INTRODUCTION

Testicular cancer represents between 1% and 1.5% of male neoplasms and 5% of urological tumours. The vast majority of tumours are diagnosed in the third and fourth decade of life. The histological type varies, although there is a clear predominance (90-95%) of germ cell tumours. The incidence of germinal cell tumours (GCTs) declines markedly towards the age of 50, and tumours in patients above the age of 60 are extremely rare, while the incidence of spermatocytic seminoma (a distinct GCT with a generally benign behavior), primary lymphoma, stromal tumors, usually of the Leydig cell type, and rarely metastasis progressively increases. In addition, although most masses encountered within the scrotal sac are within the testis, a subset (2-3%) of these tumors is extratesticular and arises from paratesticular tissue that includes the spermatic cord, testicular tunics, epididymis, and vestigial remnants. Although uncommon, these tumors have been recorded as the main urogenital site of sarcomas in the elderly, whereas primary sarcoma of the testis is a rare entity in which a diagnosis is made only after the exclusion of the more common paratesticular neoplasm.

KEY WORDS: Testicular neoplasm, Elderly, Stromal testicular neoplasm, Primary testicular lymphoma, Paratesticular sarcomas.

UNCOMMON TUMORS OF THE TESTIS


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ABSTRACT: The behaviour of testis tumors in the elderly is completely different from the younger patient one. The most frequent histological type are spermatocytic seminoma, malignant Leydig tumors and lymphomas in the testis and sarcomas in the paratesticular region. Despite the low incidence of these tumors, the testis is the first site of genitourinary involvement for sarcomas in the elderly. on account of their frequency, its diagnosis should be made only after the exclusion of the most common paratesticular neoplasm.

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TESTICULAR GERM CELL TUMORS

Testis germ cell tumors (TGCTs) can be subdivided into three different biological and clinical entities: (a) prepubertal teratoma-yolk sac tumors; (b) seminoma and nonseminoma; and (c) sperma-
Spermatocytic seminoma is a tumor that typically occurs in the elderly, with distinctive clinical and pathological characteristics. The incidence increases with age and the peak is in the sixth decade, representing the 1.3-2.3% of all patients with seminomas. Generally, spermatocytic seminoma is presented with painless and unilateral swelling, not associated with history of cryptorchidism and without increasing markers. This tumor tends not to metastasize. Usually, the tumor is well circumscribed and encapsulated, rarely extending into the paratesticular soft tissue. Microscopically, the tumor consists of a diffuse proliferation of polymorphic cells of different sizes: small, 6-8 mm, eosinophilic cytoplasm lymphocyte-like; large, 80-100 mm, sometimes multinucleated; and intermediate, 15-20 mm, which are predominant in the tumor and with a round nucleus and granular chromatin. Spermatocytic seminomas generally show an immunohistochemical expression of c-Kit in around 40% of the spermatocytic seminomas. Cytogenetic anomalies aid the differentiation of spermatocytic seminomas from conventional seminomas and other GCTs: the gain of chromosome 9 appears to be a consistent finding in all spermatocytic seminomas. Classic seminomas, in contrast, show a consistent structural chromosomal abnormality of isochromosome 12p. The neoplastic transformation of progenitor cells in spermatocytic seminoma and their relationship with other GCTs remain controversial. The best hypothesis considers the spermatocytic seminoma as derived from progenitor cells capable of maturation at least up to the stage of spermatogonia-pachytene spermatocyte. In fact, spermatocytic seminoma expressing proteins related to this range of aging in normal GC, as synaptonemal complex protein 1 (SCP1), xeroderma pigmentosa A (XPA), and synovial sarcoma on X chromosome (SSX). SCP1 and XPA are expressed normally in primary and pachytene spermatocyte stage, which SSX is normally observed in spermatogonia and primary spermatocytes, as well as in germ cells from the 17th week of intrauterine development. The absence of these proteins in conventional seminoma supports the embryonic germ cells as the cell of origin. Lim et al. have identified two subsets of spermatocytic seminoma features based on OCT2 or SSX2-4 immunoreexpression and conclude that the expression pattern of three markers reflects the origin of spermatocytic seminoma from spermatogonia and demonstrate that the tumor is a heterogeneous group. Finally, the expression profile of 156 miRNAs showed that spermatocytic seminoma cluster occurs with more differentiated tissues as normal testis and teratomas, in contrast microRNAs in seminomas and dysgerminomas, which also cluster with embryonal carcinomas. In consideration of their favorable behavior is being cured by only orchiectomy. A worst prognosis can occur when appears a sarcomatous dedifferentiation that gives a metastasizing potential.
SSTROMAL TESTICULAR NEOPLASM

Leydig cell tumors (LCTs) are rare tumors representing 1-3% of all testicular malignancies and they have two peaks of incidence: between 5 and 10 years and in men aged 30 to 82 years. Its malignant variant that represent only 10% of cases, occurred more frequently in the elderly. The frequent site of metastatization is to the retroperitoneal lymph nodes (70%), liver (45%), lung (40%), and bone (25%), usually within 2 years of the diagnosis. Frequently, the tumor cells produce testosterone, but it can be characterized by an increase in estrogen, either because of the direct production of estradiol or because of peripheral aromatization of the testosterone. Thus, androgen-secreting tumors in adults and in elderly patients are asymptomatic, whereas in estrogen-secreting tumors, patients generally present with endocrinological disorders such as gynecomastia, impotence, infertility, and loss of libido. Clinically, patients commonly show painless testicular enlargement or a palpable mass. This kind of tumor can be pure or mixed with germ cell tumors or other sex-cord stromal tumors. Histologically, we can observe four types of cells: (a) large polygonal cells with abundant granular eosinophilic cytoplasm, oval nuclei, and indistinct cell borders; (b) cells similar to type 1, but with distinct cell borders and smaller nuclei; (c) small cells with grooved nuclei; and (d) spindle cells. The cytoplasm less frequently may be clear for the presence of abundant lipid and lipofuscin. The degree of malignancy is defined by more tumor size (> 5 cm), infiltrative margins, foci of necrosis, absent signs of hormonal activity cancer (gynecomastia), vascular and lymphatic invasion, nuclear atypia, mitotic count greater than 3/10HPF, increased MIB-1 and DNA aneuploidy. The positive immunohistochemical markers for LCT are inhibin, vimentin, Melan-A, and calretinin. The benign variant can be cured by surgery, such as orchiectomy and retroperitoneal lymph adenectomy. Most cases are diagnosed in men beyond the sixth decade. According to the current literature, PTL should be considered when no other tumor masses are observed on the rest of the body or when such tumors are smaller in volume than the testicular tumor mass. In HIV-positive patients, the incidence of PTL is increased and it is found at an earlier age, where it is associated with a poor prognosis. In adult testis, primary diffuse large B cell lymphoma (DLBCL) is the most observed lymphoma (80-90%). The most common clinical presentation of TL is with unilateral painless scrotal swelling. In 25-41% of patients the disease presentation is with fever, night sweats, and weight loss but are more frequent in the advanced stage. The involvement of retroperitoneal lymph nodes often leads to pain and ascites. In 43% of patients is found hydrocele without evidence of a testicular mass. On clinical examination, TL appears as a firm mass. Bilateral testicular involvement synchronous at diagnosis or, more frequently, asynchronous has been documented in up to 35% of patients. Local lymphoma diffusion through the epididymus, spermatic cord, is quite frequent, whereas dissemination to several extranodal sites including the controlateral testis, central nervous system (6-16%), skin (0-35%), Waldeyer’s ring (5%), lung, pleura, and soft tissue is less frequent. The diagnosis of TL is better made on orchiectomy samples rather than on fine needle biopsy. In addition, orchiectomy provides good local tumor control and facilitates the removal of a sanctuary site, as the blood-testis barrier makes testis tumors a chemotherapy sanctuary. Most TLs are B-cell lymphomas. DLBCL represents 80-90% of all cases. Burkitt’s and Burkitt’s-like lymphomas are found in only 10-20% of cases, mainly in HIV+ patients. B-cell lymphoma, unclassifiable, with characteristics intermediate between DLBCL and Burkitt lymphoma, has also been reported. Follicular or T cells lymphomas have rarely been described. Most common expressed markers are CD19, CD20, CD79a and CD22 (B cell marker), while CD10 MUM1 are found in 30-65% of cases and the nuclear BCL6 expression has been reported in 60-90% cases. DBCLs can be distinguished into two subclasses based on the expression of CD10, BCL6, and MUM1: germinal Center B-cell-like and a center nongerminall B-cell-like, the germinal center B-cell lymphomas as is the most frequent at this site. The diagnostic definition of these diseases is of primary importance infact an error in differential diagnosis, may cause fatal consequences in view of the completely different treatment. Unfortunately, in view of the high disease aggressivity, the prognosis is very poor and often patients with stage I/II show early recurrence. Overall survival at 5 and 10 years for stage I patients PTL was 58 and 29%, and for stage II patients PTL,
was 46 and 29%, respectively. Stage IV patients show a higher rate of recurrence of 90% and a 5-year survival of 20-25%. It has been proposed several prognostic factors such as age, performance status, tumor burden greater than 9 centimeters, the spermatic cord involvement, lactate dehydrogenase serum levels, histologic grade, vascular invasion, degree of sclerosis and stage of the disease. In IELSG series of 373 patients PTL, the parameters associated with a long overall survival were low/low-intermediate risk, according to the international prognostic index, absence of B symptoms, anthracycline-based chemotherapy, and prophylactic scrotal radiotherapy.

PARATESTICULAR SARCOMA

Paratesticular sarcoma is an uncommon disease. It is so difficult to provide a summary of various factors in the natural history of these tumors and the treatment results. According to the Memorial Sloan-Kettering Cancer Center large case series, 2.1% of soft tissue sarcomas arise in the genitourinary tract, and almost 44% are paratesticular. Usually, a paratesticular tumor appears as a scrotal mass occasionally associated with a hydrocele. Seventy percent of all cases are benign and 30% are malignant. The most frequent benign tumors are lipomas, adenomatoid tumors, and leiomyomas. Among the paratesticular sarcomas, liposarcoma is the most frequent, followed by leiomyosarcoma, both found mainly in the elderly.

PARATESTICULAR LEIOMYOSARCOMA

Leiomyosarcoma is the most commonly reported histologic type of paratesticular sarcoma. The reported average age for paratesticular leiomyosarcoma was 60 years and most cases were in the 40-70 age group. Rarely, pure intratesticular leiomyosarcomas are reported as single case reports, with an average age of 50 years. Definitive diagnosis requires a histologic examination of a resected specimen to observe morphological and immunohistochemical smooth muscle differentiation, neoplastic cells immunostain for smooth muscle actin, muscle-specific actin, and desmin; moreover, h-caldesmon may be used to confirm smooth muscle differentiation and myogenin to exclude spindle cell rhabdomyosarcoma. The preferred site of involvement is the spermatic cord, rarely epididymis. It appears as a generally painful mass or swelling, often near the spermatic cord, occasionally accompanied by a small hydrocele. Histologically, leiomyosarcoma is characterized by typical features of spindle cell neoplasm with a fascicular architecture, foci of cytologic atypia, and mitoses, the presence of a large amount of necrosis is generally observed in high-grade tumors. The clinical and biological behavior of paratesticular leiomyosarcoma is generally unpredictable. The main prognostic factors of leiomyosarcomas are the site, size, grade of primitive tumors and nodal or distant metastasis. The best treatment remains controversial but radical inguinal orchietomy is the primary treatment including high ligation of the spermatic cord. Local recurrence is common for

PARATESTICULAR LIPOSARCOMA

Liposarcoma is the most common type of soft tissue sarcoma, accounting for 30% of all mesenchymal tumors, whose peak occurs in the sixth to seventh decade. Paratesticular liposarcoma is low-grade malignancy. It appears as a painless, fluctuant, slow-growing mass, with a maximum diameter of 5-10 cm. Rapid growth, large size, and pain are indicative of more aggressive histotypes. Histologically, they are classified into five categories, as the WHO Committee for the Classification of Soft Tissue Tumors proposed in 2002: well differentiated, dedifferentiated, myxoid, pleomorphic, and mixed. The most frequent histotype in paratesticular site is the well-differentiated variant, characterized by diffuse mature lipomatous differentiation associated with the presence of lipoblasts in fibrous septa. It is a low-grade tumor with no metastatic potential, but with high rate of local recurrence. De-differentiation can occur ab-initio or in case of relapse with potential hematogenous and lymphatic spreading. The prognosis for well-differentiated liposarcoma remains good, with overall 5- and 10-year survivals of 75 and 55%, respectively. The high relapse rate and metastasis observed in high-grade liposarcoma worsen the prognosis significantly. Initial treatment consists of orchietomy with high ligation of the spermatic cord at the inguinal canal. Surgery can be combined with radiation therapy. Spermatic cord liposarcoma is the most radiosensitive of all sarcomas. This therapy has been particularly indicated in the relapse of intermediate-grade or high-grade lesions. The role of retroperitoneal lymph node dissection is uncertain and is recommended in case of intermediate/high-grade disease with evidence of lymphnode involvement by a computed tomographic scan. The role of adjuvant chemotherapy remains uncertain, in case of high-grade liposarcoma can be represented by the use of combined chemotherapy (vincristine, cyclophosphamide, ifosfamide and anthracyclines).
high grade tumor and for positive margins, difficult to obtain in the paratesticular region. Adjuvant loco-regional radiation after surgery may be recommended to reduce the rate of local recurrence. The role of chemotherapy is unknown.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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