Phyllodes-type prostate sarcoma

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RESUMEN

Los sarcomas de la próstata son responsables del 0.1% a 0.2% de todos los tumores malignos de la próstata, y sobre todo los de origen estromal. El rabdomiosarcoma es el tumor mesenquimatoso de la próstata y se observa exclusivamente en la infancia, no expresa CD34 ni progesterona. Los leiomiosarcomas son los sarcomas que comprometen con mayor frecuencia el tejido prostático en los adultos, se expresan con actina y desmina en los estudios inmunohistoquímicos. El subtipo filodes es una neoplasia muy poco frecuente. Tiene un potencial maligno incierto, pero en la mayoría de los casos desarrolla metástasis de forma rápida y suele ser recidivante.

Presentamos el caso de un hombre de 79 años quién desarrolló un sarcoma de próstata tipo filodes de alto grado, con gran poder metastásico de manera rápida y poco frecuente.

Palabras clave: Sarcoma, próstata, filodes, metástasis, México.

ABSTRACT

Sarcomas of the prostate, especially those of stromal origin, are responsible for 0.1- 0.2% of all malignant prostate tumors. Rhabdomyosarcoma is a mesenchymatous tumor of the prostate that does not express CD34 or progesterone and is seen exclusively in infancy. Leiomyosarcomas are the sarcomas that more frequently involve prostate tissue in adults and they express actin and desmin in immunohistochemistry studies. The phyllodes subtype is a rare tumor that has an uncertain malignant potential, but it rapidly develops metastases in the majority of cases and tends to be recurrent.

We present the case of a 79-year-old man that developed a high-grade phyllodes-type prostate sarcoma with unusually rapid and extensive metastasis.

Keywords: Sarcoma, prostate, phyllodes, metastasis, México.
INTRODUCTION

Prostate tumors are the most frequent neoplasia in men. Tumors of mesenchymal origin represent only 0.1 to 0.2% of malignant prostate tumors and therefore little is known about them. Phyllodes-type prostate sarcoma is a very rare entity, with only approximately 30 cases reported in the medical literature. First diagnosed in 1960, it is also known as phyllodes-type of atypical prostatic hyperplasia, cystoadeno-leiomyofibroma, cystosarcoma phyllodes, and prostatic stromal tumor of uncertain malignant potential.

Prostatic stromal sarcoma is characterized by the expansion of specialized prostatic stroma, associated with a glandular non-neoplastic component that typically expresses CD34 and progesterone receptors. This characteristic expression lends support to the theory that these lesions are the result of an abnormal hormone-dependent response of the specialized prostatic stroma. Many authors have associated this type of lesion with mixed epithelial-mesenchymal tumors that occur in other organs, such as the phyllodes tumor of the breast.

It has a fusiform cell morphology and can have histologic and/or immunohistochemical characteristics of leiomyosarcoma, rhabdomyosarcoma, and fibrosarcoma.

The cardinal sign of this pathology is severe urinary obstruction and in some cases the serum creatinine and urea levels are also elevated. Tumors measure from 4 to 25 cm in diameter and their weight is variable. Prostate specific antigen (PSA) can be normal or elevated.

Phyllodes tumor is characterized by its infiltrating growth and its potential for metastatic propagation to the bladder, rectum, lung, abdominal wall, bones, and lymph nodes.

Treatment is radical surgery, chemotherapy, or radiotherapy. After carrying out transurethral resection of the prostate (TURP), cystoscopic surveillance especially of the periurethral zone can be done and is usually performed in older men presenting with associated comorbidities. However, initial aggressive treatment is the best option.

CASE PRESENTATION

A 79-year-old man presented with a past medical history of partial pancreatectomy plus necrosectomy plus open cholecystectomy secondary to biliary pancreatitis 30 years prior. Ten years prior he had a right inguinal plasty and TURP at a private hospital. In 2007 and 2008 he underwent TURP again at the Hospital Regional Lic. Adolfo López Mateos. All histopathologic reports (HPR) were negative for malignancy and serum creatinine and hemoglobin levels were normal. PSA value was between 0.4 and 2.4 ng/mL, respectively.

Eighteen months later he returned, presenting with acute urine retention, gross hematuria, anemia, postrenal kidney failure, and with a serum creatinine level of 4.1 mg/dL, PSA of 19.78 ng/mL, and hemoglobin de 8.1 g/dL. Pharmacologic treatment and surgical protocol were begun. Retropubic prostatectomy was offered to the patient but he refused it and TURP was performed instead.

Histopathologic study revealed low-grade phyllodes-type prostate sarcoma with intense prostatic stromal proliferation that either replaced or surrounded the normal glands. The stromal cells were small and thin with a fibroblastic appearance. Collagenization was scant and the relaxed and myxoid aspect of the proliferation was predominant. A duct-type epithelial component was recognized in some of the fragments as outer sheathing or as glands. There was little stromal atypia, mitotic activity was scant, and necrotic zones were observed (Figures 1 and 2). The immunohistochemistry study was positive for CD34 and negative for estrogen and progesterone receptors. The S100 protein was positive, there was focal positivity for smooth muscle actin, desmin, and calponin, and proliferative activity with Ki 67 was 10% (Figure 3). The patient was released presenting with no hematuria.

He was re-admitted three months after TURP with hematuria, urosepsis, and physical and clinical deterioration. The patient was given multidisciplinary support and was stabilized. Adenomectomy was performed (Figures 4 and 5) and the HPR stated high-grade phyllodes-type prostatic stromal sarcoma. The obtained tissue weighed 600 g and multiple fragments measured up to 10 cm. On this occasion, tumor differentiation showed a higher degree of cellularity and atypia. An epithelioid component that was not identified in the previous resections was observed that was negative for anti-keratin antibodies (Pan K) and the reaction for CD34 was negative, as well as that for muscle markers.

Proliferative activity was intense with 40% Ki 67. Low-grade phyllodes-type areas were found that were similar to those described in the previous resections.

After being given the diagnosis and treatment options, the patient accepted only surveillance and so he was released and given an appointment in the out-patient service to continue the surgical protocol. The patient did not keep his appointment and 45 days later he was readmitted in very poor physical health, with hematuria, abdominal surgical wound dehiscence, and tumor and evisceration of the abdominal wall. Surgical exploration revealed an eventrated small bowel with no other pathology and a bladder-dependent tumor.
extending to the abdominal wall. Due to the patient's general condition the abdominal wall was closed. After the surgery the patient presented with multiple organ failure and died seven days later.

**DISCUSSION**

Prostate cancer (CaP) is the most frequent malignant tumor in men. Epithelial lesions are common, but mesenchymal tumors have a frequency of only 0.2% in prostate malignancies and little is known about them, especially those of stromal origin. They were first described in 1960 and are histologically very similar to phyllodes tumors of the breast. The prostate has a hormone-dependent specialized stroma with a complex relation between stromal and epithelial tissue. This relation is responsible for the formation of prostatic epithelium and for the differentiation, proliferation, and expression of specific proteins in the prostate. Therefore, it is thought that proliferative lesions of the prostatic stroma are the result of a faulty interaction between the stroma and the epithelium. Phyllodes-type prostate sarcomas are associated with a non-neoplastic glandular component and they typically express CD34 and progesterone receptors.

From an anatomopathologic perspective, differential diagnosis is made with tumors such as rhabdomyosarcoma, leiomyosarcoma, carcinosarcoma, and low-grade fibromyxoid sarcoma. Rhabdomyosarcoma is a tumor that occurs during infancy within the first decade of life and does not typically express CD34 or progesterone. In immunohistochemistry studies, leiomyosarcoma tends to express actin and desmin and often lacks an
epithelial component. Carcinosarcoma is a low-grade fibromyxoid sarcoma that does not present with an associated benign epithelial component and does not express CD34, unless only focally.\(^1,5-7,8\) Histologically, phyllodes-type prostate sarcoma is divided into low-grade (benign), intermediate grade (malignant), and high-grade (malignant), depending on its mitotic activity, on stromal cellularity, and on the relation between the stroma and the epithelium.\(^1,10,13\)

Low-grade tumors show limited stromal cellularity, minimal atypia, scant or absent mitosis, an absence of necrosis, and a weak stromal/epithelial relation. High-grade tumors have a marked stromal cellularity, considerable atypical cytology and frequent mitotic figures, a very strong stromal/epithelial relation, and moderate or abundant necrosis. The intermediate-grade tumors have characteristics of the other two grades.\(^1,10-13\)

In the few reported cases, the disease presents at a mean age of 56 years and a range of 20 to 86 years. Patients typically present with obstructive urinary symptoms, hematuria, dysuria, rectal pain, a palpable mass in the abdomen or rectum, and stabbing hypogastric or perineal pain. Severe urinary obstruction is the cardinal sign and there is serum creatinine and urea level elevation in some cases. Upon rectal examination, the prostate is large, soft, and spongy. The tumors range in size from 4 to 25 cm and weight varies from 0.5 to 11.2 Kg. PSA is normal or slightly elevated, even in those patients with metastasis.\(^1,5-8\) Radiologically, phyllodes-type prostate sarcoma is viewed as a lobulated or cystic lesion.\(^7\)

The majority of these tumors involve the lateral wall of the peripheral zone and the periphery of the verumontanum and they are identified in the histopathologic result of TURP or prostatectomies, and usually are not discerned in transrectal biopsy of the prostate due to their unusual architecture.\(^1-3,7\) The phyllodes tumor is characterized by its infiltrating growth and its potential for metastatic propagation to the bladder, rectum, lung, abdominal wall, and bones. Its metastasis to the lymph nodes is very rare.

The histology of metastases has not yet been clearly defined.\(^1,10-12\) Recurrence after TURP in low-grade tumors is 65%, and in high-grade tumors is 100%. Recurrence is accompanied with biological aggressiveness, progressively increasing the sarcomatous transformation with metastasis, and a fatal outcome.\(^7,10\)

There is a tendency towards a higher recurrence incidence and a decrease in survival in high-grade tumors when compared with low-grade tumors. However, the majority of low-grade tumors become high-grade and at the same time present with metastasis. The phyllodes tumor can coexist with adenocarcinoma, leiomyosarcoma, and rhabdomyosarcoma.\(^1,5\)

Treatment is prostatectomy or radical cystoprostatectomy. Chemotherapy immediately after diagnosis is recommended (cisplatin and etoposide) (cisplatin and doxorubicin), four to five cycles. Radiotherapy is not recommended as a first instance therapy because of the resulting disease progression, recurrence, and secondary effects in comparison with surgery plus chemotherapy results.\(^1,5\)
**CONCLUSIONS**

Prostate sarcomas are very rare lesions and the phyllodes-type is even rarer, with very few reports in the medical literature. They usually present as lower obstructive uropathy and when the HPR is obtained, initial radical treatment is suggested due to their uncertain potential malignancy and high recurrence.

The most important problem involved in phyllodes-type prostate sarcoma is that its clinical progression is unpredictable and does not seem to correlate exactly with the histologic parameters of cellular pleomorphism, mitotic index, and necrosis.

Even though surgical resection appears to be the treatment of choice, postoperative results are discouraging and not very successful since the majority of cases present with elevated recurrence, and metastases do not always respond to chemotherapy and radiotherapy.

Early indicators of progression to malignancy for the purpose of justifying radical surgery are not yet well defined. Strict follow-up is necessary for improving poor outcome. It is essential to establish adequate diagnosis as early as possible and a complete treatment that includes surgical resection and systemic adjuvant chemotherapy to improve the short and long-term success rates.10-13

**REFERENCES**