Retroperitoneal Malignant Lymphoma

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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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