Idiopathic Retroperitoneal Fibrosis

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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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C.-H. Luo (ed.), *Retroperitoneal Tumors*, https://doi.org/10.1007/978-94-024-1167-6_18

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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