Clinical case

Synchronous Primary Testicular Tumor: a case report of diffuse large B-cell lymphoma

Tumor testicular primario sincrónico: reporte de un caso de linfoma difuso de células B grandes

Silva Gilmar Pereira,[1] Xavier Grangeiro Vitor Pereira,[2] Carmelita Félix Dantas de Oliveira.[2]

Abstract

Case description: 63-year-old man of with 7-month history of progressive and gradual increase in testicular size without pain, symptoms of local or systemic infection. Biomarkers for testicular neoplasia were within the reference range: LDH(167 U/L), AFP(1.49 IU/mL), and HCG(0.2 mUI/mL). MR): enlarged testicular dimensions showing nodular lesions of heterogeneous enhancement. The patient initially underwent a inguinal orchiectomy who revealed diffuse large B-cell lymphoma.

Relevance: primary testicular lymphoma (PTL) is a rare non-Hodgkin lymphoma (NHL) that occurs in 1–2% of all cases of NHL and commonly presents as diffuse large B-cell lymphoma in 80–90% of cases. Bilateral and synchronous lesions are observed in 1–2% and 10% of cases, respectively. In this report, we describe our experience regarding this cancer.

Clinical implications: if not properly conducted, it can end in advanced disease with no prospect of cure, infertility, primary hypogonadism and psychological alterations due to the removal of the gonads.

Conclusions: PTL is a rare malignancy associated with high recurrence rates and poor prognosis, and multimodal therapy is warranted to achieve better long-term survival and cure rates.

Keywords:
Primary testicular lymphoma, diffuse large-B cell lymphoma, orchiectomy, testis cancer, testicular chemotherapy

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Resumen

Descripción del caso clínico: varón de 63 años de edad con antecedentes de aumento de tamaño testicular progresivo y gradual de 7 meses de evolución sin dolor, síntomas de infección local o sistémica. Los biomarcadores de neoplasia testicular estuvieron dentro del rango de referencia: LDH (167 U/L), AFP (1,49 UI/mL) y HCG (0,2 mUI/mL). RM: agrandamiento de las dimensiones testiculares que muestra lesiones nodulares de realce heterogéneo. Inicialmente, el paciente se sometió a una orquiectomía inguinal que reveló un linfoma difuso de células B grandes.

Relevancia: el linfoma testicular primario es un linfoma no Hodgkin (LNH) poco común que ocurre en el 1-2 % de todos los casos de LNH y comúnmente se presenta como un linfoma difuso de células B grandes en el 80-90% de los casos. Se observan lesiones bilaterales y sincrónicas en el 1-2% y el 10% de los casos, respectivamente. En este informe, describimos nuestra experiencia con respecto a este cáncer.

Implicaciones clínicas: si no se realiza correctamente, puede terminar en enfermedad avanzada sin posibilidad de curación, infertilidad, hipogonadismo primario y alteraciones psicológicas por la extirpación de las gónadas.

Conclusiones: el linfoma testicular primario es una neoplasia maligna rara asociada con altas tasas de recurrencia y mal pronóstico, y la terapia multimodal está justificada para lograr mejores tasas de curación y supervivencia a largo plazo.

Palabras clave: Linfoma testicular primario, linfoma difuso de células B grandes, orquiectomía, cáncer de testículo, quimioterapia testicular

Introduction

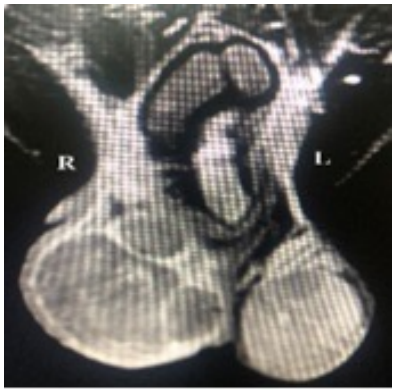
Testicular cancer represents 1% of all male malignancies and 5% of urological tumors, with prevalence of 3–9 new cases per 100,000 males/per year. This cancer occurs more frequently in industrialized countries and is histopathologically characterized by germ-cell tumors in 90–95% of cases.[1] Primary testicular lymphoma (PTL) is a rare non-Hodgkin lymphoma (NHL) that occurs in 1–2% of all cases of NHL and commonly presents as diffuse large B-cell lymphoma in 80–90% of cases.[1,2] Bilateral and synchronous lesions are observed in 1–2% and 10% of cases, respectively.[3,4] In this report, we contribute with our clinical experience and keep the urologist alert for the differential diagnosis of testicular enlargement.

Clinical case: Clinical and laboratory findings: 63-year-old man of African descent, non-smoker, with a normal body mass index and a history of hyperuricemia visited the Uro-

logy Outpatient Clinic at the Hospital of the Regional North of Brasília, Federal District, Brazil for evaluation of a 7-month history of progressive and gradual increase in testicular size. He denied any accompanying pain, symptoms of local or systemic infection, weight loss, or symptoms of sexual dysfunction. On physical examination, we observed bilateral testicular enlargement (right and left testes measured 7 cm and 5 cm, respectively). The testes were hard in consistency but without pain to palpation and showed a smooth and regular surface, which excluded infectious diseases (for example, tuberculosis) and testicular neoplasia.

The following biomarkers for testicular neoplasia were within the reference range: serum lactate dehydrogenase 167 U/L, alpha-fetoprotein 1.49 IU/mL, and human chorionic gonadotropin 0.2 mUI/mL. Analysis of cerebrospinal fluid obtained via lumbar puncture did not reveal malignant cells, which is relatively common. Diagnostic imaging and interpretation (Figure 1).

Figure 1. Magnetic resonance imaging (MRI)



Enlarged testicular dimensions showing nodular lesions of heterogeneous, enhancement, the right measuring up to 65 x 50 mm and the left measuring 32 x 20 mm. Bilateral inguinal cord thickening that achieves lymph node enlargement in the internal iliac chain, mainly on the right (19 x 15 mm).

Histopathological evaluation of gonadal tissue (hematoxylin and eosin) showed a solid malignant neoplasm that consisted of small atypical and homogeneous cells, which were diffusely distributed and occupied and expanded the entire testicular parenchyma. We observed a solid diffuse cell growth pattern accompanied by a few thin bundles of interstitial fibrosis with testicular tissue destruction. Evaluation showed atypical cells with vesicular irregular nuclei and some prominent nucleoli and infiltration of the vessel walls and nerves across the entire organ. Surgical margins of the spermatic cord were compromised (pT2 staging).

The immunohistochemical panel most commonly associated with diffuse large B-cell lymphoma are the proteins Bcl-2,[5] Bcl-6,[6] CD20,[7] Ki67,[8] and MUM-1,[9] as shown in Figure 2 & 3 below.

Figure 2. Histology hematoxylin and eosin staining

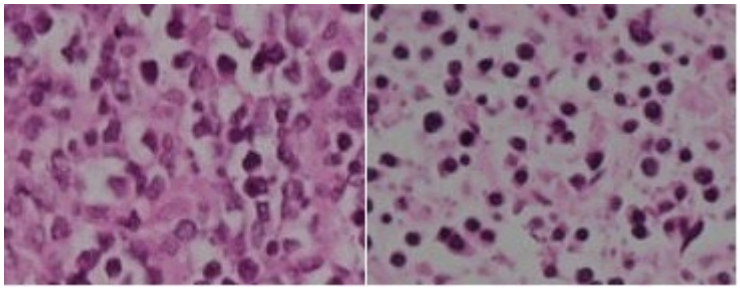
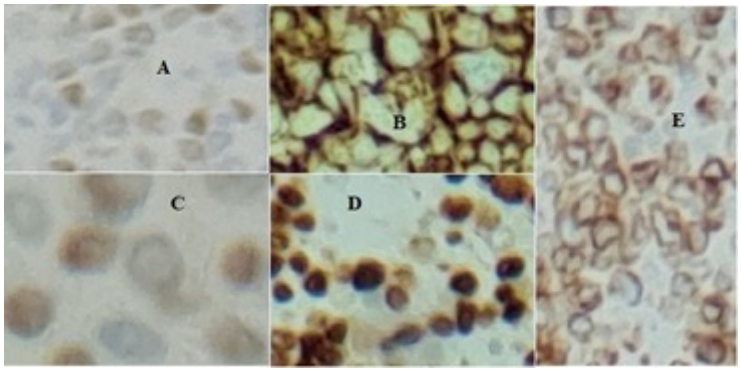


Figure 3.



Positive immunostaining for Bcl-2-membrane marker (A); Bcl-6- membrane marker (B); CD20- nuclear marker (C); Ki67-nuclear marking of cell proliferation index, 70% (D) and MUM-1: nuclear marker (E).

Whole-body 18-fluorodeoxyglucose positron emission tomography computed tomography showed no indication of a hypermetabolic state, and chest and abdominal computed tomography findings were unremarkable.

Considering the previously mentioned diagnostic hypotheses, the patient initially underwent a spinal cord block for D unilateral inguinal orchiectomy. After confirmation of PTL, we performed left contralateral inguinal orchiectomy 15 days later, and anatomopathological examination showed that it was in the same line as the contralateral testicle. The patient received six cycles of the rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapeutic regimen, followed by adjuvant radiotherapy (30 Gy) to the scrotum and inguinal regions. Currently, the patient is in good general condition and is being followed-up as an outpatient, 6 months after treatment.

Discussion: PTL should be considered in the differential diagnosis of testicular masses, particularly in patients aged >60 years in whom diffuse large B-cell lymphoma is the predominant histopathological subtype (detected in >80% of cases).[10]

Our patient was 63 years old and was diagnosed with PTL class II according to the Ann Arbor classification.[11] PTL classically presents as a painless, swollen and hard testis or testicular mass (bacterial epididymo-orchitis, primary testicular tumors, testicular infarction,

and genitourinary tuberculosis should be considered in the differential diagnosis) without preference for either side or synchronous bilateral involvement in approximately 6–10%,[6] and asynchronous lesions in 30–35% of all cases.[3] In addition to imaging and laboratory tests, accurate characterization of the tumor requires spinal fluid analysis because the central nervous system is affected in approximately 40% of cases.[12]

Dysregulated NFkB signaling via the MYD88, JAK/STAT, and B cell receptor signaling pathways are implicated as genomic alterations that contribute to the etiopathogenesis of testicular lymphoma and activating mutations in MYD88 and CD79B are most commonly identified.[13,14]

Standard treatment for PTL remains unavailable. Initially, we preferred to perform right unilateral orchiectomy considering the diagnostic uncertainty and the possible complications of psychological effects and hypogonadism associated with bilateral orchiectomy;[15,16] however, we performed left contralateral orchiectomy after diagnosis of PTL was confirmed, to verify whether the lesion belonged to the same histological lineage. R-CHOP chemotherapy followed by scrotal radiotherapy is the standard treatment for localized PTL stages I–II.[9,10]

The major limitation of this case presentation is the absence of follow-up after application of the treatment protocol for the presented neoplasia. PTL is a rare malignancy associated with high recurrence rates and poor prognosis, and multimodal therapy is warranted to achieve better long-term survival and cure rates.

List of abbreviations

PTL(Primary testicular lymphoma)
NHL(Non-Hodgkin lymphoma)
Nuclear factor kB(NF-kB)

CRediT taxonomy

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Conflict of interest

None of the authors have any conflicts of interest or financial ties to disclose.

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