CLINICAL CASE

Bladder paraganglioma: a rare disease with controversial treatment

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KEYWORDS
Bladder paraganglioma; Pheochromocytoma; Hematuria; Bladder tumor; Colombia.

Abstract
The case is described herein of a man presenting with intermittent hematuria of 8-month duration, headache during micturition, dysuria, and hypogastric pain. Cystoscopy and nuclear magnetic resonance (NMR) imaging of the abdomen and pelvis showed a bladder mass. It was surgically resected and the pathologic study reported a bladder paraganglioma. Biochemical test (free plasma metanephrines) results were high and the patient underwent cystectomy, confirming the diagnosis. MIIB scintigraphy did not report evidence of disease in other organs.

It was concluded that bladder paraganglioma is a rare pathology whose diagnosis involves a high degree of suspicion, along with biochemical and imaging studies. Treatment depends on the lesion characteristics and is not yet standardized.

PALABRAS CLAVE
Paraganglioma vesical; Feocromocitoma; Hematuria; Tumor vesical; Colombia.

Paraganglioma vesical: una entidad poco frecuente con tratamiento controversial

Resumen
Se describe el caso de un paciente masculino con 8 meses de hematuria intermitente, cefalea durante la micción, disuria y dolor hipogástrico. La cistoscopia y la resonancia nuclear magnética (RNM) de abdomen y pelvis mostraron una masa vesical, la cual se resecó quirúrgicamente y su patología reportó un paraganglioma vesical. Los estudios bioquímicos (metanefrinas libres en plasma) fueron elevados, siendo llevado a cistectomía donde se confirmó el diagnóstico. Se realizó gammagrafía MIBG, que no reportó evidencia de enfermedad en otros órganos.

Se concluyó que el paraganglioma vesical es una patología poco frecuente cuyo diagnóstico implica alto índice de sospecha, estudios bioquímicos e imagenológicos. El tratamiento depende de las características de la lesión y aún no está estandarizado.

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Introduction

The term “paraganglioma” is used to refer to extra-adrenal pheochromocytomas.¹ They derive from the ganglion tissue located in the paravertebral and para-aortic region, from the base of the cranium to the pelvis.² They most commonly present in patients between the ages of 20 and 40 years and are slightly more frequent in women. Their main location is the organ of Zuckerkandl and the adrenal glands, the bladder is the 3rd most frequently compromised organ (11%), and the other cases are sporadic.²,³ Bladder paraganglioma correspond to 1% of all the pheochromocytomas and to less than 0.06% of all bladder tumors.⁴ Their malignancy potential is low, calculated at 10%, and the majority of these lesions are found to be metabolically active.⁵ Those that correspond to familial syndromes have up to a 50% possibility of being associated with neoplasia. However, there are no specific malignancy criteria and no difference among races has been reported.³,⁶

The aim of the present clinical case was to carry out an up-to-date review of the literature in relation to bladder paraganglioma as an uncommon entity whose diagnosis is often a challenge and whose management is still controversial.

Case presentation

A 30-year-old black man sought medical attention for an 8-month history of bilateral colicky lumbar pain irradiating to both flanks, intermittent hematuria, headache particularly during micturition, dysuria, and hypogastric pain. Laboratory tests were done upon his admittance to the emergency department showing: creatinine and clotting time in normal ranges, Hb: 14.7 g/dl, no alterations in the hemogram, and a negative urine culture.

An ultrasound study of the kidney and urinary tract was ordered that identified bilateral renal lithiasis. Three stones measuring 1, 3, and 5 mm in the left kidney were shown, as well as 2 stones measuring 9 and 6 mm in the right kidney. There was no hydronephrosis. In addition a pedunculated 3.6 x 2.5 x 2.5 cm piriform mass was found in the fundus of the bladder.

Cystoscopy revealed a pedunculated, hypervascularized lesion that was dependent on the bladder dome measuring approximately 3 cm in diameter. There was no active bleeding, but there was mucoid production. Given these findings, transurethral resection of the bladder lesion was programmed. During the procedure and upon the first cut of the lesion, the patient presented with severe bradycardia and elevated blood pressure values of 240/140 mmHg. The procedure was suspended and the sample was sent to the pathology department. The pathologic report was bladder paraganglioma. Nuclear magnetic resonance (NMR) imaging was ordered (fig. 1), as well as a plasma free metanephrines test, whose results were: metanephrine 49 pg/mL (<58 pg/mL), normetanephrine 711 pg/mL (<149 pg/mL), and total metanephrines 760 pg/mL (>206 pg/mL). The NMR image showed a hyperintense lesion at T2 in the bladder dome of approximately 4-5 cm.

The patient was premedicated 10 days prior to the partial cystectomy with an alpha blocker (prazosin) and then 3 days prior with a beta blocker (metoprolol). In addition, he was over-hydrated to maintain an adequate plasma volume. Surgery revealed a pedunculated and highly vascularized mass in the bladder dome that measured 4-5 cm in diameter (fig. 2). The final pathologic report was bladder paraganglioma extending into the muscularis propria. The resection margins were tumor-free (fig. 3).

During the first control, the free metanephrines continued to be high, requiring MIBG scintigraphy; no disease was shown. In the later control, the metanephrines were negative. Currently, the patient does not present with high blood pressure or hematuria.

Discussion

Cases of bladder paraganglioma continue to attract attention due to their rareness and the fact that they are still a diagnostic and management challenge. Even though paraganglioma is regarded as an extra-adrenal or

Figure 1 Bladder paraganglioma in magnetic resonance (hyperintense lesion in T2).

Figure 2 Bladder paraganglioma during the surgical procedure.
Bladder paraganglioma: a rare disease with controversial treatment

Heterotopic pheochromocytoma, its morphology, endocrinologic tests, clinical presentation, and treatment can be completely different.6 The symptomatology is the result of an excessive production of catecholamines. Sixty percent of the patients present with hematuria, headache, palpitations, facial flushing, and sweating. Hypertensive crises can be triggered by micturition, bladder over-distension, bowel movements, sexual activity, ejaculation, and bladder instrumentation.4 Symptoms such as hematuria present in other bladder tumors, and so it is important to distinguish these lesions from urothelial tumors. Paraganglioma typically arises from within the bladder wall and when it becomes measurable, it is possible that the muscularis propria is already compromised. Histologically, the cells are large, polygonal, and with slightly granular, eosinophilic cytoplasm. The nuclei are rounded with soft contours.7 The microscopic description of the resected lesion reported on in this clinical case concurs with the abovementioned, and therefore the diagnostic impression was paraganglioma.

Diagnosis of this entity is made through biochemical and imaging studies. The biochemical tests include the 24-hour urine tests for measuring metanephrines and catecholamines, as well as the determination of plasma free metanephrines.2 The sensitivity and specificity of the urine test for measuring metanephrines is calculated at 86% and 88%, and for catecholamines it is 77% and 95%, respectively. In the case of plasma free metanephrines, the reported sensitivity is up to 99% and the specificity is 89%. There is still discussion as to which test to choose based on the patient risk for having or not having paraganglioma. Some studies state that the urine tests should be done on the low risk patients and the plasma tests on the high risk ones.4 Our patient already had the histologic diagnosis before the tumor marker analyses, and so they were decided upon based on the information in the literature.

Cystoscopy generally shows a submucosal, yellow, hypervascularized tumor and manipulation during the procedure should be avoided to prevent a hypertensive crisis.4 Abdominopelvic computerized tomography (CT) has very good sensitivity that varies between 93%-100% for detecting tumors in the adrenal gland, and in the case of extra-adrenal pathology, it is 95%. It has the advantages of availability and lower cost, with respect to NMR, which has similar sensitivity figures and also has the advantages of less radiation and less exposure to contrast medium. The specificity of both studies is low, and is reported at up to 50%.8 NMR was chosen in the present case, because it was available and because there could be a possible increase in the exposure to radiation in the future follow-up studies. Despite its great sensitivity,123-I metaiodobenzylguanidine (MIBG) scintigraphy has been reserved for those cases in which the lesion is not visualized through CT or NMR and there is biochemical evidence of its existence, in adrenal masses >10 cm, or in some cases of paragangliomas with suspected metastatic disease.3,8 This scintigraphy was done on our patient due to the persistent high tumor marker levels (metanephrines), despite the tumor resection. They can present in some types of high blood pressure (HBP), chronic kidney failure, and some forms of heart disease, but HBP was the only aspect related to our patient.

Surgical preparation is essential for preventing a hypertensive crisis, which is one of the complications that can present during resection. Adequate intravascular volume must be reached and optimized with a high-sodium diet to avoid collapse upon tumor resection, once there is a cessation in catecholamine production. An alpha blocker should be administered 7 to 10 days before the procedure and then, once the block has been achieved, therapy with a beta blocker should be started.3 The type of surgery has yet to be standardized, taking into account the rareness of this pathology. Partial cystectomy or radical cystectomy, whether open or laparoscopic, plus lymphadenectomy, are the proposed procedures and their choice depends on tumor location, size, and perivascular tissue involvement.6 In the present case, partial cystectomy was chosen because of the location of the mass in the bladder dome, and because the imaging studies showed that the perivesical fat and other adjacent tissues were not compromised.

Conclusions

Bladder paraganglioma is a rare pathology whose diagnosis requires a high level of suspicion, along with biochemical and imaging studies. Treatment depends on the characteristics of the tumor and is not yet standardized.

Conflict of interest

The authors declare that there is no conflict of interest.

Financial disclosure

No financial support was received in relation to this article.
References