Chapter

Testicular Lymphoma: Primary and Secondary Involvement

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Abstract

This chapter explores the testicular involvement of lymphoma. Testicular lymphoma may either represent secondary involvement by systemic disease or primary malignancy. Regarding primary testicular lymphoma (PTL), it is a rare form of extranodal lymphoma and the most frequent malignant testicular neoplasm in men over the age of 60 years. The diffuse large B-cell lymphoma (DLBCL) accounts for the majority of cases. The morphologic manifestation of PTL on imaging may be in the form of a localized mass or a diffuse enlargement of the testis. On ultrasonography, PTL usually appears as a hypoechoic area with hypervascularity. MRI and positron emission tomography with computed tomography (PET/CT) are useful diagnostic tools. The latter is crucial in staging and follow-up of these patients. The treatment of PTL is based on orchiectomy, chemotherapy, and radiotherapy. The prognosis is poor and PTL exhibits a propensity to relapse in the central nervous system (CNS) and in the opposite testis. Secondary involvement of the testis by non-Hodgkin lymphoma (NHL) is more frequent than PTL. Patients may develop the relapsed or refractory disease in the testis in the context of disseminated lymphomas due to the existence of the blood-testis barrier. This chapter discusses the treatment of secondary involvement by lymphoma.

Keywords: testicular lymphoma, non-Hodgkin lymphoma, testis, sanctuary sites, primary testicular lymphoma

1. Introduction

Approximately 30% of all non-Hodgkin lymphomas (NHL) arise from extranodal sites. The management of primary extranodal presentation often implies site-specific diagnostic and therapeutic strategies [1].

Testicular lymphoma often represents secondary involvement, although primary testicular lymphoma (PTL) may occur. Secondary testicular involvement is frequent in advanced NHL cases and is observed in up to 20% of patients in autopsy findings [2]. Furthermore, the testis is considered a "sanctuary" site for chemotherapy and is commonly the site of residual cancer after adequate treatment with chemotherapy [3].

PTL is the most common malignant testicular neoplasm in men over sixty years. It is an aggressive and rare form of extranodal lymphoma and represents 1–2% of NHL and 1–9% of all testicular tumors [4].

2. Primary testicular lymphoma

2.1 Histological subtypes

There are several histological subtypes of PTL, such as follicular lymphoma, Burkitt's lymphoma, and diffuse large B-cell lymphoma (DLBCL). Primary DLBCL is the most common subtype of lymphoma (80%) in the adult testis, whereas most of testicular lymphomas in children consist of secondary involvement by lymphoblastic lymphoma, DLBCL, or Burkitt's lymphoma [5].

Infrequent histological subtypes in testis include mantle cell lymphoma, the extranodal natural killer–cell lymphoma, peripheral T-cell lymphoma, extranodal marginal zone lymphoma, and activin receptor-like kinase-1–negative anaplastic large cell lymphoma. **Table 1** summarizes PTL subtypes and their frequency.

Patients with HIV (human immunodeficiency virus) infection often exhibit more aggressive variants of PTL [6]. Follicular lymphoma (FL) of the testis is very uncommon and has been reported mainly in childhood.

2.2 Epidemiology

Regarding the incidence of extranodal NHLs, it is similar to other lymphomas: in countries with high NHL incidence, there is an increased incidence of extranodal disease. An important geographic variation of the distribution across the diverse anatomic sites of onset as well as the overall frequency of the extranodal presentation has been reported.

Extranodal lymphomas can derive from practically each and every organ. The published data from large series have shown bone, skin, brain, and gastrointestinal (GI) tract to be the most frequent sites of extranodal involvement. Ann Arbor staging system classifies the Waldeyer's ring and tonsils as lymphatic locations, so their designation as extranodal sites remains a controversy. However, when they are included in the extranodal lymphoma series, the neck and head are the second most frequent locations. Furthermore, the incidence of primary extranodal presentation is variable across the different B-cell histologic subtypes, including less than 10% of follicular lymphomas (FL), up to 50% of DLBCL, and the majority of Burkitt's

Subtype	Frequency (according to SEER data) [7]
Diffuse large B-cell lymphoma (DLBCL)	78.1%
DLBCL, immunoblastic variant	3.7%
Burkitt's lymphoma	1.3%
Diffuse non-Hodgkin's mixed small and large cell lymphoma	1.2%
Small lymphocytic lymphoma	0.8%
Lymphoplasmacytic lymphoma	0.6%
Mantle cell lymphoma	0.4%
Others/not specified	8.8%

Table 1.
Histological subtypes of PTL.

lymphomas (BL). The histologic subtypes can be site-specific for some localizations such as central nervous system (CNS) or testis, where the majority of cases are DLBCL. Contrarily, in the GI tract, a wide spectrum of lymphoma types can be found, including mantle cell lymphoma (MCL), marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) BL, FL, and DLBCL [1].

The annual incidence of PTL is 0.09–0.26/100,000 per year and the median age at diagnosis of PTL is 67 years old [7]. Moreover, PTL is both the most common testicular malignancy in men age > 60 years and the most frequent bilateral testicular neoplasm [6].

2.3 Risk factors and genetics

Despite the fact that there are limited data about risk factors for PTL, HIV infection is a well-known risk factor for aggressive NHL, with lymphomas in HIV-positive patients more frequently developing in extranodal sites, such as the testis.

HIV-infected patients with PTL are younger (36 years is the median age). In these patients, Burkitt-like, plasmablastic and immunoblastic histological types are more habitual [6].

With regard to genetic risk factors for lymphoma, plasmacytoid differentiation, that is shown in some cases of PTL, with somatic hypermutation of immunoglobulin heavy-chain genes (IgH) and the presence of a high rate of T-cell infiltrate, suggest that antigen-driven stimulation could be implicated, as well as in extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (eMZL of MALT).

Other characteristics usually observed in PTL that raise the possibility of an antigen-driven mechanism in their pathogenesis are a higher frequency of the loss of HLA-DR and DQ expression, along with homozygous deletions of the corresponding genes, and the frequency of HLA-DRB1–15 and HLA-DRB1–12 [8].

2.4 Clinical features

Testicular lymphoma can be the initial presentation of clinically occult disease or a primary extranodal disease. It must be considered in the differential diagnosis of a testicular mass, especially in patients over 60 years old [9].

The classic presentation consists of a painless, swollen, and hard testis or a testicular mass, without preference for either side. An associated hydrocele is found in about 40% and synchronous bilateral involvement occurs in approximately 6% of cases. Systemic B symptoms are usually present only in an advanced stage. Moreover, patients can present abdominal pain or ascites. In addition to the contralateral testis, the disease typically spreads to other extranodal sites such as the skin and subcutaneous tissue, the lungs, the bone, and mainly the CNS [1].

2.5 Diagnosis and stages

In clinical practice, ultrasonography and magnetic resonance imaging (MRI) are the most commonly used imaging modalities, which allow simultaneous evaluation of both testicles, paratesticular space, and spermatic cord.

Staging workup is the same as used for other forms of aggressive NHL. It consists of bone marrow biopsy and FDG PET/CT, with the addition of specific CNS staging with a lumbar puncture for cerebrospinal fluid analysis and cranial MRI. CNS is the most frequent metastatic location with a reported incidence of 45%. Furthermore, 64% of CNS relapses involve the brain parenchyma [10].

Stage I: Involvement of a single extralymphatic organ or site or of a single lymph node region.
Stage II: Localized involvement of an extralymphatic organ or site or involvement of two or more lymph node regions on the same side of the diaphragm.
Stage III: Involvement of lymph node regions or structures on both sides of the diaphragm.
Stage IV: Diffuse or disseminated involvement of one or more extralymphatic organs, or either: • Involvement of the liver, bone marrow, pleura or cerebrospinal fluid. • Isolated extralymphatic organ involvement without adjacent regional lymph node involvement, but with the disease in distant sites.
Additional sub staging variables include: • **A:** Asymptomatic • **B:** Presence of B symptoms (including fever, night sweats, and weight loss of ≥10% of body weight over 6 months.) • **E**: Involvement of a single, extranodal site, contiguous or proximal to a known nodal site (stages I to III only; additional extranodal involvement is stage IV). • **S**: Splenic involvement. • **X:** Bulky nodal disease: nodal mass > 1/3 of intrathoracic diameter or 10 cm in dimension.

Table 2.
Ann-Arbor staging system used in PTL.

The Ann Arbor staging system is the most widely utilized for lymphoma staging, for both HL and NHL. It is named after the town of Ann Arbor in the US state of Michigan where the Committee on Hodgkin's Disease Staging Classification met in 1971 to agree on it. It updated and replaced the earlier Rye staging system (**Table 2**) [11].

The disease is limited to the testis (stage IE) in the majority of patients and nearly 20% of patients have stage II disease. Disseminated disease is rare. A stage IV testicular lymphoma is virtually indistinguishable from a nodal one with testicular involvement [1].

2.5.1 Ultrasound scan

Scrotal ultrasound is useful to confirm the diagnosis of a solid intratesticular tumor, but it does not provide sufficiently reliable information to precisely determine the T stage: whether the tunica albuginea, tunica vaginalis, epididymis, or spermatic cord are affected [12].

Generally, ultrasonography demonstrates focal or diffuse areas of hypoechogenicity with hypervascularity in an enlarged testis. MRI allows detailed evaluation of both testes, paratesticular spaces, and spermatic cord [6].

In the series of Bertolotto et al., these authors described a group of 43 patients with pathologically proven testicular lymphoma investigated with grayscale and Doppler ultrasound scan. Doppler ultrasound findings confirmed that testicular lymphomas present as hypoechoic lesions of the testis, either focal or diffuse, predominantly with a hypervascular appearance. In 72% of cases, normal testicular vessels traversing the lesion can be found. This sonographic feature is only indicative of the infiltrative nature of the pathologic process, but it is not specific for lymphoma, because it has been reported in other infiltrative neoplasms, such as plasmacytoma and leukemia infiltration. On the other hand, non-neoplastic disorders and other inflammatory diseases, such as chronic granulomatous orchitis, may present as hypervascularity of the entire testis or a striated pattern, decreased echogenicity, diffuse enlargement, or multifocal hypoechoic hypervascular lesions,

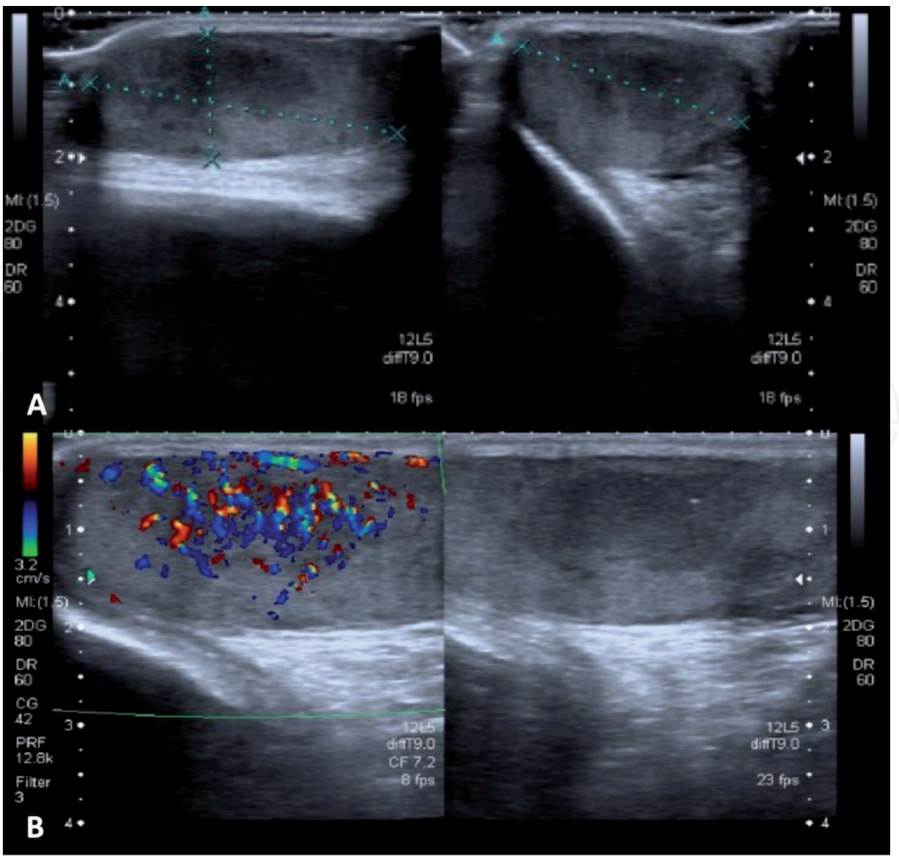

Figure 1.
Testicular ultrasound scan of a patient with suspected testicular lymphoma showing an enlarged right testicle (11 cc) with heterogeneous echogenicity, with poorly defined hypoechoic areas (A). The Doppler study (B) shows increased vascularity of the testicular parenchyma.

identical to the grayscale and Doppler sonographic characteristics of lymphoma. An accurate interpretation of these findings could be difficult if clinical features of inflammation are absent. In these cases, biopsy should be considered, and often orchidectomy is performed to establish the final diagnosis (**Figure 1**) [13].

2.5.2 Magnetic resonance imaging

MRI of the testes seems to be more accurate than ultrasound for detecting involvement of the tunica albuginea, the epididymis and the spermatic cord (**Figures 2** and **3**) [12].

2.5.3 PET/CT

PET/CT and bone marrow biopsy, along with the specific CNS staging (lumbar puncture for cerebrospinal fluid analysis by cytology and flow cytometry and brain MRI) are used at the initial staging of patients with PTL [6].

Nowadays, PET with glucose analog 18F-fluorodeoxyglucose (18F-FDG) is the most commonly used imaging modality for evaluating tumor metabolism. PTL usually shows increased 18F-FDG uptake. Despite the growing use in clinical practice of FDG PET/CT, its role in PTL has neither been clearly defined (**Figures 4** and **5**) [10].

2.5.4 Bone marrow biopsy and lumbar puncture

Because of the high tendency of PTL to disseminate to particular extranodal sites, some specific diagnostic procedures are required for complete staging. The

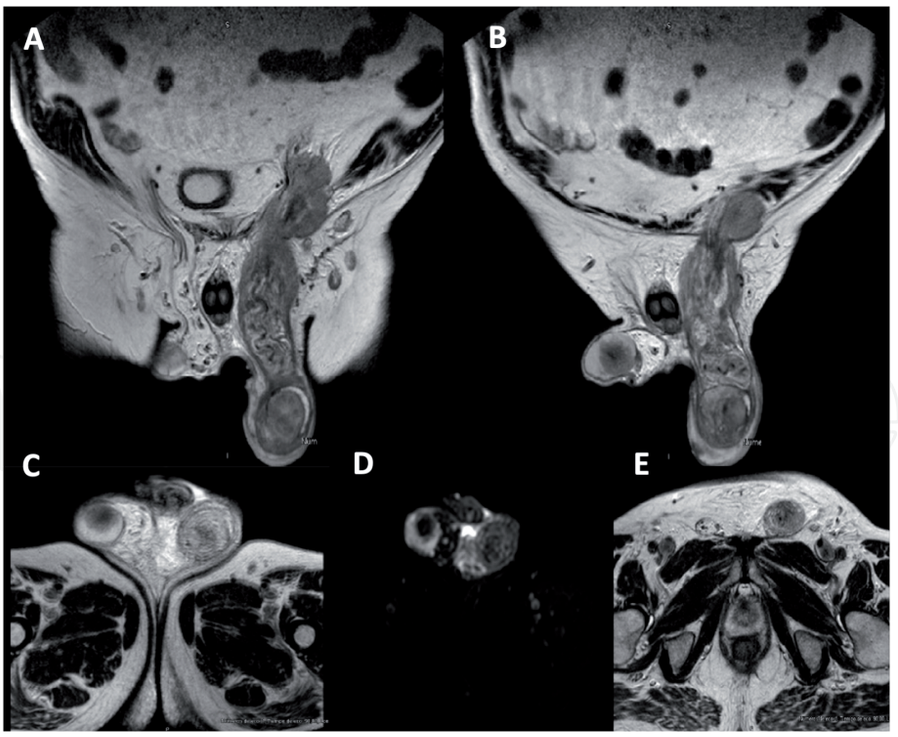

Figure 2.
Coronal and axial MRI in a patient with diffuse large cell lymphoma B (activated phenotype). The images show thickening of the left spermatic cord from its intra-abdominal segment to the interior of the scrotum, with involvement of the epididymis and testis (A and B). The right testis shows a low signal, hyper-uptake lesion, 3 cm in size (C-E).

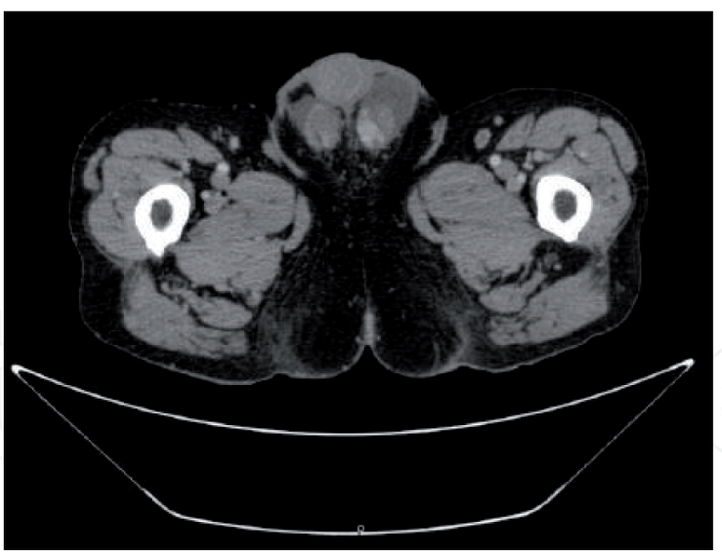

Figure 3.
An axial MRI image shows a testicular nodule in a patient with generalized lymphadenopathy.

presence of pulmonary mass, pleural effusion, skin, or Waldayer's ring lesions needs histological confirmation.

An accurate examination of the skin is recommended due to the association of PTL with cutaneous "leg-type DLBCL" and testicular DLBCL. Additionally, skin is a frequent site of extranodal relapse of PTL, especially in HIV-positive patients.

Lumbar puncture with cytological and flow cytometric analysis on CSF is mandatory to exclude CNS involvement. Benevolo et al. conducted a study comparing the diagnostic and prognostic value of conventional cytological (CC) examination and flow cytometry (FCM) of a base-line sample of cerebrospinal fluid in 174

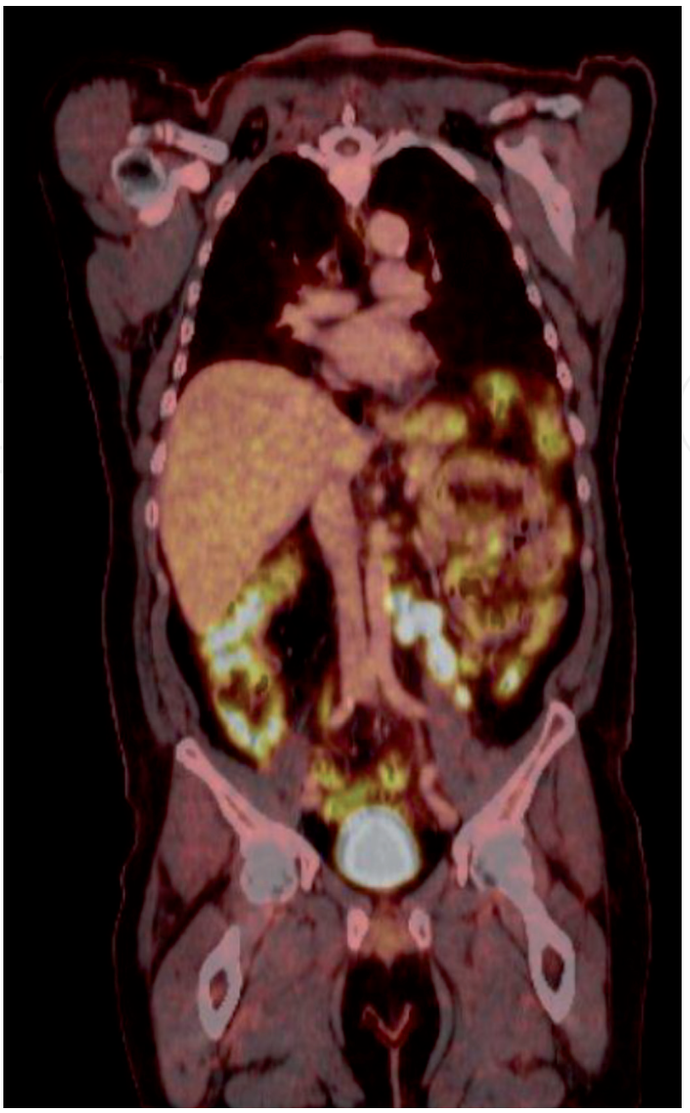

Figure 4.
PET/CT in a patient diagnosed with a PTL (diffuse large B-cell lymphoma). Numerous hypermetabolic left paraaortic lymphadenopathy (16 mm and SUVmax: 18), located in the anterior aspect of the psoas.

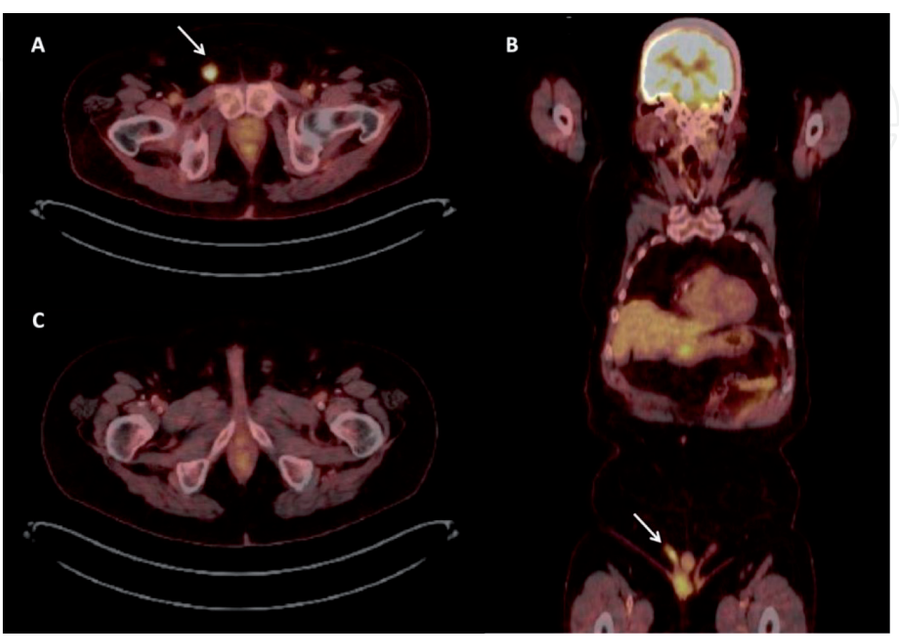

Figure 5.
Burkitt's lymphoma relapse in the testicle. Radiotracer uptake is observed in the right inguinal canal (arrow, A and B). The last image (C) corresponds to the control PET/CT after right orchiectomy.

patients with aggressive NHL. The results showed a significantly higher risk of CNS progression in patients with FCM-positive and CC-negative patients, compared to patients who are both FCM- and CC-negative. Therefore, FCM is a highly sensitive test to rule out CNS involvement, and it should be recommended in all NHL patients at high risk of CNS relapse, including testicular lymphoma. Moreover, HIV serology should be checked in all cases, because testicular lymphoma is more frequent in HIV-positive patients [8].

2.6 Differential diagnosis

Bacterial epididymal-orchitis, primary testicular tumors, testicular infarction, and genitourinary tuberculosis must be considered in the differential diagnosis of PTL. Several germ cell tumors, such as classic seminoma, spermatocytic seminoma, and embryonal carcinoma, should be included in the differential diagnosis of primary testicular DLBCL. Granulomatous and viral orchitis can also mimic lymphoma. Unlike the majority of lymphoma cells, seminoma cells have a distinctive histologic pattern, including rounded but focally flattened central nuclei, glycogen-rich cytoplasms, and distinct cell membranes. The cells of spermatocytes seminoma are polymorphous and they can be divided into three types. Embryonal carcinoma has a classic epithelioid appearance that usually forms papillary, tubular, or glandular structures. Lymphomas usually consist of smaller cells with a higher nucleo-cytoplasmic ratio. Furthermore, these neoplasms exhibit diffuse intertubular infiltration with recognizable tubular remnants. This characteristic intertubular growth pattern of lymphoma is initially suggestive of the diagnosis in numerous cases. Contrary to seminoma and embryonal carcinoma, lymphomas lack precursor intratubular germ cell neoplasia. Viral and granulomatous orchitis have heterogeneous and benign-appearing inflammatory cellular infiltrates, in contrast to the more homogeneous and malignant-appearing infiltrate of lymphoma [5].

2.7 The role of testicular biopsy

The diagnosis of primary testicular lymphoma is often confirmed through orchiectomy or testis biopsy [14]. Over the past decades, there has been a trend towards primary orchidectomy [15].

Coad et al. found needle biopsy to be a safe and simple method of examining the testes of patients with acute leukemia and non-Hodgkin's lymphoma. The procedure is quickly carried out under a short general anesthetic on an outpatient basis. Only one out of 102 cases provided insufficient material for histological examination. Using needle biopsy, a good correlation between clinical assessment and histological appearance was found. Out of 70 clinically normal testes, in 6 (8.5%) cases testicular infiltration was detected [16].

2.8 Pathology

According to prior work, lymphoma can infiltrate the epididymis and spermatic cord. The macroscopic observations showed that the cut surface of the tumor is usually solid, and testicular masses measures around 5.5 cm (range: 2.5–9 cm). Regarding macroscopic tumor appearance, they were gray or gray-red in color, tender, and spongy, and had clear boundaries [17].

The large majority of PTLs (80–98%) are DLBCLs, although patients with HIV infection commonly present with more aggressive variants. B-cell markers, such as CD19, CD20, CD79a, and PAX5 are typically expressed by DLBCL-type PTL. Bcl-2 protein is expressed in 70% of cases, but Bcl-6 is rarely positive.

The median MIB1 proliferative index is 40%, and in the non-HIV population, Epstein–Barr virus is usually negative (**Figure 6**) [6].

2.9 Treatment

The treatment of primary testicular lymphoma is based on orchiectomy, chemotherapy, and occasionally radiotherapy, but there is not a standardized regimen. It is an extremely aggressive neoplasm with poor progression-free survival and overall survival [14]. A study from the International Extranodal Lymphoma Study Group (IELSG) has reported that R-CHOP chemoimmunotherapy with intrathecal methotrexate prophylaxis and radiotherapy to the contralateral testis could reduce CNS relapse (6%) [18].

Orchiectomy is usually required for the pathological diagnosis and its removal avoids the potential chemotherapy "sanctuary" site as a consequence of the blood-testis barrier.

In the largest series of patients with testicular lymphoma, the IELSG observed a 10- and 5-year incidence of CNS relapse of 35% and 20%, respectively. Therefore, CSF cytology should be included in the staging. Nevertheless, the pattern of CNS involvement is characterized by parenchymal involvement and late relapses. This contrasts with primary nodal DLBCL, in which the CNS relapse rate is lower (approximately 5%) and relapses are common of early-onset and leptomeningeal presentation.

Testicular lymphomas are very aggressive malignancies, with a poor outcome. Indeed, in spite of initial chemoradiation (CR), patients with stage I-II disease

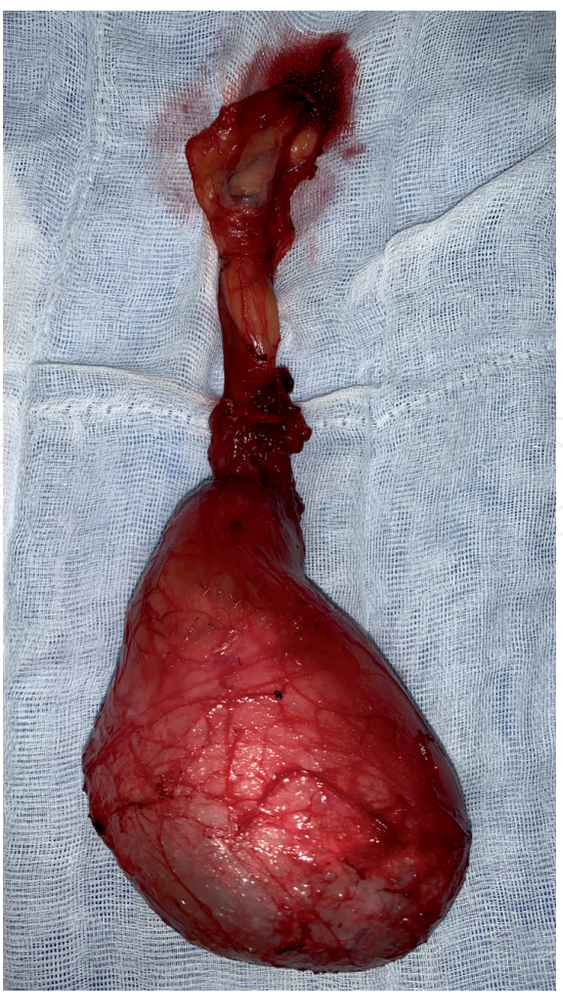

Figure 6.
Macroscopic findings in a surgical specimen (orchiectomy) of PTL.

frequently relapse. The large retrospective IELSG series, that enrolled 373 patients, reported a 10- and 5-year OS rate of 27% and 48%, respectively. The OS and PFS survival curves showed no clear evidence of plateau, suggesting no cure for these patients, including those with stage I-II disease. The majority of patients did not receive CNS prophylactic chemotherapy, but in patients who received anthracycline-based chemotherapy plus intrathecal prophylaxis and scrotal irradiation, a reduction of the risk of progression by administering CNS prophylaxis was observed (5-year PFS, 72%). IELSG-10 phase II trial showed that combined treatment with six cycles of R-CHOP-21, intrathecal MTX, and contralateral testis irradiation was associated with better outcomes in stage I-IIE disease (5-year PFS and OS rates were 74% and 85%, respectively). Moreover, radiation therapy reduced the risk of contralateral testis relapse.

According to the guidelines for the treatment of advanced stage nodal DLBCL, patients with disseminated PTL should be treated with the addition of prophylactic scrotal radiotherapy and intrathecal chemotherapy. Routine CNS prophylaxis is recommended in testis lymphoma of any stage because of the high rate of CNS relapse (**Figure 7**) [1].

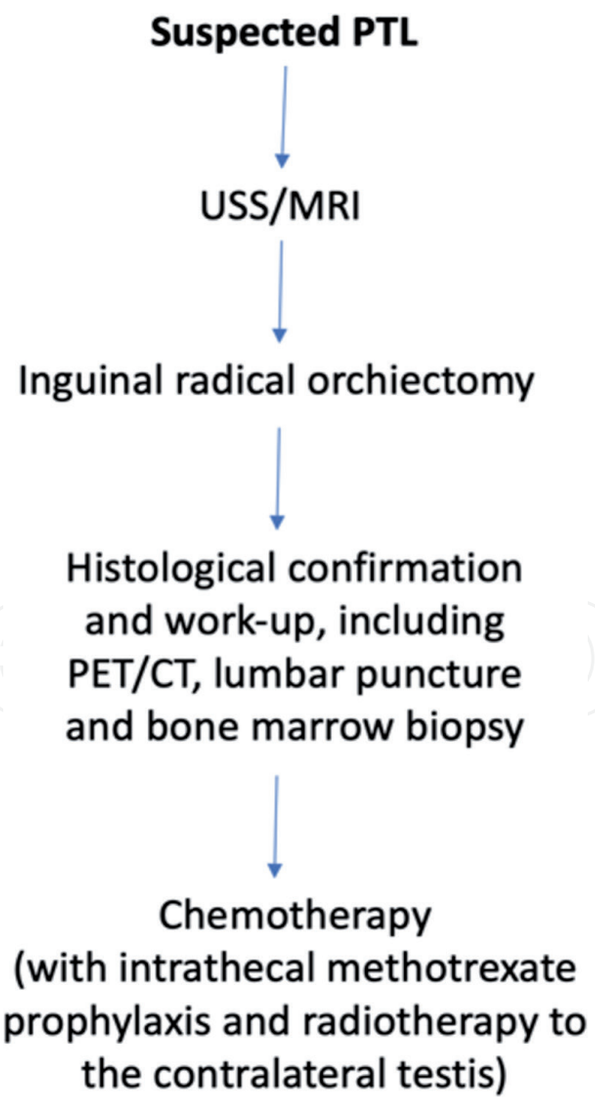

Figure 7.
Diagnostic algorithm and treatment of the PTL. USS, Ultrasound scan; MRI, Magnetic resonance imaging.

2.10 Prognosis

Historically, PTL has been associated with poor prognosis with an overall 5-year survival rate ranging from 17 to 48%, mainly primary testicular DLBCL, which is a very aggressive neoplasm with a clear tendency to spread to the skin and the CNS at presentation and relapse [5].

Testicular lymphoma has been reported to have a poor prognosis compared to other extranodal lymphomas and NHL and may need a more prolonged course of chemotherapy. Pathologic grading and stage are the main predictive factors for outcome. Early-stage and younger age, which are part of the International Prognostic Index (IPI), have been shown to be independent prognostic factors affecting the overall and disease-free survival (**Table 3**) [19].

3. Secondary involvement of the testis

3.1 Testicular involvement at diagnosis or relapse

Three types of presentation of testicular lymphoma have been documented:

- Primary extranodal: very rare, most cases are primary testicular DLBCLs.
- Extranodal relapse after chemotherapy: usually in aggressive lymphomas, such as Burkitt. The testicle is a "sanctuary organ" thanks to the blood-gonad barrier, which inhibits the accumulation of chemotherapeutic agents. This phenomenon has been described most frequently in children with acute lymphoblastic leukemia; however, it has also been documented in patients with lymphomas.
- The primary manifestation of unknown systemic disease [20].

>1 extranodal site
Adverse prognostic factors for PFS in studies of PTL
Age > 70 years
Advanced stage
ECOG performance status >1
B symptoms
Hypoalbuminemia
Involvement of extranodal sites other than testis
Involvement of the left testis
Raised serum LDH
Raised serum β2-microglobulin
Tumor diameter > 10 cm

Table 3.
Prognostic factors for PFS identified in PTL [6]. ECOG, eastern cooperative oncology group; LDH, lactate dehydrogenase.

Overall, secondary involvement of the testis by NHL is more common than primary extranodal disease [19].

3.2 Testicles as "sanctuary sites" for chemotherapy

The testis is an immunologically privileged site. The blood-testis barrier interferes with the delivery of chemotherapeutic agents, making the testicle a potential site for relapse or residual disease.

Testicular relapse of leukemia and lymphoma is a well-recognized phenomenon: testicular relapse of lymphoma is more frequent in the adult population, whereas leukemia relapse is most commonly seen in the pediatric population. With the advent of F-18 fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) in the evaluation of lymphoma, it is possible to detect PTL or testicular relapse on the FDG-PET examination. Testicular relapse of NHL detected on FDG-PET has been reported previously. Prior studies have examined normal standardized uptake value maximum (SUVmax) values in the testicle, with normal values ranging from 2.81 (30–39 years) to 2.18 (80–89 years), depending upon age. Elevated activity in one testicle or lateralizing activity should be deemed suspicious, and etiologies can include primary testicular tumor, primary or secondary testicular lymphoma, and metastatic disease with other etiologies less likely.

Autopsy findings have demonstrated testicular involvement is identified in 64.3% of male patients with acute leukemia, in 22.4% of male patients with chronic leukemia, and in 18.6% of patients with lymphosarcoma (NHL) [21].

3.3 Management of residual testicular disease

Lymphoma and leukemia are the predominant secondary tumors of the testis. Acute lymphoblastic leukemia (ALL) is a frequent cause of prepuberal testicular mass. Indeed, microscopic involvement of the testis has been found in autopsy in 66% of patients with ALL.

The management of testicular lymphoma and leukemia relapses is similar. The finding of a palpable mass on physical examination in a patient with recently diagnosed lymphoma or leukemia should prompt a scrotal ultrasound scan. This commonly demonstrates a homogeneous hypoechoic mass.

Currently, literature discourages testicular biopsy in patients before initiating chemotherapy as no survival benefit has been reported. However, a patient with new or persistent enlarged testis undergoing chemotherapy, especially in leukemia, could imply a relapse while on therapy. This scenario should prompt a biopsy to guide therapeutic decisions. In this case, additional chemotherapy is typically needed to eradicate the residual disease in "sanctuary" sites and possible systemic disease, as well as radiation to the affected testis.

In 25% of cases, testicular lymphoma is a manifestation of widespread systemic involvement, another 25% present with Ann Arbor stage II disease and the remaining 50% have disease confined to the testis (Ann Arbor I) [22].

If residual tumor within the gonad after chemotherapy persists, delayed orchiectomy should be considered, because the blood-testis barrier limits anticancer drug penetration [3].

For example, in the management of testicular relapse of BL, radical orchiectomy is indicated in cases in which the testicle has been completely replaced by a tumor, or is persistent after chemotherapy. Additionally, this procedure can be beneficial in tissue diagnosis and staging (**Figure 8**) [23].

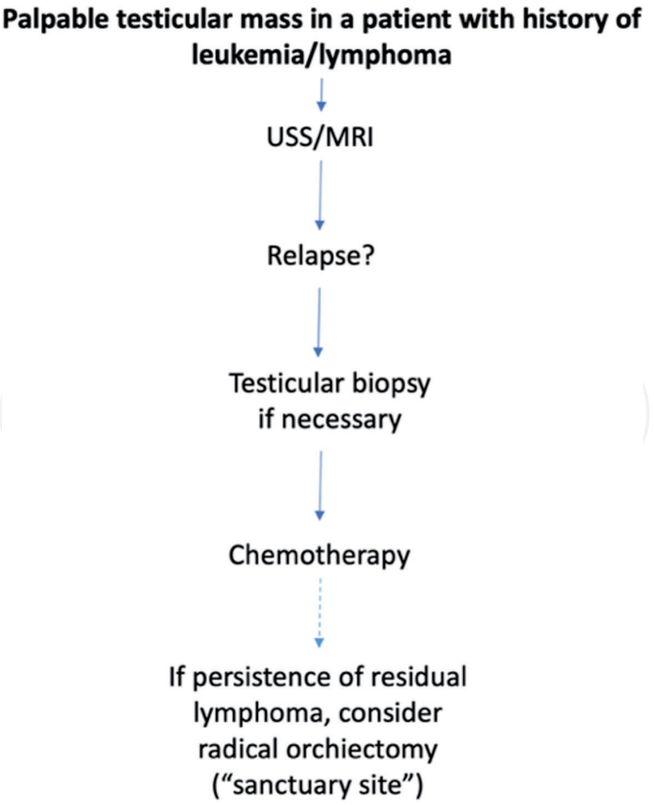

Figure 8.
Management of suspected testicular relapse in systemic lymphoma.

4. Conclusions

Testicular lymphoma is the most common testicular tumor in patients over the age of 60 years. The clinical and radiologic features of PTL should be known because it is the most common secondary testicular cancer. A painless, swollen, and hard testis or a testicular mass are the most common presenting signs and symptoms of PTL. The imaging studies used to diagnose and evaluate the stage of PTL are ultrasonography, MRI, and PET/CT. After diagnosis of PTL, lumbar puncture for cerebrospinal fluid analysis and brain MRI provide information regarding CNS staging.

PTL may mimic germ cell tumors and other diseases, such as orchiepididymitis or testicular tuberculosis. The treatment includes radical orchiectomy, chemotherapy, and occasionally radiotherapy, although there is not a well-established regimen. PTL is an extremely aggressive neoplasm with poor progression-free survival and overall survival. According to the results from the study by IELSG, the recommended therapeutic strategy of primary testicular DLBCL should include R-CHOP chemoimmunotherapy with intrathecal methotrexate prophylaxis and radiotherapy to the contralateral testis in order to reduce the risk of CNS and testicular relapses.

Regarding secondary involvement of the testis, testicular relapse of leukemia and lymphoma usually occur due to the existence of a blood-testis barrier. If residual tumor within the testis after an adequate course of chemotherapy persists, delayed orchiectomy should be considered.

Conflict of interest

The authors declare no conflict of interest.

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