carrying only 1–2 copies. The i(12p) can be accurately determined in metaphase and interphase by fluorescence in situ hybridization.

3.3 Histological Classification of Retroperitoneal Teratoma

The old histological classification system of teratoma was established based on cytological features of testicular germ cell tumors, which played

Table 30.1 Histological classification of retroperitoneal teratoma

Benign teratoma
a. Mature teratoma
i. Grade 0: All components exhibit well differentiated
ii. Grade 1: Occasionally microscopic foci contain undifferentiated tissues, less than 10% of the samples
b. Immature teratoma, benign
i. Grade 2: Immature tissues make up 10–50% of the section samples
ii. Grand 3: Over half of the samples is composed of undifferentiated tissues of uncertain metastatic potential;
Malignant teratoma
a. Areas of germ cell tumors present in the teratoma
i. Germinoma (seminoma, dysgerminoma)
ii. Embryonal carcinoma
iii. Choriocarcinoma
iv. Yolk-sac tumor
v. Mixed (any combination of the above)
b. Areas of non-germinal malignant tumor present in the teratoma
i. Carcinoma
ii. Sarcoma
iii. Malignant embryonal tumor
iv. Mixed
c. Immature teratoma, malignant
i. A teratoma was otherwise classified as benign immature teratoma histologically, except it subsequently became metastatic

a limited role in assessing the malignant potential or accurately diagnosing the tumors. The classification system of teratoma proposed by Gonzalez-Crussi (1978) (Table 30.1) was established based on the natural distribution, proportion, and characteristics of tumors. At least 10 specimens should be collected for each centimeter of the maximum diameter.

As shown in the above table, benign teratoma consists of mature and immature types. Benign teratoma can be determined when undifferentiated tissue accounts for <10% of the sample collected from a mature teratoma. Immature teratoma contains >10% of undifferentiated tissue without malignant components and metastasis, which is most common in the nervous system.

Identification of tumor components is essential. The presence of germ cell components as well as immature or undifferentiated tissue is the major pathological evidence for malignancy. Malignant teratomas can be further classified into subtypes based on the presence of malignant germ cell components, which is vital for prognosis and treatment.

As the presence of germ cell components in teratomas indicates a poor prognosis, a comprehensive treatment should be taken actively. The presence of choriocarcinoma or endodermal sinus tumor indicates rapid invasion and poor prognosis. The presence of endodermal sinus tumor in teratoma is closely associated with reduced survival.

In addition to the germ cells, teratomas may contain lots of other undifferentiated tissue components, of which neuroectodermal tissue is the most common. Non-germline malignant components are reported in adult cases and should be closely followed up. Rhabdomyosarcoma with neuronal differentiation results in dismal prognosis. No immature somatic tissue has been found in children.

The mechanism underlying malignant transformation of mature teratoma remains controversial. The present study suggests that the malignancy rate in adults is significantly higher than that in children (25.8% vs. 6.8%). The malignancy rate of teratoma is 7.6% in pediatric patients under 1 year of age, 63.2% in those aged 1–2 years, and remains unchanged in those aged more than 2 years. Unlike children, adults with retroperitoneal teratoma may experience a long-term malignant process.

It has been reported that 1% of patients with dermoid cysts may undergo malignant transformation. Squamous cell carcinoma is the most common form of transformation, which is developed locally and more invasive than teratoma.

Malignant transformation of retroperitoneal teratoma is less frequently than that of mediastinal teratoma. Common cell types predisposed to malignant transformation include primitive neuroectodermal tumor, intestinal adenomas, and leukemia (the latter is more common in mediastinal teratoma). These tumors were traditionally

considered resistant to chemotherapy; however, recent studies indicate that some patients may benefit from chemotherapy, particularly those with rhabdomyosarcoma and primitive neuroectodermal tumor components.

Ohno and Kanematsu (1998) propose that all mature teratomas are of malignant potential and should be considered as pre-cancerous tumors. Tiny areas with malignant lesions should be carefully examined, which may help predict a higher risk of relapse. When adjacent structures are identified in completely differentiated teratoma, it would be speculated that the immature tissue has been missed in original specimens.

4 Clinical Manifestation

It is estimated that retroperitoneal teratomas frequently occur close to the central axis, on both sides of the spine and in pre-sacral region, commonly in the left upper quadrant if located in the upper abdomen. These tumors vary in size, and the biggest one weighs 3.6 kg.

Benign teratomas are usually asymptomatic and discovered incidentally. Due to the special location, retroperitoneal teratomas often have grown quite large before they are found. With an increase in tumor size, a series of visceral obstruction symptoms will appear, mainly including abdominal pain or back pain, urinary symptoms (hydronephrosis), gastrointestinal symptoms (nausea, vomiting, constipation, and peritonitis), as well as edema in the lower extremities or scrotum caused by blockage of lymphatic flow. Clinical signs related to a teratoma include a definite abdominal mass, abdominal tenderness, and progressive abdominal bulge. In physical examination, a midline or para-median abdominal mass with limited mobility in the abdomen may be detected. Common signs in infants include an abdominal mass and progressively increased abdominal circumference. Malignant teratoma develops rapidly and is usually diagnosed when symptoms get worse in advanced stage. Retroperitoneal malignant teratomas can cause nausea, weight loss, fever, dyspnea, and chest discomfort, as well as secondary infection if the tumor invades through the diaphragm into the lungs.

Retroperitoneal teratomas that invade forward through the peritoneum and inferiorly into the pelvic cavity are often misdiagnosed as tumors of abdominal or pelvic origin. The majority of teratomas in children presents as an exogenous sacrococcygeal mass that is easily found (Ugarte N et al., 1980). Teratomas in adults are mostly pre-sacral which grow slowly within quite a long time and are easily ignored due to lack of obvious symptoms.

5 Examination and Diagnosis

Since germ cell tumors usually spread to the retroperitoneum, primary gonadal teratoma and metastatic tumors from those in abdominal cavity and pelvis should be ruled out in all cases of extragonadal teratomas. Retroperitoneal teratomas are also easily confused with a variety of tumors, including sarcoma, so an accurate preoperative differential diagnosis is required. Some imaging features of teratomas, such as lipid–fluid level and calcification formed by limited fluid, lipid regions, adipose tissue and/or sebum in hybrid lesions, can help make an accurate diagnosis.

Anteroposterior and lateral plain radiographs of the abdomen were once recommended for patients with retroperitoneal teratoma. The plain image elicited irregular calcification in 61.5% of retroperitoneal teratoma cases, such as calcification or teeth and bone tissue on the margin of the cyst, therefore, tooth-like calcification indicates a teratoma. Irregular calcification does not absolutely indicate a benign tumor, because 12.5% of cases with calcification are malignant. In the absence of calcification, the displacement of adjacent organs caused by a transparent or translucent mass may be observed under the radiation. The excretory urography may help predict the displacement of kidney and ureter, compression of bladder, and urinary retention.

Ultrasound for mature teratoma can suggest a solid cystic mass accompanied by multiple hyperechoic spots with acoustic shadowing. Fat and calcification contribute to the diagnosis of a

teratoma, although cannot be clearly distinguished by ultrasound (Davidson et al. 1989).

Arterial angiography of benign retroperitoneal teratoma may reveal avascular feature and displacement of digestive arteries. Abdominal aorta angiogram may be used to assess tumor resectability in addition to tumor blood supply.

CT is the optimal tool for diagnosis of retroperitoneal teratoma. CT is superior to ultrasound in identifying lipid tissue, regardless of fatty tissue or sebum. The identification of sebum by CT depends on the type of fluid (through fatty attenuation and horizontal boundary with another tissue), which is vital for the diagnosis of teratoma. The enhancement of intracapsular solid mass is the reliable standard for diagnosing a malignant retroperitoneal teratoma, with a sensitivity of 75%, a specificity of 81%, and an accuracy of 80%.

MRI has superior image resolution on soft tissue compared to CT. MRI helps determine if the tumor has wrapped or invaded the blood vessels, and identify the displacement of abdominal aorta and multiple structures within the mass. It can clearly display the blood vessels, internal features, and location of the tumor, thus playing a vital role in predicting malignant potential, resectability of retroperitoneal teratoma, as well as the necessity of wider excision. Bellin et al. (1991) reported that MR could help identify non-infiltrating adjacent structures. The presence of fat is suggestive of a teratoma. MR can display some characteristics of a teratoma so that it is more easily distinguished from fibrous pseudotumor. T1-weighted MR images present the fat as a high intensity signal.

Alpha-fetoprotein (AFP) is produced during fetal life by the liver and the visceral endoderm of the yolk sac during embryogenesis. AFP may appear in a series of diseases, including non-seminoma germ cell tumors, hepatocellular carcinoma, and hepatitis (induced by infection, drugs, or alcohol). It is commonly seen in germ cell tumor and embryonal carcinoma containing yolk sac. A few immature teratomas show no evidence of yolk sac differentiation, they also secrete AFP, albeit at a low level. Teratomas with abnormally elevated levels of AFP should be highly suspected as advanced cancer. Elevated levels of AFP subside in 8–10 days after surgery, and reemerge if the tumor recurs. Thus, tumor recurrence can be determined by asymptomatic elevation of AFP level. Billmire et al. found that AFP level is elevated in malignant teratoma (100%), immature teratoma (50%), and mature teratoma (6%) by analyzing 142 cases of infant teratoma. Elevated levels of CEA and CA19-9 were reported to be occasionally observed in retroperitoneal teratoma. However, there is no reproducible evidence for clinical significance of this finding, which also occurs in other malignant tumors besides teratoma.

The final diagnosis of retroperitoneal teratoma depends on surgical resection and histological evaluation. Rapid increase in tumor size within a short term or compression of adjacent organs can result in pain and difficulty in urination and defecation, or elevated levels of certain tumor markers such as HCG, CEA, and AEP. The emergence of carcinoid syndrome and gynecomastia are signals of malignant retroperitoneal teratoma.

Teratoma components may come from a single or three germ layers. Cystic teratoma is typically benign, while solid teratoma is typically malignant. However, "solid and cyst" cannot be the synonyms of "benign and malignant," as most tumors appear as a mixture of solid and cystic elements. Mixed tumors are commonly seen in elder patients. A mixed tumor may transform into low-degree malignancy mostly from a single component in the late stage. By contrast, a solid tumor is commonly seen in younger patients and may transform into high-degree malignancy from multiple components in the early stage. Notably, the presence of a large amount of jelly-like mucus and bleeding necrotic tissue, accompanied by enlargement of adjacent lymph nodes or infiltration of the surrounding tissue in the tumors indicates an extremely high suspicion of malignancy.

Retroperitoneal teratoma is often misdiagnosed as ovarian or adrenal tumors (e.g., adrenal medullary tumors) as well as other renal and retroperitoneal tumors (e.g., Wilms tumor, renal cysts, retroperitoneal fibromatosis, sarcoma, hemangioma, and giant lymph node).

6 Treatment

As primary retroperitoneal teratomas in adults have tendency to malignant transformation, a complete resection should be conducted as early as possible in principle. Surgical resection is the mainstay for treatment of retroperitoneal teratoma. Patients with multiple-drug resistant tumors who undergo radical resection may achieve a long-term survival. Surgical resection is crucial for both diagnosis and treatment, as the final diagnosis depends on histological findings of the specimens. The presence of ligament-like vessels around the tumors and/or significant infiltration of the adjacent organs may interfere with the complete removal of the tumor. A one-stage resection may be performed in most cases, while two-stage resection should be performed if necessary.

In children with retroperitoneal teratoma, trans-abdominal approach can be used to expose a wider field and control drainage vessels in the early stage. The median and transverse abdominal incisions are adopted in most patients. The thoracoabdominal incision is indicated for a giant tumor in the upper abdomen. If possible, a laparoscopy resection may be applied to shorten operation length and recovery period, as well as reduce complications, given that the surgeons master sufficient skills of laparoscopic surgery and an appropriate preoperative plan has been made. In the setting of a benign teratoma, if the imaging displays a well-defined tumor without evidence for invasion of blood vessels, laparoscopic resection would be recommended.

Intraoperatively, tumors with abundant blood supply, adhesion to surrounding organs or invasion of muscles of posterior abdominal wall, or containing a large amount of mucus should be suspected of malignancies. In this setting, the extent of resection should be extended appropriately. Tumors closely adherent to surrounding tissue should be destroyed by electric coagulation to prevent recurrence if partial cystic wall is not completely removed. When teratoma results in severe vascular or ureteral obstruction, nephrectomy and resection and/or ligation of the inferior vena cava should be performed if necessary. The transcoccygeal approach is appropriate for the presacral surgery, particularly for the presacral tumor at the lower position, as this approach results in less trauma and bleeding, provides easy access to the site of operation, and shortens operation period. If tumors reach above the S2 (the 2nd sacral) plane, an abdominal incision should be made.

Patients with non-seminoma germ cell tumors show poor response to chemotherapy or radiotherapy. If the progressive germ cell cancer (yolk sac or embryo-derived) is identified after surgery, adjuvant chemotherapy should be conducted to achieve a short-term response and a longer survival. The treatment strategy for extragonadal germ cell tumors is identical to that for the same lesion in testis, and cisplatin-based chemotherapy is the major choice. Retroperitoneal germ cell tumors are similar to progressive testicular germ cell tumors, with a total effective rate of 61%. 50–69% of patients have achieved a long-term disease-free survival. The occasional presence of non-germ cell components, such as cancer or sarcoma, in patients with teratoma indicates clonal variation. In this regard, adjuvant chemotherapy is not necessary, although recent data show that the surgical resection combined with chemotherapy may significantly increase the response rate in cases with dominant single histological type.

It needs to be emphasized that the surgery should not be considered until the tumor markers (e.g., AFP and β-HCG) have returned to normal levels in patients with metastatic retroperitoneal non-seminoma germ cell tumors after receiving initial chemotherapy. Such patients present with a progressive disease and need additional chemotherapy. Furthermore, for patients who have received chemotherapy, if residues are detected by imaging system and tumor markers have returned to normal, surgical resection should be performed to consolidate the curative effect. Since these patients may be cured possibly, active measures should be taken to improve the therapeutic effect. Radiotherapy often exerts positive effects on the radiation-sensitive germ cell tumors such as seminoma.

7 Efficacy and Prognosis

The clinical outcome is determined by tissue components within the retroperitoneal teratoma. Patients with benign teratoma who have undergone complete resection have an excellent prognosis. The prognosis of patients with malignant teratoma is not optimistic, except that cystic teratoma is low-grade malignant after transformation and maybe alleviated for many years following treatment. Malignant teratomas (including germ cell tumors) containing germ cell components are high-grade malignant and frequently metastasize via lymphatics and blood, so the prognosis of patients is dismal even in early stage. Patients who have undergone malignant transformation have a poor prognosis, if they present with metastatic lesions.

Patients who have undergone complete resection have significantly prolonged survival. Retroperitoneal teratomas frequently recur, so all patients should be closely followed up, in order to monitor the progress of malignant lesions. Arai et al. (1997) reported that patients with malignant teratoma and an elevated AFP level had response to chemotherapy but mostly recurred after extensive surgery and chemotherapy, with the median survival time of 6 months; patients with nerve or rhabdomyosarcoma-like differentiation were more susceptible to relapse after surgery and had a poor prognosis.

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Retroperitoneal Extragonadal Germ Cell Tumors

31

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1 Introduction

Extragonadal germ cell tumor (EGGCT) represents 5–10% of germ cell tumors and frequently occurs in mediastinum, retroperitoneum, pineal gland, or sacral area. EGGCTs are mostly benign, such as teratoma and yolk sac tumor. Typical malignant EGGCTs mainly include malignant teratoma and embryonal carcinoma, while seminoma and choriocarcinoma are rarely seen. Less than 1000 cases of primary retroperitoneal seminoma have been described worldwide; as a subtype of EGGCT, it commonly occurs in young adult aged 30–50 years (Schmoll, 2002).

2 Etiology

The occurrence of retroperitoneal seminoma may be derived from (a) primitive germ cells in the early embryo due to the displacement of yolk sac endoderm and (b) residual pluripotent stem cells during embryonic development.

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3 Pathology

All retroperitoneal germ cell tumors arise from the testis; and only those derived from mediastinum are really atopic. Primary testicular tumor may be small and even invisible to naked eyes, which can only be histologically confirmed by biopsy. When space-occupying lesions are found in the retroperitoneum, the testis should be carefully examined and removed (removal of the ipsilateral testis is usually recommended) for a comprehensively histologic evaluation. Patients with normal histological findings of testicular biopsies should be closely followed up.

4 Clinical Manifestations and Diagnosis

Retroperitoneal seminomas often grow extensively and present with non-specific clinical manifestations, thus making its diagnosis very challenging. A patient is commonly diagnosed in his thirties. Most cases are diagnosed by surgical exploration. Symptoms vary from dysphagia, abdominal or back pain, a palpable mass, to edema in the limbs, which are determined by the tumor's location. The tumor may be accompanied with constitutional symptoms (e.g., fever and weight loss). Eighty-five percent of patients have a palpable mass. The presence of seminomatous and nonseminomatous elements on biopsy histopathologically confirms its diagnosis. During the

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diagnosis, it should be noted that multicenter metastases may occur while the tiny testicular tumor lesions spread through the lymphatic system to the retroperitoneum. A tiny seminoma originated in the testis can spread to the retroperitoneum and form a large lump, which mimics a primary tumor. Therefore, a primary retroperitoneal germ cell tumor must be diagnosed with special caution, while the possibility of metastatic lesions from testicular seminoma must be ruled out (Atmaca et al., 2009). For differential diagnosis, routinely performed testicular biopsy can be avoided because scrotal ultrasound can easily differentiate a retroperitoneal EGGCT from primary testicular tumor metastases. It will be very challenging to differentiate a primary retroperitoneal seminoma from carcinoma originated in cryptorchidism that metastasizes to the retroperitoneum; however, the differential diagnosis plays a significant role in guiding clinical treatment.

5 Treatment and Prognosis

Seminoma can be treated by surgery, radiotherapy, or chemotherapy. Surgical approach should include retroperitoneal tumor resection, lymph node dissection, and stage II ipsilateral orchiectomy. Patients with distant metastases should be actively treated, and their clinical outcome is comparable to primary testicular tumors. Seminomatous histology predicts a very good prognosis regardless of retroperitoneal or mediastinal EGGCT. Goss et al. (1994) proposed that the 5-year survival rate of extragonadal seminoma was more than 80% regardless of its origin; and extensive surgery in combination of cisplatin-based chemotherapy may achieve a higher survival rate.

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Retroperitoneal Endodermal Sinus Tumor

32

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1 Introduction

Germ cell tumors can be divided into seminomas and non-seminomatous tumors, which include embryonal carcinomas, endodermal sinus tumors, choriocarcinomas, teratomas, and mixed germ cell tumors. The vast majority originates in ovary and testis gonads, and a small number occurs beyond gonads. Retroperitoneum is the second most common site of extragonadal germ cell tumors (Ueno et al., 2004). Primary retroperitoneal extragonadal germ cell tumors are rarely encountered neoplasms that occur without an apparent gonadal primary lesion (Bokemeyer et al., 2002). Primary retroperitoneal endodermal sinus tumor (PREST), also known as primary retroperitoneal yolk sac tumor (PRYST), is an extremely rare tumor that has only previously been described in case reports and occurs principally in girls and women of childbearing age.

2 Etiology and Pathology

Primary extragonadal germ cell tumors are thought to arise from primordial germ cell nests that fail to migrate properly during embryogenesis and are usually midline in location (Meyer and Gilbertson-Dahdal, 2010). Extragonadal germ cell tumors show immunoreactivity patterns identical to those of their gonadal counterparts (McKenny et al., 2007). The histogenesis of PREST remains controversial. The PREST represents a highly malignant germ cell neoplasm in adult cases, which is a non-capsulated soft tissue mass and mostly invades into adjacent tissue and organs directly. In the majority of cases, the tumor has invaded the crucial nerves and blood vessels, such as the abdominal aorta and inferior vena cava, and may have formed tumor thrombus in the inferior vena cava.

Tumor section often looks like jelly, characterized by the coexistence of solid, cystic, and necrotic area. PREST tissue exhibits variable morphologies under the microscope, such as loose network structure composed of stellate-shaped tumor cells, endodermal sinus-like structure based on the monolayer of columnar or cubic tumor cells wrapping around capillaries, or vesicle-like structure consisting of squamous epithelium and cubic or low columnar tumor cells. Eosinophilic bodies can be seen within tumor cells and intercellular space. In immunohistochemical examination, tumor cells display AFP-positive staining in cytoplasm and eosinophilic bodies.

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C.-H. Luo (ed.), *Retroperitoneal Tumors*, https://doi.org/10.1007/978-94-024-1167-6_32

3 Clinical Manifestations and Diagnosis

PRYST shows non-specific clinical symptoms and signs and is difficult to be identified at its early stage. The tumor is commonly identified when it has grown to a considerable size. Typically, patients present with abdominal pain, low back pain, weight loss, fever, venous thrombosis, scrotal edema, and dysphagia. Positive α-fetoprotein (AFP) staining and elevated serum AFP level can be found in PREST tissue. AFP is produced by endodermal sinus tumors either alone or in association with other types of germ cell tumors and exhibits a good correlation with the severity of the lesion. AFP is an important tumor marker of PREST. Measurement of serum AFP can not only establish an important basis for the diagnosis of PREST but also play a role in evaluating and predicting clinical outcome of patients. Levels of AFP can also be used to differentiate PREST from other subtypes of mediastinal germ cell tumors (MGCT). Classically, immunohistochemistry reveals that AFP is positive in embryonal carcinoma cells; however, serum AFP is not elevated in most of these patients. Serum AFP may be elevated in some cases of immature teratoma but is undetectable in human chorionic cancer. PREST also presents with an elevated human chorionic gonadotropin (hCG) level. The hCG is only produced by syncytiotrophoblasts as a component of choriocarcinoma. These are useful serum markers in the diagnosis, prognosis, and treatment of patients with germ cell tumors.

4 Treatment and Prognosis

The appropriate treatment of PREST is currently unclear. The preservation of fertility is particularly important, and maintaining reproductive function to the greatest extent has become the primary strategy in treatment. The operative principle for PREST is to perform en bloc resection of the tumor without any residual tumor tissue as possible. If necessary, a combined resection of adjacent organs and blood vessels, in parallel with revascularization, should be conducted. Even for recurrent cases, surgical resection remains an ideal therapeutic approach (International Germ Cell Cancer Collaborative Group, 1997). Particularly for patients with PREST who are not suitable for receiving en bloc resection, their serum AFP levels can return to normal after treatment with one to three cycles of chemotherapy postoperatively. PREST is insensitive to radiotherapy, so surgery and chemotherapy are the major choices. Due to lack of appropriate chemotherapy drugs, not to mentioned proper combination chemotherapy, the 2-year survival is less than 20% and the 3-year survival rate is as low as 13% in most patients with PREST.

Since the 1980s, various platinum-based chemotherapy regimens (such as BEP [bleomycin, etoposide, cisplatin] and BVP [bleomycin, vinca alkaloid, and cisplatin]) have been widely used and have markedly improved the prognosis of patients with MGCTs. The BEP regimen has become the most effective treatment for MGCTs after the 1990s and is considered to be the first line chemotherapy regimen for MGCTs. The platinum-based chemotherapy regimens remain effective for PRYST patients even when there is a tumor relapse following the first platinum-based chemotherapy. By contrast, platinum-based chemotherapy regimens may not be effective in cisplatin refractory patients with repeated tumor relapses. AFP is an important biomarker for monitoring tumor recurrence, which is used to assess preoperative or postoperative residual tumors, monitor the response to chemotherapy treatment, and contribute to a long-term follow-up. The observation of elevated serum AFP levels during chemotherapy indicates a poor prognosis. Approximately 10–20% of patients experience a yolk sac tumor (YST) relapse following the first treatment, and their AFP levels may be associated with tumor recurrence and prognosis (Zanagnolo et al., 2004; Zanetta et al., 2001). Mitchell et al. (1999) reported that relapses were principally observed among patients with an AFP level >1000 ng/ml, with regard to the prognosis of YST.

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Retroperitoneal Synovial Sarcoma 33

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As a very rare type of tumor, soft tissue sarcomas (STS) constitute only 1% of all malignancies. Synovial sarcoma morphologically mimics synovium during development. Synovial sarcoma mostly affects adults aged 30–60 years and accounts for 8–10% of all types of sarcomas. About 85–95% of this group of tumors arises from the extremities close to the large joints; and 5–15% occurs in the head and neck, mediastinum, abdominal wall, and retroperitoneum. Primary retroperitoneal synovial sarcoma is extremely rare, making up 0.8–8.3% of all synovial sarcomas (Fisher, 1998). Meanwhile, retroperitoneal synovial sarcomas represent approximately 1% of all retroperitoneal tumors (Fisher et al., 2004). The disease was firstly described by Pack and Tabah (1954); up to now, 35 cases in total have been reported.

1 Etiology and Pathogenesis

Potential origins of synovial sarcomas include normal synovium, arthrogenous mesenchyme, and primitive pluripotent mesenchyme. A primary retroperitoneal synovial sarcoma should be defined as a tumor located in retroperitoneum with a precursor of mesodermal components exclusive of renal, bony, adrenal, visceral, and pancreatic tissues (Ziarn et al., 1996). The etiology of synovial sarcoma remains unknown. Two cases reported by (Egger et al. 2002) were associated with previous radiation. Molecular biology studies mostly revealed a representative chromosomal translocation t(X;18) (p11.2; q11.2) (Ladanyi et al., 2002).

2 Presentation

Generally, a retroperitoneal synovial sarcoma manifests as a nonspecific soft tissue mass without distinct clinical presentation, which is differential from other types of mesenchymal tumor. Its symptoms are vague and nonspecific, such as tenderness, discomfort, and abdominal pain, due to compression on adjacent organs.

3 Diagnosis

Early diagnosis of retroperitoneal synovial sarcoma contributes to reduced morbidity and mortality. Preoperative diagnosis may be obtained through radiography. It is difficult to distinguish retroperitoneal synovial sarcoma from other mesenchymal tumors since it often presents as a nonspecific soft tissue mass lacking specific imaging features. Soft tissue calcifications being delicate or specifically located in complex anatomic setting can be identified by CT imaging. Intratumor hemorrhage, cyst formation, or necrosis can be present. CT imaging

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can define the tumor and demonstrate bone involvement. To differentiate the tumor from the adjacent neurovascular structure and muscles, intravenous contrast is employed. On MRI, the lesion displays a nonspecific heterogeneous mass. Its signal intensity is very similar to skeletal muscle on T1WI whereas higher than subcutaneous fat on T2WI. Signal intensity can change compatibly with prior hemorrhage and fluid–fluid levels. CT and radiograph but not MRI may detect soft tissue calcifications. Large calcifications can be identified as reduced signal intensity on all pulse sequences (Alhazzani et al., 2010).

A retroperitoneal soft tissue mass present in young adults should be suspected as synovial sarcoma. The diagnosis of a retroperitoneal synovial sarcoma is pathologically confirmed by surgical resection or fine needle biopsy (Miyashita et al., 1994). Morphologically, synovial sarcomas exhibit in two main variants: monophasic and biphasic. The monophasic tumors contain spindle cells organizing in fascicles, displaying whorled configurations or presenting like a hemangiopericytoma or fibrosarcoma (Buiga-Potcoava et al., 2005). In contrast, biphasic tumors consist of glandular components embedded in the spindle cells. Sometimes the glandular structures are subtler, being revealed by a reticulin stain. The presence of stromal mast cells may represent a valuable diagnostic clue. Cystic synovial sarcomas are a rare finding (Morrison et al., 2001). Poorly differentiated forms or sarcoma with rhabdoid features have been reported (Jun et al., 2004). Synovial sarcoma may mimic desmoplastic round cell tumors (Cole et al., 1999). Immunohistochemically, synovial sarcomas are universally or focally positive for cytokeratin (either AE1/AE3 or CAM5.2), epithelial membrane antigen, vimentin, CD99, and calretinin. A significant number of cases are immunoreactive for bcl-2, calponin, Her2/Neu, and MAGE-CT; some cases are focally positive for S-100 protein (Rosai, 2004).

4 Treatment

The treatment of choice for retroperitoneal synovial sarcoma is a wide surgical resection, including the regional lymph nodes, followed by postoperative radiotherapy. Chemotherapy appears to be ineffective; however, chemotherapy may be considered in high-grade lesions (Borden et al., 2003). Unfortunately, complete resection rate is approximately 50%. Despite adequate surgical resection and adjunctive therapies, 28–36% of patients develop relapse or progression (Ko et al., 1998).

5 Prognosis

Retroperitoneal synovial sarcoma has a poor prognosis. Generally, 20–29% of patients can survive for 5 years after diagnosis (Ariel and Pack, 1963; Felix et al., 1981). Well-accepted indicators for poor prognosis include poorly differentiated small cell subtype (as the worst factor), extensive necrosis, and highly mitotic figures (>10–15 mitoses per 10 HPF). In contrast, favorable predictors include a tumor size <5 cm, young age (≤15 years), and distal rather than proximal location in the extremities (Kransdort, 1995). Metastasis from synovial sarcomas usually occurs via the bloodstream with the lungs being the most frequent site. However, literature review yielded no reported case with distant metastasis from retroperitoneal synovial sarcoma (Miyashita et al., 1994).

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Malignant Peritoneal Mesothelioma

34

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1 Introduction

In 1908, Miller and Wynn firstly described a malignant mesothelioma (MPM), a type of aggressive and dismal malignancies that originates in the serosal layer of pleura, peritoneum, pericardium, and tunica vaginalistestis (Bridda et a l ., 2007). MPM is mostly located in the pleural region and accounts for 30% of all mesotheliomas, with an estimated annual incidence of approximately 10,000 cases in China. Notably, the prevalence of MPM has been increased rapidly worldwide since 1970 and is not expected to reach the peak in another 1–2 decades (Robinson et al. , 2005). It has been reported that the lifetime probability of developing a peritoneal mesothelioma is 1/10,000 in women and 1–1.5/10,000 in men (Moolgavkar et al., 2009). In developed countries, MPM is the most common peritoneal malignancy. Because of high malignancy and frequent recurrence, either untreated or conventionally treated, the life expectancy of patients is restricted to be 4–12 months (Chua et al., 2009a).

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2 Etiology

Certain risk factors contribute to the pathogenesis of MPM. Previous studies have implicated that asbestos exposure highly correlates with MPM carcinogenesis. Although the odds ratio of peritoneal mesothelioma attributed to asbestos exposure may differ between the genders, the difference may stem from misclassification of exposure in women (Carbone et al., 2007). Three molecular mechanisms may be involved in asbestos-induced carcinogenesis: (a) Free radicals generated by asbestos directly cause lesions in coding regions of multiple genes, which promotes cancer initiation and progression; (b) Asbestos mediates chronic inflammation, local release of free radicals, as well as hypersecretion of cytokines/growth factors by effectors; and (c) Asbestos fibers exert co-carcinogenic effects on target cells and function as adaptors for chemical carcinogens (Clin et al., 2009). Other potential factors associated with peritoneal mesothelioma development are previous abdominal radiation and mineral erionite. Less substantiated and more controversial putative risk factors include a diet low in vegetable consumption, and simian virus (SV) 40 infection from contaminated polio vaccines (Yan et al., 2007).

C.-H. Luo (ed.), *Retroperitoneal Tumors*, https://doi.org/10.1007/978-94-024-1167-6_34

3 Clinical Manifestation

As a very rare tumor, MPM has unspecific symptoms and is commonly diagnosed at an advanced stage and confused with ovarian cancer and peritoneal disseminations, leading to misdiagnosis and mistreatment (Hassan et al., 2006). The most common presenting symptoms are abdominal pain and increasing abdominal girth, the latter of which is probably caused by ascites (Sugarbaker et al., 2003). The less-common symptoms are weight loss and fever. In some cases, a palpable abdominal mass could be detected on physical examination. MPM has been classified into 3 subtypes according to prognosis and clinical presentation: (a) classical type, characterized by abdominal swelling due to ascites and an abdominal mass associated with abdominal pain and weight loss; (b) surgical type, characterized by requirement for an immediate operation, and (c) medical type, featured with weight loss, diarrhea, fever, and acute-phase responses, which resemble intestinal inflammatory bowel disease (de Pangher Manzini, 2005).

4 Diagnosis and Extent of Disease Evaluation

Histologically, MPM is generally presented as either a low-grade adenomatoid and tubulopapillary tumor or a high-grade epithelioid, sarcomatoid, and biphasic tumor (Suzuki, 1992). A biphasic mesothelioma contains sarcomatoid and epithelial components and characteristics. High-grade tumors account for 62–76% of MPMs. Among them, the epithelioid subtype is the most common one and has the best prognosis (Yano et al., 2009). Immunohistochemistry is critical for the diagnosis of MPM. Tumor specimens could be obtained through diagnostic laparoscopy or CT guided biopsy. Diagnostic laparoscopy has the special advantage of enabling direct visualization of tumor burden and consequent selection of patients whose disease is qualified for operative intervention (Deraco et al., 2008). Commonly used biomarkers for MPM include calretinin, cytokeratin 5/6, EMA, WT1, human mesothelial cell-1, and mesothelin. MPM is usually negative for B72.3, Ber-EP4, CEA, and MOC-31 (Nonaka et al., 2005). However, these immunohistochemical markers rarely stain consistently as positive or negative (Husain et al., 2009). Therefore, using at least two mesothelioma markers and two carcinoma markers is necessary when establishing the diagnosis of MPM.

Several tumor markers including CA125, CA15-3, osteopontin, and serum mesothelin related protein (SMRP) may assist in diagnosis, however, they are more suitable in evaluating response to treatment and disease progression (Chua et al., 2009b). N-ERC/mesothelin and C-ERC/mesothelin are potential candidate markers for diagnosis of mesothelioma.

CT scan is essential to evaluate the tumor and help selection of treatment strategy. CT imaging can illustrate features that distinguish MPM from other peritoneal malignancies, either primary or secondary. Radiographically, manifestations of MPM vary significantly on CT, such as thickening of the peritoneum, mesentery or pleura, nodules of varying shapes and sizes, omental and mesenteric infiltrations, bone destruction, lymphadenopathy, and ascites (Low et al., 2009; Park et al., 2008). Lymph node metastasis mostly occurs in common, internal, and external iliac lymph nodes, and ileo-colic lymph nodes (Yan et al., 2006).

It has been proposed that, although their manifestations on CT scan may vary greatly, MPM tumors can be classified into 3 types: dry, wet, and mixed. A "dry" type appears as a single or multiple peritoneal-based soft tissue masses that could be either large or confluent. A "wet" type consists of thickened peritoneum that could be

Table 34.1 TNM staging system of Malignant Peritoneal Mesothelioma

Stage	T (Tumor)	N (Node)	M (Metastasis)
I	T1	N0	M0
II	T2-3	N0	M0
III	T4	N0-1	M0-1
	T1-4	N1	M0-1
	T1-4	N0-1	M1

either nodular or diffuse, accompanied with ascites (peritoneal fluid). The "mixed" one has simultaneously "dry" and "wet" appearance (Bridda et al., 2007). Moreover, colonoscopy and gastroscopy are commonly performed to exclude intraluminal malignancies in the stomach (e.g., gastric cancer) and intestine (e.g., colorectal cancer).

A new staging system is highly recommended as it is based on a multi-institutional registry and can stratify patients' survival by stages: the 5-year survival rate for stage I, II, and III is 87%, 53%, and 29%, respectively (Tables 34.1) (Yan et al., 2011).

5 Treatment

MPM was previously considered as untreatable, and managed with systemic and palliative chemotherapy. Recently, with the advancement of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), overall survival of these patients has been significantly improved. Due to the peritoneal confinement and rarely distant metastasis, a locoregional approach composed of CRS plus perioperative intraperitoneal chemotherapy is a curative treatment strategy for MPM over the past 10 years (Mohamed et al., 2011).

Compared to traditional debulking surgery, CRS adopts a brand-new concept, which requires to remove as much visible tumor as possible to create an optimal environment for intraperitoneal chemotherapy. In order to resect or strip MPMs from all intra-abdominal surfaces, the surgery consists of six peritonectomy procedures: (1) greater omentectomy-splenectomy, (2) left upper quadrant peritonectomy, (3) right upper quadrant peritonectomy, (4) lesser omentectomy-cholecystectomy with stripping of omental bursa, (5) pelvic peritonectomy with sleeve resection of the sigmoid colon, and (6) antrectomy (Sugarbaker, 1996).

Currently, CRS in combination with HIPEC and mitomycin C or cisplatin is largely considered to be a first-line initial treatment for selected patients. The actual extent of disease in the abdominal cavity is defined by using peritoneal cancer index (PCI) by CT scan. The abdominal cavity is divided into 9 squares, while the small bowel mesentery is separated into 4 quadrants. Each part is scored based on disease burden, on a scale of 0 (no gross disease) to 3 (extensive disease). Therefore, the extent of disease will range from 0 to 39, and the patients with a PCI of lesser than 30 are generally thought to be qualified for a complete gross cytoreduction. Completeness of cytoreduction (CCR) score records the volume of residual disease following CRS. A CCR of 0 signifies that no gross disease remains after CRS; a score of 1 indicates that tumor nodules remain but are all 2.5 mm or less in diameter; whereas a score of 3 is assigned for a residual disease >2.5 cm in diameter. Cytoreduction is considered to be therapeutic when a CCR of 0 or 1 is obtained, and is independently associated with prolonged survival (Table 34.2) (Yan et al., 2009).

Table 34.2 Completeness of cytoreduction (CCR) scoring system of Malignant Peritoneal Mesothelioma

CCR score	Residual tumor nodule in diameter
0	No visible tumor
1	<2.5 mm
2	Between 2.5 mm and 2.5 cm
3	>2.5 cm or a confluence of tumor nodules remaining at any site

After a therapeutic CRS is obtained, HIPEC is performed, during which a chemotherapeutic agent, typically mitomycin C or cisplatin, is circulated throughout the abdominal cavity under hyperthermic conditions for 90–120 min (Mongero et al., 1999). Temperature probes and large catheters will be placed within the abdominal cavity. The abdominal cavity is then closed temporarily, then the catheters are connected to a closed extracorporeal circuit consisting of a reservoir bag, heat exchanger, and roller pump. Thermal enhancement of chemotherapeutic agents would be maximized at temperature of 40.5–43 °C, which is referred to as moderate hyperthermia (Sugarbaker et al., 2007). Perfusate volume of 3–6 L is used and circulated at a rate of 1–1.5 L/min to ensure uniform warming of the peritoneal cavity. During perfusion, the abdomen should be gently manipulated to minimize any streaming effect of the perfusate from the inflow to the outflow catheter. At the completion of

treatment, the perfusate is drained from the abdominal cavity. For a MPM, HIPEC with doxorubicin (at a concentration of 15 mg/m^2) and cisplatin (at a concentration of 50 mg/m^2) in 3 L of 1.5% dextrose peritoneal dialysis solution with stirring at 42 °C for 90 min can be employed every 15 min to improve pharmacologic distribution.

The advantages of CRS plus HIPEC include: (a) surgery itself not only separates the adhesions but also resects the mass to release tumor burden, leaving a residual disease much more sensitive to chemotherapy agents; (b) intraperitoneal chemotherapy has much higher concentration of drug at the intraperitoneal tumor site compared with systemic chemotherapy, and less systemic side effects, and (c) heat enhances the cytotoxicity of chemotherapeutic drugs and their penetration into cancerous tissue (Al-Shammaa et al., 2008).

While, what about unresectable MPM tumors? Chemotherapy is considered to be a palliative approach for the patient ineligible for CRS. A substantially promising non-surgical treatment is the use of combinatory chemotherapy consisting of pemetrexed and cisplatin or gemcitabine. Pemetrexed alone or in combination with cisplatin obtains a similar disease control rate and overall response rate, suggesting that either regimen could be used as first-line chemotherapy. In recent years, regimens commonly used in systemic chemotherapy include combinatory irinotecan, cyclophosphamide, cisplatin, dacarbazine, pemetrexed, doxorubicin, and gemcitabine. It seems there are plenty choices, however, a definitely efficient regimen is yet to be developed to prolong survival for these patients.

Laparotomy and cytoreduction surgery related complications are wound infection, sepsis, bleeding, and fistula. Chemotherapy related complications are always caused by myelosupression.

6 Prognosis

Generally, for MPM patients who have undergone CRS plus HIPEC, the median overall survival time is 35.6 months, and the 5-year survival rate is 29%. Consistently, the median overall survival time in the cohort selected for CRS is significantly longer than its counterpart. According to a multi-institutional registry study, CRS plus HIPEC may achieve a 5-year survival rate of 47% in well-selected patient population.

Both tumor histology and biology affect prognosis. A recent study has shown that epithelioid histology is the most common and favorable feature of MPM (Schaub et al., 2013). Both the status of surgery and the extent of disease are important prognostic indicators (Yan et al., 2011). CCR (complete cytoreduction) can exert significantly positive effects on overall survival and progression-free survival of patients with MPM, just like other members of peritoneal malignancies.

According to a series of study, histologic type and nuclear size of tumor cells are the most important variables predicting the patient's survival. Male gender, poor performance status, a low level of hemoglobin, a high count of white blood cells, and non-epithelioid histologic type have been clarified as clinicopathologic factors predicting reduced survival for patients with MPM (Davidson, 2008). However, in another study, predictors for improved survival were good health status, female gender, minimal previous surgery, low peritoneal cancer index, undergoing a second-look surgery and complete cytoreduction.

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Retroperitoneal Malignant Lymphoma

35

Yuhong Zhou and Weiqi Lu

1 Introduction

Primary retroperitoneal tumors refer to tumors originating in adipose, loose connective tissue, fascia, muscle, blood vessels, neural tissue, lymphatic tissue, and the residual embryonic tissue in the retroperitoneal space. Two thirds of these tumors are malignant, which are typically soft tissue sarcoma, gastrointestinal stromal tumor (GIST), lymphoma, germ cell tumor, or other malignant tumors with lymph node metastasis. One third are benign, including typical lipoma, peripheral nerve sheath tumors, teratoma, and paraganglioma.

Lymphoma is a common lymphoid hematopoietic tumor that frequently occurs in the lymph nodes and may involve any tissue and organs in the body. Lymphadenopathy is the most common and typical clinical manifestation of lymphoma, which may not only invade superficial lymph nodes but also infiltrate deep lymph nodes in the mediastinum, abdominal cavity, retroperitoneum, and mesentery. However, simple enlargement of retroperitoneal lymph nodes is rarely seen in patients, mostly accompanied by simultaneous enlargement of lymph nodes at other sites of the body or the involvement of extranodal organs.

2 Clinical Features

Patients with retroperitoneal lymphoma present nonspecific symptoms such as abdominal pain, bloating, abdominal discomfort, and abdominal mass. With the increase in size of the tumor, patients may experience low back pain, gross hematuria, and lower extremity edema, which resulted from the invasion or compression of adjacent organs, such as the pancreas, duodenum, adrenal gland, and kidney. Those with disease progression may present with ascites, sometimes accompanied by fever, night sweats, weight loss, and other systemic symptoms. Patients with primary retroperitoneal lymphoma are considered at higher risk of secondary central nervous system involvement; however, its specific mechanism is unclear. Currently, the routine prophylactic intrathecal injection has not been recommended for these patients.

3 Diagnosis and Differentiation

Due to special characteristics of the anatomical structure, the diagnosis of retroperitoneal lymphoma is a challenging task, and the tumor is easily confused with other abdominal tumors.

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3.1 Imaging Characteristics

The ultrasound shows relatively homogeneous hypoechoic masses of various sizes next to large retroperitoneal blood vessels and the spine. The mass is nonencapsulated, nodular, and lobulated. Color Doppler displays plenty of blood flow signal in spot or bar shape, sometimes accompanied by the involvement or compression of adjacent organs.

CT scanning plays a vital role in the diagnosis and staging of retroperitoneal lymphoma. Plain image typically exhibits a nodular or irregular mass that is solitary or fused into a lump in the retroperitoneum, with an irregular margin and uneven density; after injection of contrast media, the mass is mildly enhanced. Enlarged lymph nodes may cross the midline and fuse into clumps that push or wrap mesenteric blood vessels, abdominal aorta, and inferior vena cava, resulting in typical "vascular silence sign" and disappearance of fat component from aorta and inferior vena cava. Castellino et al. (1984) confirmed the feasibility of CT scanning in the diagnosis and staging of lymphoma. Chen et al. (2005) reported the observation of 32 hematologic cases with primary retroperitoneal presentation, concluding that retroperitoneal lymphoma may lead to compression and involvement of surrounding tissue and organs, which are manifested as external compression of the bowel lumen, involvement of the kidney, adrenal glands, and pancreas or obstruction of urinary tract. CT of the chest, abdomen, and pelvis help determine the involvement scope of lymphoma as well as the pathological staging.

In MRI image, those enlarged lymph nodes involved by lymphoma typically display low-intensity signal on T1 image whereas iso-/high-intensity signal on T2 image, sometimes accompanied by hepatosplenomegaly.

It is now recognized that PET/CT is essential to the staging, efficacy evaluation, and prognosis prediction of aggressive diffuse large B-cell lymphoma and Hodgkin lymphoma. However, its role in the diagnosis of indolent lymphoma remains unclear, so PET/CT is not currently recommended for a routine detection.

3.2 Histopathological Examination

Malignant lymphoma is a group of highly heterogeneous tumors. Its two major forms are non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL). It can be further divided into dozens of subtypes, such as indolent follicular cell lymphoma (FL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), aggressive diffuse large B-cell lymphoma (DLBCL), and highly invasive Burkitt lymphoma in NHL, as well as different subtypes in HL. All of these subtypes can involve retroperitoneal lymph nodes but present with different biological characteristics and clinical outcomes. Thus, the determination of a specific pathological subtype contributes to an optimal regimen for therapy. The diagnosis of lymphoma must rely on lymph node biopsy. According to the studies reported by Cowles et al. (2000), if superficial lymph nodes are enlarged concurrently, the excision of lymph nodes or incisional biopsy under local anesthesia is a direct and simple method for establishing the diagnosis. However, the diagnosis may be challenging due to lack of superficial lymph nodes for biopsy.

The surgery cannot be used as a primary treatment for malignant lymphoma, as laparotomic biopsy simply for qualitative diagnosis can cause excessive trauma. With the development of CT, MR, and other diagnostic techniques, the diagnosis of lymphoma can be generally established by B ultrasound or CT-guided percutaneous biopsy that is simple, safe, economical, and minimally invasive, in combination with flow cytometry analysis. The effectiveness has been reported by Erwin et al. (1986), Nishino et al. (2003) and Yu et al. (2006). Especially for those with previous history of lymphoma, the fine needle aspiration is an ideal diagnostic tool to predict the efficacy, recurrence, or histological conversion. Nevertheless, the amount of tissue obtained by needle aspiration is limited, so its robustness is inferior to that of surgical specimen in pathological value of newly diagnosed patients. Sometimes, the diagnosis can only be established based upon multiple biopsies rather

than a single biopsy. Moreover, the determination of subtypes is more challenging. Additionally, percutaneous biopsy operation is technically difficult and risky due to enlarged retroperitoneal lymph nodes surrounded by large blood vessels, bowel, and other parenchymal organs. With the advancement of minimally invasive surgery, laparoscopic surgery may be an ideal approach to achieve a safe and effective surgical biopsy for retroperitoneal tumors. Malignant lymphomas can be classified by pathologists into different subtypes based on the morphology, immunohistochemistry, and molecular biology.

3.3 Differential Diagnosis and Staging

The possibility of the following tumors should be ruled out: soft tissue sarcoma, Castleman's disease, idiopathic retroperitoneal fibrosis, autoimmune lymphadenitis, lymph nodes tuberculosis, Wilms tumor, chromaffin tumor, paraganglioma, and malignant tumors metastasizing to retroperitoneal lymph nodes. Once the diagnosis of lymphoma is established, imaging examination (enhanced CT) should be performed for determination of staging. Ann Arbor staging system is commonly used for staging of lymphoma.

4 Therapeutic Management

Malignant lymphoma is highly sensitive to chemotherapy, while surgical treatment is limited to specific subtypes of indolent lymphoma. Since there is lack of effective methods with high sensitivity and specificity for the early diagnosis of primary retroperitoneal lymphoma, a surgery should not be performed blindly if a lymphoma is suspected based upon clinical manifestation and imaging findings. In this setting, pathological specimen should be harvested with minimally invasive techniques, and then further therapeutic regimen should be determined on the basis of pathological findings. If primary retroperitoneal lymphoma is misdiagnosed as other tumors, the excessive extent of surgical resection will not only increase the incidence of postoperative complications but also cause unnecessary harm to the quality of life. For those cases which are difficult to diagnose preoperatively, with wide intraoperative exploration range and involvement of multiple organs and large retroperitoneal blood vessels, a combined multiple-organ resection should not be performed until the pathological findings of rapid intraoperative frozen sections have been obtained, and if lymphoma is diagnosed, the surgery should be given up.

4.1 Chemotherapy

CHOP (cyclophosphamide, hydroxydaunorubicin, Oncovin/vincristine, and prednisone or prednisolone) protocol is a commonly used chemotherapy regimen. When in combination with CD20 monoclonal antibody such as rituximab, CHOP can effectively target B-cell lymphoma and improve EFS (event-free survival), PFS (progression-free survival), and OS (overall survival) of patients. Specific regimens may refer to those recommended for different types of lymphoma.

4.2 Radiotherapy

For patients with residual lesions after chemotherapy or with a large primary lesion ($\geq$10 cm in diameter), radiotherapy can be administered after chemotherapy. With the improvement in radiotherapy technology, three-dimensional conformal radiotherapy or intensity-modulated radiation therapy (IMRT) can increase an irradiation dose at the local tumor and reduce the potential damage to surrounding tissue and organs.

5 Prognosis

The patient's prognosis can be predicted with reference to the subtypes, clinical staging, performance status score, age, and lactate dehydrogenase levels of malignant lymphoma.

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Retroperitoneal Lymph Node Metastases

36

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Many malignant tumors produce retroperitoneal nodal metastases. Retroperitoneal metastases may be secondary to squamous cell carcinoma of pelvic, urinary, or gynecological systems, gastrointestinal (GI) tract adenocarcinoma, renal cell carcinoma, and unknown origin (Levi et al. 2002). Up to now, we have treated 17 cases of retroperitoneal metastatic cancer, including metastatic adenocarcinoma, squamous cell carcinoma, and sarcoma. Metastatic tumors that mostly occur in the retroperitoneal lymph nodes and lymph tissue may be differentiated from primary retroperitoneal tumors that commonly arise from the connective tissue beyond the lymph nodes.

1 Retroperitoneal Lymph Node Metastasis of Testicular Seminoma

Testicular germ cell tumors (TGCTs) mostly metastasize to the retroperitoneum. Lymph node involvement varies from micrometastases to huge intra-abdominal retroperitoneal masses. Primary extragonadal germ cell tumors (EGCTs) are extremely rare, accounting only 2–5% of all germ cell tumors. EGCTs occur in many sites in adults, including the pineal gland, retroperitoneum, and anterior mediastinum. Thus, they arise mostly along the sagittal midline. Whether an EGCT essentially metastasizes from a primary testicular tumor or develops originally in the retroperitoneum remains debated and controversial. It is critical to identify a primary testicular tumor in patients with a presumed EGCT due to a high risk for persistent testicular malignancy in almost 1/2 of such patients even treated with systemic chemotherapy (Scholz et al. 2002).

So-called primary retroperitoneal EGCTs are extremely rare. Until proven otherwise, it should be considered as metastasis of a burned-out/viable testicular cancer. An intensive urological examination including testicular ultrasound is mandatory for patients with retroperitoneal germ cell tumors. All ipsilateral testicular lesions identified by testicular ultrasound, clinical examination, and the patient's medical history should be treated adequately with orchiectomy since they could become the origin for tumor recurrence (Coulier et al. 2008).

After orchiectomy, if nonseminomatous testicular germ cell tumors show no evidence of metastases, either surveillance or retroperitoneal lymph node dissection would be recommended. On CT scan, using a size criterion of 10 mm has a false-negative rate of 63%, which can be reduced to as low as 7% if a size criterion of 4 mm is used (McMillan et al. 1982); however, specificity would be correspondingly decreased. When detecting enlarged lymph nodes (≥4 mm), especially for those located anterior to the midportion of the aorta, metastases should be highly

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suspected (Hilton et al. 1997). For patients with TGCT, especially young cases, MRI and CT have an almost equal sensitivity in detecting retroperitoneal tumors, indicating that MRI can replace CT in the surveillance of disease, so that ionizing radiation may be avoided. MRI is a noninvasive method, with a value equivalent to laparotomy in determining the anatomical localization and size of residual mass after chemotherapy as well as retroperitoneal lymph nodes that metastasize from testicular nonseminomatous germ cell tumors (Hogeboom et al. 1993). Components of the metastatic retroperitoneal lymph nodes respond differently to chemoradiation therapy, which can be tracked with MRI according to tumor homogeneity or signal intensity on T1-/T2-weighted imaging.

2 Retroperitoneal Lymph Node Metastasis from Ovarian Cancer

Very few studies have been focused on retroperitoneal spread through the lymphatics system in ovarian cancer. Chen and Lee (1983) examined nodal biopsy from 61 ovarian cancer cases who were randomly recruited into a prospective study. The incidence of metastasis to para-aortic nodes from ovarian cancer was 37.7%. Another study (Wu et al. 1989) reported the incidence of retroperitoneal nodal involvement as 50% in ovarian cancer. Aortic lymph node metastasis was first described by Knapp and Friedman in 1974, in which 26 patients with Stage I ovarian cancer were subjected to para-aortic lymphadenectomy. Retroperitoneal lymphadenectomy would relieve tumor burden by resecting the metastatic lymph nodes and slow down the later upward spread of cancer along the lymphatics. For Stage III ovarian cancer, surgery is the most important predictor for improved prognosis (Burghardt et al. 1986). The 5-year survival rate was 53.0% in 70 cases with lymphadenectomy while only 13.0% in 40 cases without lymphadenectomy (Burghardt et al. 1986).

3 Retroperitoneal Metastases from Unknown Primary Tumors

Among the referred patients with solid tumors, metastatic carcinoma of an unknown primary site (CUP) generally constitutes 3–5% (Levi et al. 2002). More than a half of CUP affects multiple sites (Briasoulis and Pavlidis 1997); however, incidence of metastases in retroperitoneal area is unknown. Retroperitoneal metastases from unknown primary is defined when patients are diagnosed with histopathologically confirmed retroperitoneal metastatic cancer; however, the primary tumor site cannot be identified despite complete medical/family history, blood count and biochemistry, urinalysis and stool occult blood testing, pelvic and rectal examination, cytologic evaluation of biopsy specimens using H&E and immunohistochemistry, chest radiography, CT/MRI of the abdomen/pelvis, and mammography (Karsell et al. 1982).

3.1 Clinic Characteristics

When mediastinum/retroperitoneum are predominantly affected by CUP, "extragonadal germ cell syndrome" is defined, which was first reported in 1979 and later characterized by Greco et al. (1986). Males younger than 50 years old are more susceptible to extragonadal germ cell syndrome, with clinical features of midline distributed metastatic cancer, involving mediastinal and retroperitoneal lymph nodes and accompanying pulmonary lesions (Fox et al. 1979). Patients are histopathologically confirmed with either undifferentiated or poorly differentiated cancer (Van der Gaast et al. 1990). Although CUP progresses very rapidly and aggressively, a certain portion of this group can respond substantially to chemotherapy and obtain a durable remission (Hainsworth et al. 1988). Elevated levels of α-fetoprotein (AFP) and human chorionic gonadotropin (β-hCG) are commonly detected in patients' serum. Although few cases have all the components of extragonadal germ cell

syndrome, any single feature of the entity indicates the diagnosis (Richardson et al. 1979).

3.2 Diagnostic Evaluation

How to obtain adequate specimens of tumor tissues is of utmost importance, which allows serial studies to be performed, such as light microscopy, immunohistochemistry, identification of diagnostic markers and molecular therapeutic targets, electron microscopy, and genomic/epigenomic analysis (Parada et al. 2007). Several commonly used initial diagnostic procedures including fine-needle aspiration always provide insufficient sample for optimal histopathology, especially in the setting of poorly differentiated tumor. To obtain detailed medical history, clinical manifestation, and laboratory results, the pathologist must work together with the clinicians. Undoubtedly their seamless teamwork can maximize the opportunity to make an accurate diagnosis of CUP.

CT scan of the pelvis and abdomen has been widely used in the setting of CUP, which can detect a primary site in 30–35% of cases (Richardson et al. 1981). CT can also determine the status of the metastasis and provide instruction in selecting an optimal strategy for biopsy (Karsell et al. 1982; McMillan et al. 1982). However, the value of CT as a modality to differentiate retroperitoneal metastases from primary retroperitoneal tumors has not been evaluated. FDG-PET scan is another critical imaging technique for detecting retroperitoneal CUP (Fig. 36.1). FDG-PET scan also provides pivotal information that may influence therapy inpatients with metastases evident in the retroperitoneum (Van der Gaast et al. 1990). In this circumstance, local treatment would be required.

3.3 Therapeutic Management

Poorly differentiated retroperitoneal CUP is treated based on guidelines for poor prognosis germ cell tumors, using platinum-based combinatory chemotherapy. For those patients, the overall response rate can reach >50%, with 15–25% complete response rate and 10–15% long-term disease-free rate (Ries et al. 2007). Surgery would be indicated for locally distributed retroperitoneal metastases without distant lesions.

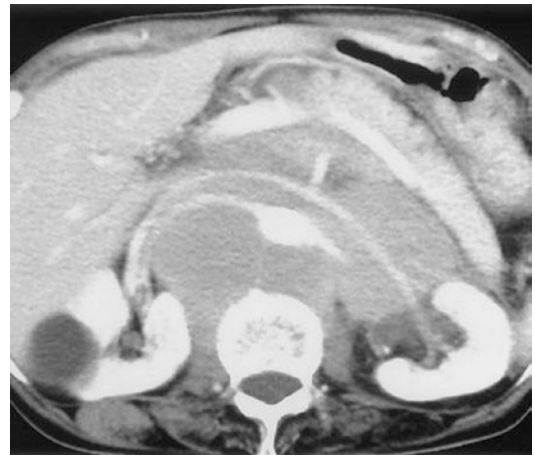

Fig. 36.1 CT scan of locally distributed retroperitoneal metastases

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