Testicular Lymphoma: Clinical and Imaging Features

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ABSTRACT
Objective: To review the clinical presentation and imaging features of testicular lymphoma.
Methods: We retrospectively reviewed the clinical data, and grey-scale and colour Doppler ultrasound features of 11 patients with proven testicular lymphoma between January 2000 and September 2013. The patients were aged 35 to 84 years (mean, 59 years). The diagnosis was established by orchidectomy in eight patients, by compelling evidence including bone marrow and lymph node biopsy in two, and autopsy in one.
Results: Of the 11 patients, seven presented with painless scrotal mass(es), three presented with an afebrile painful scrotal mass, and one presented with a febrile painful scrotal mass. Disease was unilateral in nine patients and bilateral in two. Primary testicular lymphoma was diagnosed in six patients and secondary testicular lymphoma in five, of which nine were non-Hodgkin’s lymphoma with diffuse large B-cell lymphoma (DLBCL) and two were T-cell lymphoma. Ultrasonography revealed diffuse hypoechoic involvement in seven patients, a solitary hypoechoic mass in two patients, and bilateral multiple hypoechoic masses in two patients. All lesions showed hypervascularity. Enlarged epididymis with hypervascularity was present in two patients mimicking epididymoorchitis.
Conclusion: Testicular lymphoma is predominantly DLBCL. Patients may present with painless or painful scrotal mass(es). Lymphoma should be considered in a man older than 50 years who presents with testicular mass regardless of pain with focal or diffuse hypervascular hypoechoic testicular lesion(s) on ultrasound. The associated hypervascular enlarged epididymis does not exclude the diagnosis of testicular lymphoma.

Key Words: Lymphoma; Orchitis; Scrotum; Testicular neoplasms; Ultrasonography

中文摘要
睾丸淋巴瘤的临床和影像学特征

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目的：探討睾丸淋巴瘤的臨床表現和影像學特徵。
方法：回顧分析於2000年1月至2013年9月期間共11個睾丸淋巴瘤確診病例的臨床資料，以及其灰度和彩色多普勒超聲特徵。患者年齡介乎35至84歲，平均59歲。患者中有8例經睾丸切除術而確診，2例經包括骨髓和淋巴結活檢等確診，另1例則通過屍檢而確診。
結果：11例睾丸淋巴瘤中，7例表現為無痛性陰囊腫塊，3例無發燒但有陰囊腫塊並感覺疼痛，1例有發燒症狀兼有陰囊腫塊和疼痛，單側睾丸淋巴瘤9例，雙側睾丸淋巴瘤2例。原發性和繼發性睾丸淋巴瘤
INTRODUCTION

Testicular lymphoma accounts for 1% to 9% of all testicular neoplasms and 1% of all non-Hodgkin’s lymphoma. Although uncommon, they are the most common testicular malignancy in men older than 50 years and the most common cause of bilateral testicular tumours. Clinical features are variable. Patients usually present with a unilateral painless scrotal swelling, but sharp scrotal pain or a painful scrotal mass may occur. Because the treatment is different, lymphoma is to be distinguished from other testicular germ cell tumours when patients present with scrotal masses and from infection when patients present with scrotal pain. Ultrasonography (US) is the imaging of choice to evaluate patients with scrotal problems. Familiarity with US features of testicular lymphoma will help to differentiate lymphoma from other germ cell tumours or inflammation and provide appropriate management. Since reports of US features of testicular lymphoma remain limited, we reviewed the clinical presentation and US features of testicular lymphoma at our institution to add to the current knowledge.

METHODS

This study was approved by the Institutional Review Board with informed consent waived. Clinical data, and grey-scale and colour Doppler US features of 11 patients with proven testicular lymphoma between January 2000 and September 2013 were retrospectively reviewed; one patient was revealed in a case report (Table, patient No 2). The patients were 35 to 84 years old, with a mean age of 59 years. US was performed in all patients using one of our machines (HDI 5000; Advanced Technology Laboratories, Bothell [WA], USA / Acuson Sequoia; Acuson Siemens, Mountain View [CA], USA / Logic 9; GE Medical System, Milwaukee [WI], USA / Aplio-XG; Toshiba, Tokyo, Japan). A linear transducer with frequency range of 5-14 MHz was used. Grey-scale US and colour Doppler US were performed in all patients. Two radiologists evaluated the US images by consensus. Grey-scale US images were evaluated for side of involvement, presence of focal mass(es) or diffuse infiltrative lesions, echo pattern, associated hydrocele, and involvement of extratesticular structures including epididymis, spermatic cord, and skin. Colour
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Doppler US evaluated the vascularity of the lesions. The determination of vascularity was based on comparison with the normal ipsilateral or contralateral testis. The diagnosis was established by orchidectomy in eight patients, by compelling evidence including bone marrow and lymph node biopsy in two, and on autopsy in one.

RESULTS
The Table provides the details of clinical information and US findings. Of the 11 patients, primary testicular lymphoma (PTL) was diagnosed in six patients and secondary testicular lymphoma (STL) in five. Seven patients presented with painless scrotal mass(es), three with an afebrile painful scrotal mass, and one with a febrile painful scrotal mass. The right testis was involved in four patients, left testis in five, and bilateral in two. The most common cell type was non-Hodgkin’s lymphoma with diffuse large B-cell lymphoma (DLBCL) found in nine patients and T-cell lymphoma in two. All patients had negative test results for human immunodeficiency virus (HIV).

US revealed diffuse hypoechoic involvement in seven, a solitary hypoechoic mass in two, and bilateral multiple hypoechoic masses in two. By the type of lymphoma, of six patients with PTL, a solitary hypoechoic mass was evident in two (Figure 1) and diffuse hypoechoic involvement in four (Figure 2). In five patients with STL, US showed bilateral multiple hypoechoic masses in two (Figure 3) and diffuse hypoechoic involvement in three. All testicular lesions showed hypervascularity on colour Doppler US. Enlarged epididymis was present in four and was associated with hypervascularity in two cases. Hydrocele was present in seven. No patient had skin involvement. Histologically, all patients with enlargement of the epididymis on US had epididymal involvement of lymphoma.

Lymphoma clinically mimicked epididymo-orchitis in two cases. In one patient, PTL clinically mimicked incarcerated hernia with epididymo-orchitis (patient No. 4; Figure 4). At operation, an enlarged epididymis, testis, and spermatic cord were found and radical orchietomy was performed. Histology revealed DLBCL of the testis, epididymis, and spermatic cord. Another patient with a known history of lymphoma with fever and a painful scrotal mass that did not improve with antibiotic treatment was found to have disseminated T-cell lymphoma in both the epididymis and testis (patient No. 11).

DISCUSSION
Testicular lymphoma is an uncommon tumour that affects the elderly. Although the common presenting symptom is a painless scrotal mass, it can occasionally present with scrotal pain. Systemic constitutional symptoms of lymphoma such as fever, night sweats, and weight loss are uncommon and are signs of advanced disease. Comparable with other studies, the mean age of patients in our series was 59 years (range, 35-84...
years) and 64% presented with painless scrotal mass(es). In our study, pain occurred in four (36%) patients and was associated with fever in one, mimicking a clinical presentation of epididymo-orchitis.

Testicular lymphoma may be primary as only a manifestation of malignant lymphoma or indicative of secondary involvement of the testis during the clinical course of a patient with established lymphoma. STL is more common than PTL. Nonetheless, in this study we found more cases of PTL than STL. Diagnosis of testicular lymphoma can be based solely on clinical findings in the case of STL and patients do not require US. This selection bias may affect the proportion of PTL and STL cases in our study.

US plays a major role in the evaluation of testicular lesions. Scrotal US has been used for the diagnostic evaluation of patients who present with scrotal mass or pain. Location of the lesion can suggest the nature of disease. The majority of intratesticular lesions are malignant while extratesticular lesions are usually benign. US can aid in differentiating the two with an accuracy approaching 100%. The reported US appearance of testicular lymphoma is either focal or diffuse hypoechoic enlarged testis with hypervascularity. Bilateral disease occurs in approximately 10% to 35% of cases. These US findings must be differentiated from other germ cell tumours, metastasis, and orchitis. On US, germ cell
tumours are mostly a unilateral lesion, either focal solitary mass or a diffuse lesion. The tumour is common in young adult men aged between 25 and 30 years.\textsuperscript{4,5} Bilateral germ cell tumour is uncommon, occurring in only 2\% to 3\%.\textsuperscript{1} Metastases are usually multiple with bilateral lesions occurring in patients with a known malignancy at an advanced stage. The common primary tumours include those of the prostate, lung, skin, colon, and kidney.\textsuperscript{2} Orchitis presents with a diffuse lesion with increased vascularity accompanied by enlarged epididymis and skin thickening. Isolated orchitis without epididymitis is rare.\textsuperscript{4}

It has been suggested that associated epididymal enlargement with hypervascularity is more suggestive of inflammation than of tumours.\textsuperscript{3,6,11} In this study, two patients had enlarged hypervascular epididymis and testis. Both patients presented with scrotal pain, one with fever and one without. These clinical presentations combined with US features were highly suggestive of epididymo-orchitis. One of these two patients, however, did not improve with antibiotic treatment and was found to have disseminated T-cell lymphoma involving both epididymis and testis. The other patient was diagnosed with an incarcerated hernia with epididymo-orchitis but this was later proven to be primary testicular DLBCL. To our knowledge, there are four reports\textsuperscript{3,12,14,18} of testicular lymphoma presenting as epididymo-orchitis.

Figure 4. Primary testicular lymphoma with enlarged epididymis mimicked epididymo-orchitis and incarcerated hernia. An 84-year-old man presented with a 10-day history of painful left scrotal and inguinal masses. He was afebrile. Longitudinal colour Doppler ultrasonography (US) images of the (a) right and (b) left hemiscrotum show normal blood flow in normal-sized right epididymis (RE) and testis (RT) and hypervascularity in enlarged left epididymis (LE) and testis (LT). (c) Longitudinal grey-scale US image of the left inguinal mass shows a heterogeneous hypochoic mass (M). (d) Gross specimen shows enlarged testis (T) and spermatic cord (arrow). Histology revealed diffuse large B-cell lymphoma of the testis with involvement of the epididymis and spermatic cord.
In another report by Mazzu et al., one patient had enlarged hypervascular epididymis but the presence of epididymal inflammation without histological correlation was suggested. Therefore US findings of enlarged hypervascular epididymis and testis do not exclude the possibility of lymphomatous infiltration.

Histologically, 80% to 90% of testicular lymphomas are DLCBL as in our study (81%). Less common histological subtypes found in HIV-positive patients are Burkitt’s and Burkitt’s-like types. Other rare histological subtypes include follicular lymphoma, T-cell lymphoma, and mucosa-associated lymphoid tissue lymphoma. Orchidectomy is usually performed in patients with testicular lymphoma to provide histological diagnosis and eliminate the blood-testis barrier that makes testicular tumours inaccessible to systemic chemotherapy. Further treatment with radiation and chemotherapy are often offered but the prognosis of both PTL and STL is poor. Testicular lymphoma frequently spreads to the epididymis, tunica albuginea, spermatic cord, or scrotal skin, and also has a tendency to spread to extranodal sites including the central nervous system, lung, and Waldeyer’s ring. Most patients with PTL have a relapse of their disease within the first 2 years. Unfortunately, we did not study the outcome of the patients.

**CONCLUSION**

Testicular lymphoma is an uncommon testicular tumour that affects older men, particularly those aged over 50 years. Most are predominantly DLBCL. Patients can present with unilateral or bilateral and painless or painful scrotal mass(es). US features of testicular lymphoma include hypervascular hypechoic lesions: either single, multifocal, or diffuse lesions. The disease may involve the epididymis and spermatic cord, mimicking epididymo-orchitis and hernia. To avoid diagnosis pitfalls, radiologists should keep in mind that the associated hypervascular enlarged epididymis does not exclude the diagnosis of testicular lymphoma. Suspicion should be heightened when a patient fails to respond to antibiotic treatment or has a known diagnosis of lymphoma.

**REFERENCES**