CASE REPORT

Mixed extragonadal germ cell tumour of the prostate

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SUMMARY

Extragonadal germ cell tumours (EGGCTs) originated in prostate are extremely rare, with <20 cases described in the literature. We report a case of a patient with a primary prostatic mixed EGGCT. A 47-year-old man presenting severe low urinary tract symptoms and signs of prostatic enlargement, with no malignancy suspicion, underwent transurethral resection of the prostate. The histopathological evaluation suggested the diagnosis of a retroperitoneal sarcoma. The patient underwent neoadjuvant chemotherapy and then was submitted to radical cystoprostatectomy. Histology revealed a mixed EGGCT of the prostate with yolk sac tumour and seminoma components. No testicular abnormalities were identified on the postoperative scrotal ultrasound. The patient went through four cycles of chemotherapy with bleomycin, etoposide and cisplatin. After 12 months of follow-up, the patient is alive and free of recurrence.

BACKGROUND

Germ cell tumours predominantly arise from the testis. However, about 2%–5% of these tumours have an extragonadal origin.¹ Extragonadal germ cell tumours (EGGCTs) histologically contain the same components found in gonadal tumours, however, there is no gonadal mass detectable by palpation or ultrasonography.² EGGCTs and gonadal tumours also present similar serological features such as secretion of the tumour markers beta-human chorionic gonadotropin (β-HCG) and alpha-fetoprotein (AFP).² Aetiology of EGGCTs remains unclear, with some authors believing that it may originate from pluripotent stem cells, while others think that germ cells can be sequestered during their migration along the midline of the body to the gonadal area.³

More than 90% of EGGCTs occur in male patients between 20 and 35 years of age. EGGCTs usually appear in the mediastinum and retroperitoneum, but may be found in other locations, such as the pineal gland or sacrococcygeal area.⁴ EGGCTs that originated from the prostatic gland are extremely rare, with <20 cases described in the literature.⁵ We report a 47-year-old male patient who was diagnosed with a primary EGGCT originated in the prostate.

CASE PRESENTATION

A 47-year-old Caucasian man, without previous pathology or medication, presented with an acute urinary retention and history of progressive obstructive voiding symptoms. The patient had no relevant pathological family history, neither cases of cancer

or prostatic disease in his family. He was initially evaluated by the urology department of a regional hospital. The patient reported severe obstructive urinary symptoms with 2 months of evolution. Digital rectal examination showed an enlarged prostate (>80 cc), elastic consistency, with poorly defined contours due to its size. Prostate-specific antigen (PSA) was 1.4 ng/mL. Assuming the diagnosis of benign prostatic enlargement, the patient was initially submitted to a transurethral resection of the prostate (TURP). The histopathological evaluation suggested the diagnosis of an undifferentiated sarcoma of the prostate with immunohistochemistry revealing positivity only for vimentin.

INVESTIGATIONS

After TURP, the patient underwent a CT scan. CT scan identified a 110×45 mm pelvic mass located in the recto-vesical pouch, with no apparent cleavage planes either with the prostate or the rectum. No metastatic lesions were identified (figure 1). Several analytical assays were performed, with an increase in AFP (288 ng/mL), β-HCG (3.2 mIU/mL) and the specific neuroenolase (36 ng/mL).

TREATMENT

Given the histological diagnosis of undifferentiated retroperitoneal sarcoma, the patient was referred to our hospital (tertiary hospital). A specialised team of bone and soft tissue sarcomas initially evaluated the patient and prescribed neoadjuvant chemotherapy based on doxorubicin. After ending the chemotherapy cycle, the patient was proposed for radical cystoprostatectomy. Surgery occurred about 3 months after the histological diagnosis of TURP specimens. Radical cystoprostatectomy was performed with bilateral pelvic lymphadenectomy and ureteroileostomy, without intercurrents. The resection was macroscopically complete.

Histopathological examination showed at gross examination a 5 cm white firm lesion, with extensive necrosis and lobulated boundaries, localised in the prostate and invading the bladder, seminal vesicles and vas deferens (figure 2). Histology revealed massive necrosis and fibrosis (70%), in probable relation to neoadjuvant chemotherapy. Yolk sac tumour (YST) was the predominant component (20%) and seminoma composed the remaining viable tumour (10%) (figure 3). The yolk sac tumour component was suggested by the presence of areas with microvesicular and macrovesicular patterns, papillary structures with central blood vessels and Schiller-Duval-like bodies; neoplastic cells had eosinophilic cytoplasm, moderate pleomorphic nuclei and large nucleoli. Some mitotic figures were

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Figure 1 CT scan, a large pelvic mass without cleavage planes: (A) coronal cut; (B) axial cut.

present. The seminoma component was characterised by a solid or diffuse arrangement of neoplastic cells with pale cytoplasm, moderate pleomorphic nuclei and prominent nucleoli, supported by fibrovascular septa with lymphocytic cells. The tumour was bilateral and invaded seminal vesicles, vas deferens and the lower half of urinary bladder. The minimal non-tumour prostatic tissue showed benign hyperplasia and chronic prostatitis. There was no metastasis in 12 lymphatic pelvic nodes studied.

After surgery, the patient underwent scrotal ultrasound with no testicular abnormalities identified, excluding a secondary prostatic location of a primary testicular tumour. Tumour markers decreased to normal reference values. Later on, the patient underwent adjuvant chemotherapy, which consisted of four cycles of bleomycin (30 mg, on days 1, 8 and 15), etoposide (100 mg, on days 1–5) and cisplatin (40 mg, on days 1–4). The patient tolerated the treatment without developing significant adverse effects.

OUTCOME AND FOLLOW-UP

The patient is regularly observed and evaluated in appointments of oncological urology with regular serum tumour markers, scrotal ultrasound and CT scans. At this time, 12 months after radical cystoprostatectomy, the patient is alive and free of recurrence.

DISCUSSION

Primary EGGCTs are extremely rare, most of them originate from the body midline. More than 60% of these tumours are seminomas, arising from the anterior mediastinum or retroperitoneum. Symptoms of EGGCTs are dependent on the location and size of the tumour. Patients with mediastinal and retroperitoneal EGGCTs would not present symptoms until their tumours have developed into large sizes. The clinical presentations of retroperitoneal EGGCTs include abdominal mass with or without pain,

Figure 2 (A) Tumour in the posterolateral prostate; (B) tumour in the lower third of the bladder, with extensive necrosis.

Figure 3 (A) H&E 100x, transition from YST (left) to seminoma (right); (B) H&E 40x, YST; (C) HE 100x, seminoma; (D) H&E 100x, Schiller-Duval bodies; (E) AE1/AE3 100x, YST; (F) Vimentin 100x, YST; (G) PSA 100x, seminoma; (H) ki67 100, seminoma; (I) CD117 100x, seminoma; (J) OCT3/4 100x, seminoma; (L) CD30 100x, seminoma; (M) AFP 100x, YST; (N) Glipican3 100x, YST; (O) CD30 100x, YST. AFP, alpha-fetoprotein; PSA, prostate-specific antigen; YST, yolk sac tumour.

backache and weight loss.⁶ A review of the existing literature revealed <20 cases of primary prostatic EGGCTs described.^{7,8} Mixed prostatic EGGCTs are even rarer, so far only three cases have been reported.^{3,9,10}

Similar to testis germ cell tumours, EGGCTs should be treated with cisplatin-based chemotherapy. Surgical resection should be considered for residual disease in non-seminomatous EGGCTs.¹¹ Radiotherapy may also be a therapeutic option, but only in seminomas.² In this case, surgical resection was performed prior to cisplatin-based chemotherapy due to initial suspicion of an undifferentiated sarcoma. However, the histological evaluation of the operative specimen revealed a primary prostatic germ cell tumour. We highlight the importance of the clinical suspicion of EGGCTs in cases of retroperitoneal masses. In fact, the therapeutic approach of sarcomas and EGGCTs is completely different. However, the distinction between these tumours is often a challenge. The imaging findings of most retroperitoneal soft tissue tumours are non-specific, with a definitive diagnosis established only by histopathological evaluation. Positive serum markers may suggest a diagnosis of germ cell tumours and therefore should always be evaluated, especially if there is no evidence of fat on CT scan. The majority (70%) of retroperitoneal sarcomas are liposarcomas and therefore interrogating imaging of an indeterminate retroperitoneal mass should begin with a purposeful search for the presence of abnormal macroscopic fat.¹² An accurate diagnosis after TURP would have prevented chemotherapy with doxorubicin and possibly even radical cystoprostatectomy.

The subsequent follow-up with scrotal ultrasound without identification of any testicular lesion allied to a thorough scrotal physical examination confirmed the prostatic origin. There is some debate on this subject, with some previous works reporting that many patients diagnosed with EGGCTs had evidence of testicular origin, such as scars or fibrosis in the testis.¹³ Other studies argue that germ cell tumours developed independently in extragonadal sites and testis.¹⁴ The risk of developing a metachronous testicular germ cell tumour after EGGCT treatment is also not negligible. Hartmann *et al* reported that 14.2% of patients with retroperitoneal EGGCTs developed a metachronous

testicular tumour over a 10-year follow-up.¹⁵ Although there are no specific data related to primary EGGCT of the prostate, it emphasises the importance of regular monitoring of the testis to rule out the appearance of any neoplasm.

Germ cell tumours have very favourable survival rates, >80%. However, data on survival and long-term comorbidities of patients with EGGCTs are scarce.¹⁶ EGGCTs present inferior prognosis than their gonadal counterparts. Five-year survival rate ranges from 45% to 62%, in the published series.^{2,16} Brain, liver, lungs and bones are the common sites of metastases.¹⁰ Alanee *et al* showed that patients with primary EGGCTs experience an increased risk for dying of haematopoietic malignancies and cardiovascular disorders compared with patients affected by gonadal germ cell tumours.¹⁶ The patient presented in this case continues to be clinically supervised in frequent urological oncology appointments and after 12 months of follow-up does not present any evidence of tumour recurrence or any comorbidity associated.

Learning points

- ▶ Always consider the extragonadal germ cell tumour (EGGCT) hypothesis in retroperitoneal masses suggestive of sarcoma.
- ▶ The clinical presentations of retroperitoneal EGGCTs include abdominal mass with or without pain, backache and weight loss.
- ▶ Retroperitoneal EGGCTs (and in particular those with primary prostatic origin) may present with signs typical of benign prostatic hyperplasia, which may lead to delayed correct diagnosis.
- ▶ Unlike EGGCTs, most retroperitoneal sarcomas have no presence of abnormal macroscopic fat on CT scan.
- ▶ There is a risk of developing metachronous testicular tumours in EGGCTs, so it is important to regularly monitor the testis to rule out possible late tumour development.

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