World Cancer Research Journal WCRJ 2014; 1 (2): e248

UNCOMMON TUMORS OF THE TESTIS

C. D'ANIELLO[1], C. CAVALIERE[1], S. CECERE[2], M. DI NAPOLI[2], R. DI DOMENICO[3], D. SORRENTINO[3], V. GIGANTINO[4], E. LA MANTIA[4], R. FRANCO[4], S. PERDONÀ[3], S. PISCONTI[1], S. PIGNATA[2], G. FACCHINI[2]

[1]Division of Medical Oncology, "S.G. Moscati" Hospital, Taranto, Italy
[2]Division of Medical Oncology, Department of Uro-Gynaecological Oncology, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS, Naples, Italy.
[3]Division of Urology, Department of Uro-Gynaecological Oncology, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS, Naples, Italy.
[4] Pathology Unit, Istituto Nazionale Tumori "Fondazione G. Pascale" - IRCCS, Naples, Italy.

ABSRACT: *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.*

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

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[1]. The incidence of germinal cell tumors (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[2,3]. 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[4-6].

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-

Corresponding Author: Dominique Elias, Ph.D; e-mail: dominique.elias@gustaveroussy.fr

tocytic seminoma. The first group includes tumors that develop in prepubertal age but seminoma and nonseminoma may develop also after puberty. On the contrary spermatocytic seminoma is encountered mainly in elderly men[6-8]. The developement of this histological kind of tumors starts during fetal period, through changes occurring in primordial germ cells either during migration to the embryonic genital ridges or later when cells localize in the gonads. Post-pubertal TGCTs, instead, derives from initially cellular changes defined not invasive intratubular germ cell neoplasia (ITGCNU) that following successive amendments evolve into seminoma or nonseminoma or both subtypes, around or after puberty[9,10]. In the past, in elderly were reported only sporadic cases of seminoma and non-seminoma. Seminomas and nonseminomas are also extremely rare in patients younger than 60 years of age. In a recent work of Berney and colleagues, were analyzed a large number of TGCTs in elderly patients (mean age 67 years) and 82% (41 cases) were seminomas, 12% (6 cases) were nonseminomas like yolk sac, teratoma, embryonal carcinoma, and choriocarcinoma and 6% (3 cases) mixed seminoma/nonseminoma. Tumor size was markedly larger than that in younger men and TGCTs present at a higher stage than in younger men probably because they may present to clinicians at a later stage or may be diagnostic on delay because of the lack of clinical examination of the testis. In addition, there is also a difference in the cure of the neoplasm; in fact, the tendency to present at a higher stage and less tolerance to chemotherapy in older patients make the tumors in this group less curable[3,11]. Seminomas are composed of cells similar to ITGCNU, showing a homogenous appearance, and organized in one or more nodules with a lymphocytic infiltrate in the supportive stroma. Nonseminoma could be both pure and mixed with other nonseminoma elements (embryonal cell carcinoma, yolk sac tumor, choriocarcinoma, teratoma)[8]. The management of these tumors remains the same also in elderly and the first curative approach is surgery with orchiectomy. These neoplasms are chemiosensitive (cisplatinum based therapy). The seminoma has a marked radiosensitivity too. Nonseminoma TGCT-are less sensitive to radiation and when metastatic, often requiring both chemotherapy and surgery[11].

TESTICULAR CELL TUMORS

Spermatocytic seminoma is a rare germ cell 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[13,14]. This tumors tend 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[13]. Spermatocytic seminomas cells 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[15]. Classic seminomas, in contrast, show a consistent structural chromosomal abnormality of isochromosome 12p[16]. The neoplastic transformation of progenitor cells in spermatocytic seminoma and their relationship with other GCT remain controversial[17-19]. 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 Type 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 protein in conventional seminoma supports the embryonic germ cells as the cell of origin[20]. Lim et al[17] have identified two subsets of spermatocytic seminoma features based on OCT2 or SSX2-4 immunoexpression 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[21]. In consideration of their favorable behavior is being cured by only orchidectomy. A worst prognosis can occur when appears a sarcomatous dedifferentiation that gives a metastasizing potential[22].

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, occured 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[23]. 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[24]. 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[23]. 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[25]. 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[24]. 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[26]. The positive immunohistochemical markers for LCT are inibin, vimentin, Melan-A, and calretinin[27]. The benign variant can be cured by surgery, such as orchiectomy or nodule enucleation. In adult and elderly patients, in whom malignant LCTscan be observed more frequently, the best treatment is radical orchiectomy and retroperitoneal lymphadenectomy. Malignant LCT does not respond favorably to chemotherapy and irradiation and the prognosis is poor (median, 2 years)[28].

PRIMARY LYMPHOMAS

Primary testicular lymphoma (PTL) is an uncommon disease that comprises only 1-9% of testicular neoplasm[16]. However, it is the most common malignancy in men older than 50 years of age and 85% of 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[29]. 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[30]. 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[29,31,32]. The involvement of retroperitoneal lymph nodes often leads to pain and ascites[27]. 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[29,32]. 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[31-34]. 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[35, 36]. 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[37,38]. DBCLs can be distinguished into two subclasses based on the expression of CD10, BCL6, and MUM1: germinal Center B-cell-like and a center nongerminal B-cell-like, the germinal center B-cell lymphomas as is the most frequent at this site[39,40]. 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[34]. Unfortunately, in view of the high disease aggressivity, the prognosis is very poor and often patients with stage I/II show early recurrence[41]. 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[42]. Stage IV patients show a higher rate of recurrence of 90% and a 5-year survival of 20-25%. It have been proposed several prognostic factors such as age, performance status, symptoms, 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[29,43,44]. 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[42].

PARATESTICULAR SARCOMA

Paratesticular sarcoma is an uncommon disease. It is so difficult to provide series of sufficient cases to document the natural history of these tumors and the treatment results[45]. 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[7,46]. 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[48]. Among the paratesticular sarcomas, liposarcoma is the most frequent, followed by leiomyosarcoma, both found mainly in the elderly[49].

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[50]. Paratesticular liposarcoma is low-grade malignancy[51]. It appears as a painless, fluctuant, slow-growing mass, with a maximum diameter of 5-10 cm[50]. 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[52,53]. 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[52]. De-differentiation can occur ab-initio or in case of relapse with potential hematogenous and lymphatic spreading[54-56].

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[57]. Initial treatment consists of orchiectomy 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[58]. The role of adjuvant chemotherapy remains uncertain, in case of high-grade liposarcoma can be represented by the use of combined chemotherapy (vincristine, cyclophosphamide, ifosphamide and anthracyclines)[59].

PARATESTICULAR LEIOMYOSARCOMA

Leiomyosarcoma is the most commonly reported histologic type of paratesticular sarcoma[60]. The reported average age for paratesticular leiomyosarcoma was 60 years and most cases were in the 40-70 age group[61]. Rarely, pure intratesticular leiomyosarcomas are reported as single case reports, with an average age of 50 years[62]. 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[63]. The preferred site of involvement is the spermatic cord, rarely epididymis[63,64]. 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[65,66]. The clinical and biological behavior of paratesticular leiomyosarcoma is generally unpredictable. The main prognostic factors of leiomyosarcomaa are the site, size, grade of primitive tumors and nodal or distant metastasis[67]. The best treatment remains controversial but radical inguinal orchiectomy is the primary treatment including high ligation of the spermatic cord. Local recurrence is common for

high grade tumor and for positive margins, difficult to obtain in the paratesticular region[48]. Adjuvant locoregional 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.

References

1. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Fizazi K, Horwich A, Laguna MP, Nicolai N, Oldenburg J. Guidelines on testicular cancer. European Association of Urology guidelines on testicular canncer: 2014 update.
2. Carrión López P, Pastor Navarro H, Martínez Ruiz J, Giménez Bachs JM, Donate Moreno MJ, Polo Ruiz L, Pastor Guzmán JM, Martínez Sanchiz C, Ruiz Mondéjar R, Virseda Rodríguez JA. Spermatic cord sarcomas: current status and report of four cases. Arch Esp Urol 2009; 62(3): 242-246.
3. Berney DM, Warren AY, Verma M, Kudahetti S, Robson JM, Williams MW, Neal DE, Powles T, Shamash J, Oliver RT. Malignant germ cell tumours in the elderly: a histopathological review of 50 cases in men aged 60 years or over. Mod Pathol 2008; 21: 54-59.
4. Purdue MP, Devesa SS, Sigurdson AJ, McGlynn KA. International patterns and trends in testis cancer incidence. Int J Cancer 2005; 115: 822-827.
5. Eble JN. Spermatocytic seminoma. Hum Pathol 1994; 25: 1035-1042.
6. Lioe TF, Biggart JD. Tumours of the spermatic cord and paratesticular tissue. A clinicopathological study. Br J Urol 1993; 71: 600-606.
7. Chieffi P, Franco R, Portella G. Molecular and cell biology of testicular germ cell tumors. Int Rev Cell Mol Biol 2009; 278: 277-308.
8. Looijenga LH, Oosterhuis JW. Pathogenesis of testicular germ cell tumours. Rev Reprod 1999; 4: 90-100.
9. Horwich A, Shipley J, Huddart R. Testicular germ-cell cancer. Lancet 2006; 367: 754-765.
10. Skakkebaek NE. Possible carcinoma-in-situ of the testis. Lancet 1972; 2: 516-517.
11. Masterson TA, Carver BS, Abel EJ, Pettus JA, Bosl GJ, Sheinfeld J. Impact of age on clinicopathological outcomes and recurrence-free survival after the surgical management of nonseminomatous germ cell tumour. BJU Int 2012; 6: 950-955.
12. Feldman DR, Bosl GJ, Sheinfeld J, Motzer RJ. Medical treatment of advanced testicular cancer. JAMA 2008; 299: 672-684.
13. Talerman A. Spermatocytic seminoma: clinicopathological study of 22 cases. Cancer 1980; 8: 2169-2176.
14. Carriere P, Baade P, Fritschi L. Population based incidence and age distribution of spermatocytic seminoma. J Urol 2007; 178: 125-128.
15. Robinson A, Bainbridge T, Kollmannsberger C. A spermatocytic seminoma with rhabdomyosarcoma transformation and extensive metastases. Am J Clin Oncol 2007; 4: 440-441.
16. Duncan PR, Checa F, Gowing NF, McElwain TJ, Peckham MJ. Extranodal non-Hodgkin's lymphoma presenting in the testicle: a clinical and pathologic study of 24 cases. Cancer 1980; 45: 1578-1584.
17. Lim J, Goriely A, Turner GD, Ewen KA, Jacobsen GK, Graem N, Wilkie AO, Rajpert-De Meyts E. OCT2, SSX and SAGE1 reveal the phenotypic heterogeneity of spermatocytic seminoma reflecting distinct subpopulations of spermatogonia. J Pathol 2011; 224: 473-483.
18. Looijenga LH, Hersmus R, Gillis AJ, Pfundt R, Stoop HJ, van Gurp RJ, Veltman J, Beverloo HB, van Drunen E, van Kessel AG, Pera RR, Schneider DT, Summersgill B, Shipley J, McIntyre A, van der Spek P, Schoenmakers E, Oosterhuis JW. Genomic and expression profiling of human spermatocytic seminomas: primary spermatocyte as tumorigenic precursor and DMRT1 as candidate chromosome 9 gene. Cancer Res 2006; 66: 290-302.
19. Rajpert-De Meyts E1, Jacobsen GK, Bartkova J, Aubry F, Samson M, Bartek J, Skakkebaek NE. The immunohistochemical expression pattern of Chk2, p53, p19INK4d, MAGE-A4 and other selected antigens provides new evidence for the premeiotic origin of spermatocytic seminoma. Histopathology 2003; 42: 217-226.
20. Stoop H, van Gurp R, de Krijger R, Geurts van Kessel A, Köberle B, Oosterhuis W, Looijenga L. Reactivity of germ cell maturation stage-specific markers in spermatocytic seminoma: diagnostic and etiological implications. Lab Invest 2001; 7: 919-928.
21 Gillis AJ, Stoop HJ, Hersmus R, Oosterhuis JW, Sun Y, Chen C, Guenther S, Sherlock J, Veltman I, Baeten J, van der Spek PJ, de Alarcon P, Looijenga LH. High-throughput microRNAome analysis in human germ cell tumours. J Pathol 2007; 3: 319-328.
22 Floyd C, Ayala AG, Logothetis CJ, Silva EG. Spermatocytic seminoma with associated sarcoma of the testis. Cancer 1988; 2: 409-414.
23 Mati W, Lam G, Dahl C, Thorup Andersen J, Balslev E. Leydig cell tumour a rare testicular tumour. Int Urol Nephrol 2002; 33: 103-105.
24 Al-Agha OM, Axiotis CA. An in-depth look at Leydig cell tumor of the testis. Arch Pathol Lab Med 2007; 131: 311-317.
25 Kressel K, Hartmann M. Nongerminal, benign testicular tumors--report of experiences. Urologe A 1988; 27: 96-98.
26 Cheville JC, Sebo TJ, Lager DJ, Bostwick DG, Farrow GM. Leydig cell tumor of the testis: a clinicopathologic, DNA content, and MIB-1 comparison of non metastasizing and metastasizing tumors. Am J Surg Pathol 1998; 22: 1361-1367.
27 Sengupta S, Chatterjee U, Sarkar K, Chatterjee S, Kundu A. Leydig cell tumor: a report of two cases with unusual presentation. Indian J Pathol Microbiol 2010; 53: 796-798.
28. Bertram KA, Bratlof B, Hodges GF, Davidson H. Treatment of malignant Leydig cell tumor. Cancer 1991; 68: 2324-2329.
29. Shahab N, Doll DC. Testicular lymphoma. Semin Oncol 1999; 26: 259-269.
30. Zucca E, Roggero E, Bertoni F, Cavalli F. Primary extranodal non-Hodgkin's lymphomas. Part 1. Gastrointestinal, cutaneous and genitourinary lymphomas. Ann Oncol 1997; 8: 727-737.
31. Doll DC, Weiss RB. Malignant lymphoma of the testis. Am J Med 1986; 81: 515-524.
32. Moller MB, d'Amore F, Christensen BE. Testicular lymphoma: a populationbased study of incidence, clinicopathological correlations and prognosis. The Danish Lymphoma Study Group, LYFO. Eur J Cancer 1994; 30A: 1760-1764.
33. Sampat MB, Sirsat MV, Kamat MR. Malignant lymphoma of the testis in Indians. Br J Urol 1974; 46: 569-575.

34. Vitolo U, Ferreri AJ, Zucca E. Primary testicular lymphoma. Crit Rev Oncol Hematol 2008; 65:183-189.
35. Ferry JA, Harris NL, Young RH, Coen J, Zietman A, Scully RE. Malignant lymphoma of the testis, epididymis, and spermatic cord. A clinicopathologic study of 69 cases with immunophenotypic analysis. Am J Surg Pathol 1994; 18: 376-390.
36. Moertel CL, Watterson J, McCormick SR, Simonton SC. Follicular large cell lymphoma of the testis in a child. Cancer 1995; 75: 1182-1186.
37. Swerdlow SH, Campo E, Harris NL. Pathology and genetics of tumours of hematopoietic and lymphoid tissues. World Health Organization Classification of Tumors. Lyon: IARC Press, 2008.
38. Berglund M, Thunberg U, Amini RM, Book M, Roos G, Erlanson M, et al. Evaluation of immunophenotype in diffuse large B-cell lymphoma and its impact on prognosis. Mod Pathol 2005; 18: 1113-1120.
39. Rosenwald A,Wright G, Chan WC, Connors JM, Campo E, Fisher RI, et al. The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. N Engl J Med 2002; 346: 1937-1947.
40. Al-abbadi MA, Hattab EM, Tarawneh MS, Amr SS, Orazi A, Ulbright TM. Primary diffuse large-B-cell lymphoma belongs to nongerminal center B-cell like subgroup: a study of 18 cases. Mod Pathol 2006; 19: 1521-1527.
41. Ikeda Y, Nakazawa S, Kudo M. Intracranial malignant lymphoma developing 20 years after total removal of testicular malignant lymphoma case report. Neurol Med Chir (Tokyo) 1986; 26: 68-70.
42. Zucca E, Conconi A, Mughal TI, Sarris AH, Seymour JF, Vitolo U, et al. Patterns of outcome and prognostic factors in primary large-cell lymphoma of the testis in a survey by the International Extranodal Lymphoma Study Group. J Clin Oncol 2003; 21: 20-27.
43. Sussman EB, Hajdu SI, Lieberman PH, Whitmore WF. Malignant lymphoma of the testis: a clinicopathologic study of 37 cases. J Urol 1977; 118: 1004-1007.
44. Paladugu RR, Bearman RM, Rappaport H. Malignant lymphoma with primary manifestation in the gonad: a clinicopathologic study of 38 patients. Cancer 1980; 45: 561-571.
45. Fisher C, Goldblum JR, Epstein JI, Montgomery E. Leiomyosarcoma of the paratesticular region: a clinicopathologic study. Am J Surg Pathol 2001; 25: 1143-1149.
46. Stojadinovic A, Leung DH, Allen P, Lewis JJ, Jaques DP, Brennan MF. Primary adult soft tissue sarcoma: time-dependent influence of prognostic variables. J Clin Oncol 2002; 20: 4344-4352.
47. Dotan ZA, Tal R, Golijanin D, Snyder ME, Antonescu C, Brennan MF, et al. Adult genitourinary sarcoma: the 25-year Memorial Sloan-Kettering experience. J Urol 2006; 176: 2033-2038.
48. Khoubehi B, Mishra V, Ali M, Motiwala H, Karim O. Adult paratesticular tumours. BJU Int 2002; 90: 707-715.
49. Varzaneh FE, Verghese M, Shmookler BM. Paratesticular leiomyosarcoma in an elderly man. Urology 2002; 60: 1112.
50. Pergel A, Yucel AF, Aydin I, Sahin DA, Gucer H, Kocakusak A. Paratesticular liposarcoma: a radiologic pathologic correlation. J Clin Imaging Sci 2011; 1: 57.
51. Blitzer PH, Dosoretz DE, Proppe KH, Shipley WU. Treatment of malignant tumors of the spermatic cord: a study of 10 cases and a review of the literature. J Urol 1981; 126: 611-614.
52. Christopher D, Unni K, Mertens F. Adipocytic tumors. In: Fletcher CDM, Unni KK, Mertens F, editors. Pathology and genetics of tumours of soft tissue and bone. WHO Classification of Tumors. Pathology and Genetics. Lyon: IARC press, 2002; pp. 19-46.
53. Kempson R, Fletcher CD, Evans HL, Hendrickson MR, Sibley R. Atlas of tumor pathology. Washington DC: AFIP, Armed Forces Institute of Pathology, 2001.
54. McCormick D, Mentzel T, Beham A, Fletcher CD. Dedifferentiated liposarcoma. Clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. Am J Surg Pathol 1994; 18: 1213-1223.
55. Ghosh A, Swami R, Sen PK, Dwaka S. Unusual presentation of dedifferentiated liposarcoma as paratesticular mass. Indian J Pathol Microbiol 2008; 51: 42-44.
56. Montgomery E, Fischer C. Paratesticular liposarcoma: a clinicopathologic study. Am J Surg Pathol 2003; 27: 20-47.
57. Coleman J, Brennan MF, Alektiaret K, Russo P. Adult spermatic cord sarcomas: management and results. Ann Surg Oncol 2003; 10: 669-675.
58. Littles JF Jr, Matter RC, Herman G. Paratesticular liposarcoma: a report of two cases and review of the literature. J Natl Med Assoc 1992; 84: 951-955.
59. Kalyvas K, Kotakidou R, Trantos A, Yannakoyorgos K, Hatzichristou D. Paratesticular well differentiated, adipocytic type liposarcoma presenting as inguinal hernia. Urol Int 2004; 72: 264-268.
60. Weiss SW, Goldblum JR. Enzinger and Weiss's soft tissue tumours. 4th ed. St. Louis: Mosby, 2001.
61. Rushworth GF. Leiomyosarcoma of the epididymis. Proc R Soc Med 1971; 64: 999.
62. Raspollini MR, Stomaci N, Ringressi A, Franchi A. Primitive testicular leiomyosarcoma. Pathol Oncol Res 2010; 16: 177-179.
63. Evans HL, Shipley J. Smooth muscle tumors. In: Fletcher CDM, Unni KK, Mertens F, editors. Pathology and genetics of tumours of soft tissue and bone. Lyon: World Health Organization, 2002; pp. 131-134.
64. Catton CN, Cummings BJ, Fornasier V, O'Sullivan B, Quirt I, Warr D. Adult paratesticular sarcomas: a review of 21 cases. J Urol 1991; 146: 342-345.
65. Hashimoto H, Daimaru Y, Tsuneyoshi M, Enjoji M. Leiomyosarcoma of the external soft tissues. A clinicopathologic, immunohistochemical, and electron microscopic study. Cancer 1986; 57: 2077-2088.
66. Wile AG, Evans HL, Romsdahl MM. Leiomyosarcoma of soft tissue: a clinicopathologic study. Cancer 1981; 48: 1022-1032.
67. Folpe AL, Weiss SW. Paratesticular soft tissue neoplasms. Semin Diagn Pathol 2000; 17: 307-318.