Primary urinary bladder lymphoma: presentation with bilateral hydronephrosis

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ABSTRACT

Primary urinary bladder lymphoma is an extremely rare entity, accounting for approximately 0.2% of all extranodal lymphomas and less than 1% of all urinary bladder tumours. This neoplasia usually occurs more frequently in female and elderly patients, and the most common histological type is diffuse large B-cell lymphoma. As it has non-specific clinical and imaging characteristics, its diagnosis requires a histopathological evaluation, since it can be confused with other urinary bladder neoplasms. The management of this neoplasia is mainly based on immunochemotherapy with the R-CHOP regimen, which has shown good outcomes. This article presents the case of an elderly patient who presented with isolated haematuria and hydronephrosis whose subsequent studies revealed the presence of a primary urinary bladder lymphoma consistent with diffuse large B-cell lymphoma.

Keywords: urinary bladder, diffuse large B-cell lymphoma, hydronephrosis

INTRODUCTION

Primary urinary bladder lymphoma (PBL) represents approximately 0.2% of all extranodal lymphomas and less than 1% of all urinary bladder tumours. This entity was described for the first time by Jacobs and Symington in 1953 and represents an extremely rare and not well-studied neoplasm [1].

The most common histological type is diffuse large B-cell lymphoma (DLCBL) (51.9%), followed by MALT (mucosa-assisted lymphoid tissue) lymphoma (12.5%) and follicular lymphoma (9.4%). Of these, the histological type with the worst prognosis is diffuse large B-cell lymphoma [1, 2]. This article presents the case of an 83-year-old female patient who presented with isolated haematuria and hydronephrosis, whose subsequent studies revealed the presence of a mass in the urinary bladder that turned out to be consistent with PBL.

CASE PRESENTATION

An 83-year-old female patient presented to the hospital outpatient clinic complaining of painless haematuria 1 month ago. The patient denied the presence of dysuria, urinary urgency, urinary frequency, fever, low back pain, or weight loss. The patient's medical history revealed hypertension and glaucoma. The patient had no smoking history. The physical examination revealed neither lymphadenopathy nor organomegaly. The genitourinary examination showed no abnormalities. It was decided to hospitalize the patient for further studies.

The patient's laboratory tests upon admission showed haematological counts within normal values, except for the presence of mild anaemia (Hb: 10.1 g/dL). Kidney function tests showed: creatinine: 1.4 mg/dL (normal range: 0.6 to 1.1 mg/dL), and urea: 62.7 mg/dL (normal range: 5 to 20 mg/dL). No alterations were found in the coagulation profile and liver function tests. Serology for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Cytomegalovirus (CMV), Epstein-Barr Virus (EBV) and Toxoplasma was negative. However, positivity for Hepatitis B core Antigen (HbcAg) was found. The quantitative Hepatitis B virus DNA (HBV DNA) test was 10,000 IU/mL. No other serological markers for hepatitis B were found to be positive. Urine examination showed the presence of more than 100 leukocytes per field and 25 erythrocytes per field.

A contrast-enhanced computed tomography (CT) was performed, which showed a thickening of the posterior wall of the urinary bladder of 29 mm and the presence of

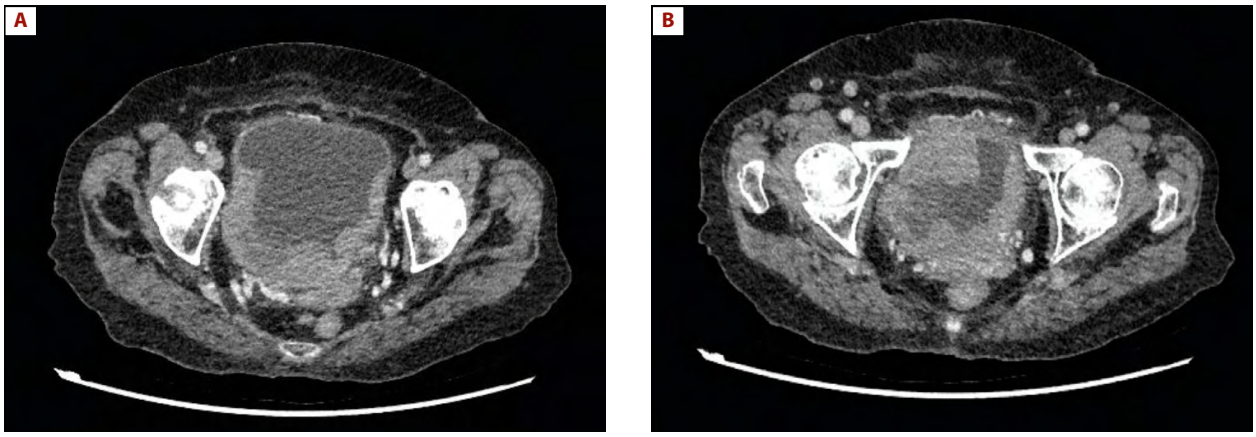

Figure 1. Computed tomography of the pelvis with contrast. There is evidence of irregular thickening of the posterior and lateral walls of the bladder

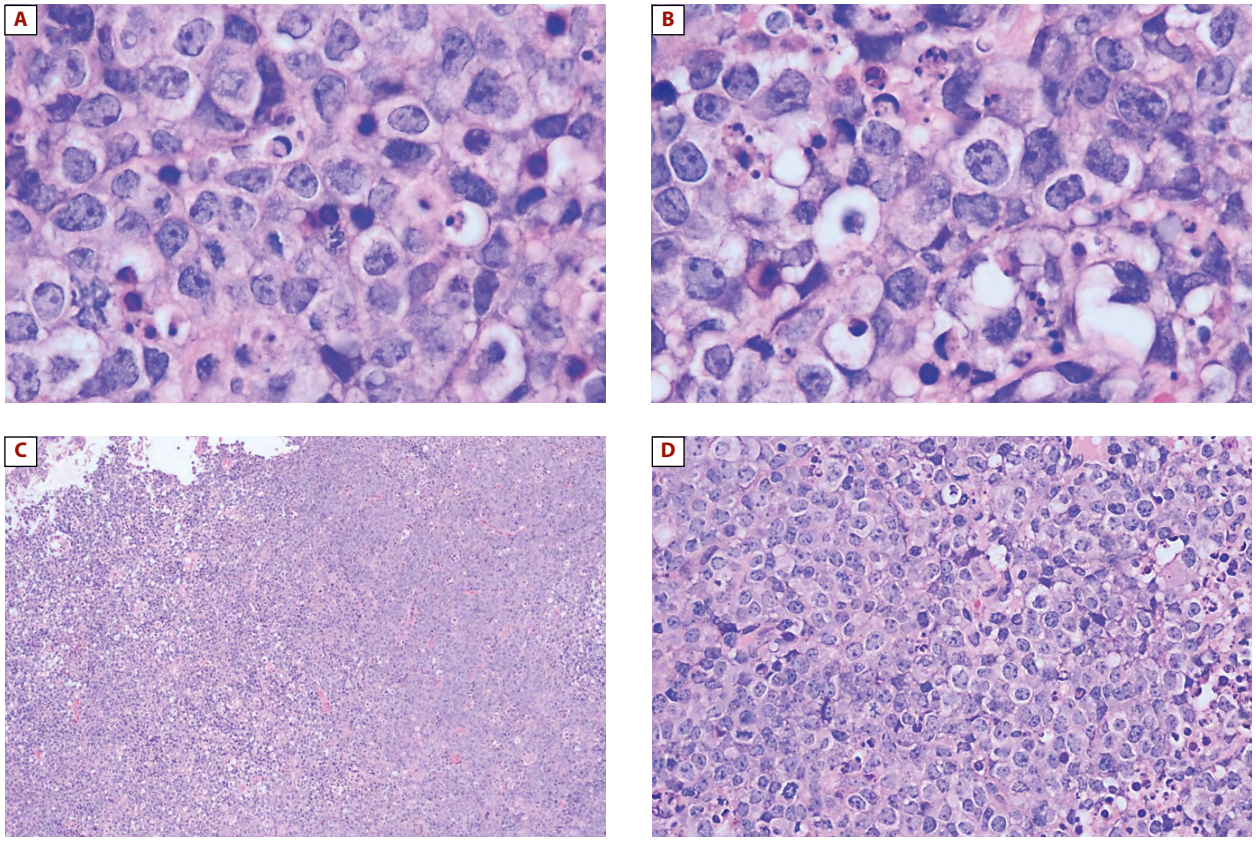

Figure 2. Histopathology with H&E staining. Microscopic examination revealed the presence of atypical lymphocytes with large nuclei at 4× (2A), 20× (2B) and 100× (2C, 2D). H&E — haematoxylin & eosin staining

bilateral hydronephrosis, predominantly on the right side with parenchymal enhancement with the administration of contrast (*see* Figure 1). Cystoscopy revealed a non-ulcerative broad-based sessile tumour measuring approximately 5 × 5 cm located on the left lateral aspect and roof of the urinary bladder. A PET scan was unavailable.

A transurethral resection was performed and histopathological examination of the biopsy specimen showed the presence of a poorly differentiated large cell malignancy (*see* Figure 2). Immunohistochemistry was positive for CD20, CD3, BCL-2, BCL-6 and MUM-1, while negative for c-MYC, CD30, P53, CD10. The Ki-67 proliferation index was greater than 90% (*see* Figure 3). The chromogenic in situ hybridization study showed negativity for EBER. A diagnosis of germinal centre B-cell-like DLBCL with high-grade features was made. The bone marrow biopsy did not reveal lymphoma infiltration. The final diagnosis was stage I DLBCL with high-grade features.

During her hospitalization, the patient suffered from a urinary infection refractory to empirical antibiotic management, so it was decided to perform a urine culture which revealed the presence of Escherichia coli ESBL, so antibiotic therapy with meropenem was started. After managing the

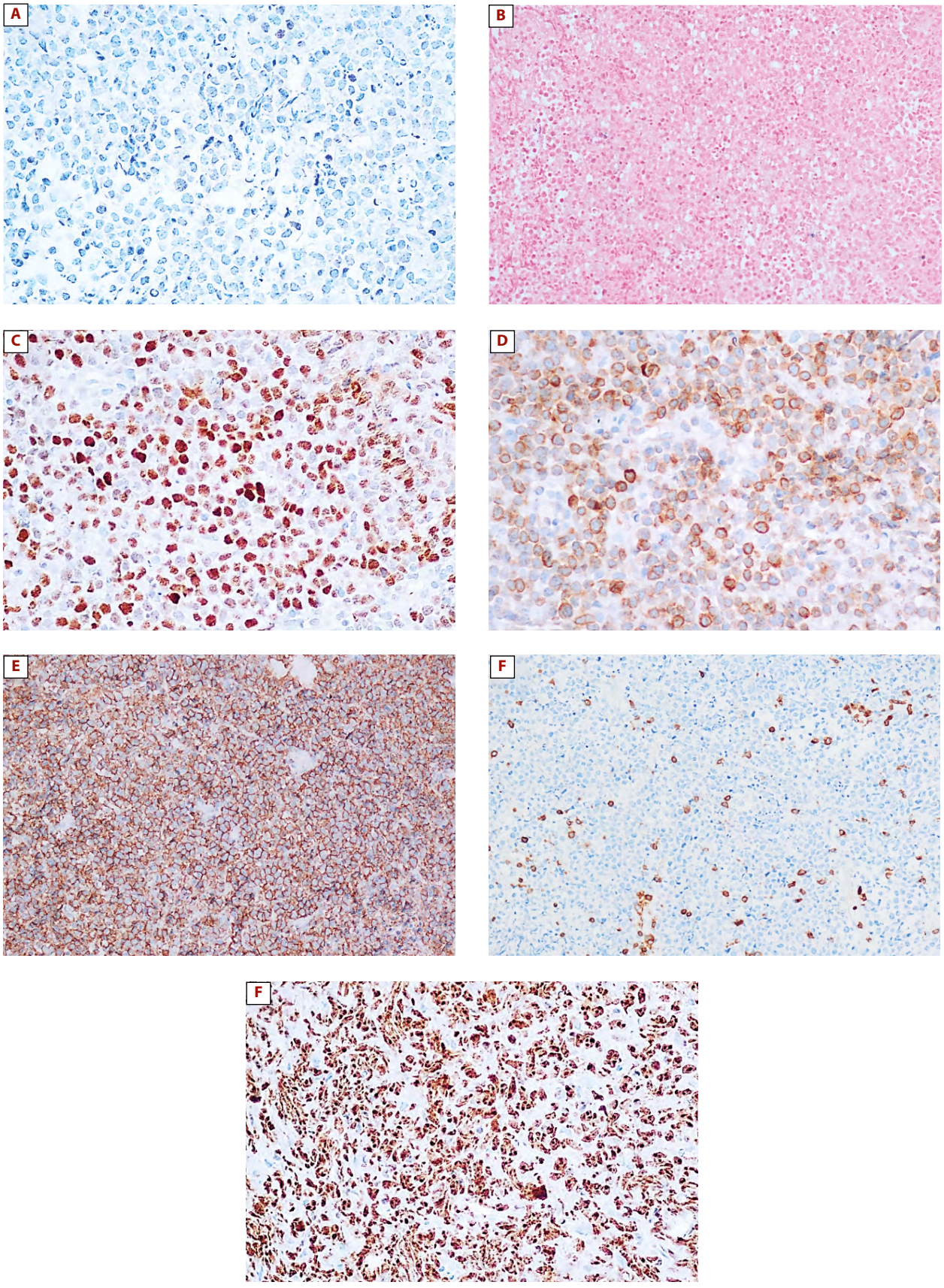

Figure 3. Immunohistochemistry showed positivity for CD20, CD3, BCL-6, BCL-2, negativity for MUM-1 and EBER. The Ki-67 proliferation index was greater than 90%

infection, it was decided to start the immunochemotherapy with the R-CHOP regimen (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone). The patient received prophylaxis with entecavir 0.5 mg orally once a day until one year after the last chemotherapy. The patient completed successfully 6 cycles of chemotherapy after which she presented complete remission demonstrated by cystoscopy and CT scan. Currently, the patient is being scheduled for adjuvant radiotherapy.

DISCUSSION

Non-Hodgkin lymphoma (NHL) with bladder involvement can be primary or secondary. In the case of PBL, it can originate from the mucosa-associated lymphoid tissue that exists in the bladder and represents approximately less than 0.2% of extranodal NHL. While secondary involvement usually occurs in advanced NHL with involvement of multiple organs and represents approximately 10 to 20% [2, 3]. According to the literature, this is the first case of PBL with the histological subtype of DLBCL reported in Latin America.

There are several hypotheses about the origin of PBL. The most accepted one is its relationship with chronic inflammation, which explains why this entity is more common in women, where chronic cystitis occurs more frequently compared with men. It is postulated that chronic inflammation caused by recurrent infections can attract lymphoid cells to the bladder tissue and that these can give rise to neoplasia. Another theory raises the possibility of the persistence of embryological residues of the cloaca that could serve as a focus of lymphoid proliferation during adulthood [2–4].

Primary urinary bladder lymphoma usually affects females twice as often as males. The average age of diagnosis is 63 years, a fact that can be explained by immunosenescence. However, the age of presentation can be variable depending on whether it is a high-grade or low-grade lymphoma. High-grade lymphomas include DLBCL, the most common histological type of PBL. While the most common histological type in low-grade lymphomas is MALT lymphoma. It must be taken into account that some low-grade lymphomas can undergo malignant transformation into DLBCL [5]. The patient in the case was an older female, which is consistent with what has been reported in the literature.

Concerning its clinical presentation, PBL usually manifests with haematuria, the most frequently reported symptom. This may be accompanied by other symptoms such as dysuria, urinary frequency, nocturia, flank pain, suprapubic pain and recurrent urinary infections [2, 5]. Although it is not usually the most common presentation, urinary bladder lymphoma can present with hydronephrosis if its location involves the bladder trigone and ureteral orifices [6, 7]. In this case patient presented bilateral hydronephrosis due to mechanical obstruction.

Urinary bladder lymphomas can be visualized on a CT scan as the presence of a solitary mass, multiple masses, or thickening of the side walls and dome of the bladder [8, 9]. In cystoscopy, non-ulcerative, oedematous, friable and even haemorrhagic solid submucosal tumours can be found. These findings are nonspecific and may mimic transitional bladder carcinoma [10]. The images of the case patient showed a thickening of the posterior wall and roof of the bladder, which is consistent with what was reported.

Regarding the genetic expression profile of DLBCL, it has been reported that the presence of EBV infection is uncommon in patients with primary urinary bladder lymphoma, so these are usually EBV-negative. Furthermore, DLBCL-EBV-positive individuals present a genetic expression profile different from the germinal centre phenotype [2]. The reported lymphoma was classified as DLBCL-EBV negative.

Approximately 56.5% of DLBCL of the urinary bladder are usually diagnosed in stage I compared to primary kidney lymphomas [2, 3]. The management of PBL of the histological type DLBCL is mainly based on immunochemotherapy with the R-CHOP regimen which has shown cure in more than 60% of cases. [2] Other management strategies include chemotherapy in combination with radiotherapy or transurethral resection surgery. However, radiotherapy has shown no superiority over surgery, and side effects must be taken into consideration in the cases of relapses. On the other hand, surgery has shown a role limited mainly to patients with hydronephrosis to relieve mechanical obstruction mainly in patients with low-grade lymphomas. In patients with high-grade lymphoma with locally advanced tumours, only chemotherapy is recommended. The use of other chemotherapy regimens in cases of non-response to the R-CHOP regimen is not yet well defined due to the infrequency of this entity [2, 11, 12].

Concerning the prognosis of PBL, it is little studied due to its rarity; however, it is known that the prognosis of DLBCL is worse compared to other histological types such as MALT lymphomas. Thus, age is an important prognostic factor, included within the International Prognostic Index adaptado por el National Comprehensive Cancer Network (NCCN-IPI) score [4]. The mortality of DLBCL of the urinary tract in patients over 75 years of age is usually 2 to 3 times higher compared to younger patients and 5-year overall survival of 27.1 % and 64.3% was reported for patients over 75 and under 60 years of age [13], respectively.

Furthermore, it has been shown that EBV-positive DLBCL of the urinary bladder has a worse prognosis compared to EBV-negative DBCL, possibly due to the presence of evasion mechanisms towards the immune response by the cells that make up the tumour microenvironment through the PD-L1 and PD-1 pathways [2, 14]).

CONCLUSIONS

Primary urinary bladder lymphoma represents an extremely rare entity that usually occurs in elderly women and whose most common histological type is diffuse large B-cell lymphoma. For its definitive diagnosis, a histopathological

examination is required, since the clinical and imaging characteristics are non-specific and it can mimic other bladder neoplasms.

Article information and declarations

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