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Case Report

Urinary Bladder Paraganglioma: a Case Report and Review of Literature

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Introduction

Non-urothelial tumors comprise less than 5% of vesical tumors, being paragangliomas responsible for only a small percentage of them. In the genitourinary tract, the bladder is the most common site for paragangliomas (79.2%), followed by the urethra (12.7%), pelvis (4.9%), and ureter (3.2%).[1]

Paragangliomas diagnosis and treatment are very challenging because our knowledge is still insufficient and based on case reports. Although it is possible to use up-to-date techniques such as immunohistochemistry, diagnosis is not always accurate.[2,3]

Papers that present most cases in the literature try to design a profile of the disease such as distribution by age, gender, and the most common site where it is found. Due to the peculiarity of these neoplasms, knowledge of pathology is important in order to choose the best treatment.

Case Report

A 20-year-old male patient presenting a 6-month recurrent painless macroscopic hematuria was initially treated for nephrolithiasis without success. Cystoscopy was then performed and showed a large polypoid lesion in the bladder right lateral wall. A tumor partial transurethral endoscopic resection was performed and histopathological test suggested less differentiated bladder carcinoma with muscle infiltration. Paraganglioma diagnosis was done by means of slide review and immunohistochemical study.

After being admitted to our institution,

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patient was submitted to excretory urograph with a normal result, but cystoscopy showed a 1cm ulcerative lesion in the right trigonal and post trigonal region with central calcification. Magnetic nuclear resonance (MRI) showed a 2cm enlargement of the right posterior-lateral wall of the bladder, with nodular component and no extension into perivesical fat. Patient was submitted to a partial cystectomy with insertion of a double J catheter due to proximity and manipulation of the right ureter. His recovery presented no intercurrences, he was discharged on the fifth day after surgery, and had vesical catheter removed on the tenth day.

Macroscopic anatomopathological assessment of the cut surface showed solid, well delimited, and lobular structure in brown-orangish color and elastic consistence. Microscopically, the tumor showed an expansive growth pattern located in the submucosal region and muscular tunica (Figure 1A). It was characterized by polygonal cells proliferation, grouped in clusters, separated by vascularized connective septa, predominantly scattered in the submucosal region (Figure 1B). Cells presented a clear, acidophilic, or granular cytoplasm, with discrete nuclear pleomorphism and evident nucleolus (Figure 1C). Mitosis figures, necrosis, and vascular invasion were not detected. Immunohistochemical panel was positive for S-100 protein, chromogranin A, neurospecific enolase, and synaptophysin compatible with diagnosis (Figure 1D). Examined surgical margins showed no neoplasm involvement.

Patient is in outpatient follow-up and presents no symptoms after 3 years.

Disucssion

Paragangliomas are neoplasms from paraganglioma tissues (chemoreceptor organs) whose origin is in the neural crest and are part of the diffuse neuroendocrine system (DNES). They produce neuropeptides and catecholamines that can work as neurotransmitters, hormones, neurohormones, or parahormones.[4]

These tumors can be classified as both sympathetic (pheochromocytoma) from the adrenal marrow, extra-adrenal paraganglia, and visceral autonomic paraganglia and parasympathetic (parasympathetic paraganglia) from which most tumors originate. Another classification is done according to site of lesion: I- branchiomeric, II- intravagal, III- aortosympathetic, and IV- visceral.[4,5]

Regarding epidemiology, they comprise a very rare entity that accounts for less than 0.05% of vesical tumors.[1] Their incidence is higher in females, a ratio of 3:1, a mean of 45 years old (16-70), which is compatible with the patient age in this case report, although he is male. He presented the common finding of painless macroscopic hematuria, but with no other typical symptoms such as headache, anxiety or palpitations.

In general, these lesions have a slow and continuous growth and most of them (97% to 99%) do not secret catecholamines and/or serotonin. In case of suspicion of a functioning tumor, it is necessary to include in laboratory investigation the following: a) urine test for metanephrine, vanillylmandelic acid, epinephrine, norepinephrine, and dopamine; b) serum test for epinephrine, norepinephrine, and dopamine, with increased sensitivity. In this case report, the patient presented a normal laboratory tests with no signs or symptoms of a functioning tumor (mictional disorders).

In this case, there was no indication of malignity. The malignant form is rare (1% of cases), and is not based on anatomopathological criteria, but on its behavior such as invasion of surrounding structures, lymph nodes impairment, and metastases, mainly to the lung, liver, bone, and spleen.[6]

MRI was effective in detecting both the lesion and its extension, being compatible with 88%-100% of sensitivity found in the literature and comparable to other imaging methods such as ultrasound (89%), computerized tomography (64%-100%), or I-MIBG scintigraphy (62%-88%).[7] If urinary bladder paraganglioma is suspected based on these tests (single submucosal or intramural lesion), cystoscopy should be done only after adrenergic blockage. Biopsy must be avoided whenever possible.

The main differential diagnosis to be considered is invasive urothelial carcinoma, which can present a large morphological variety, including rare cases with a discrete pattern in

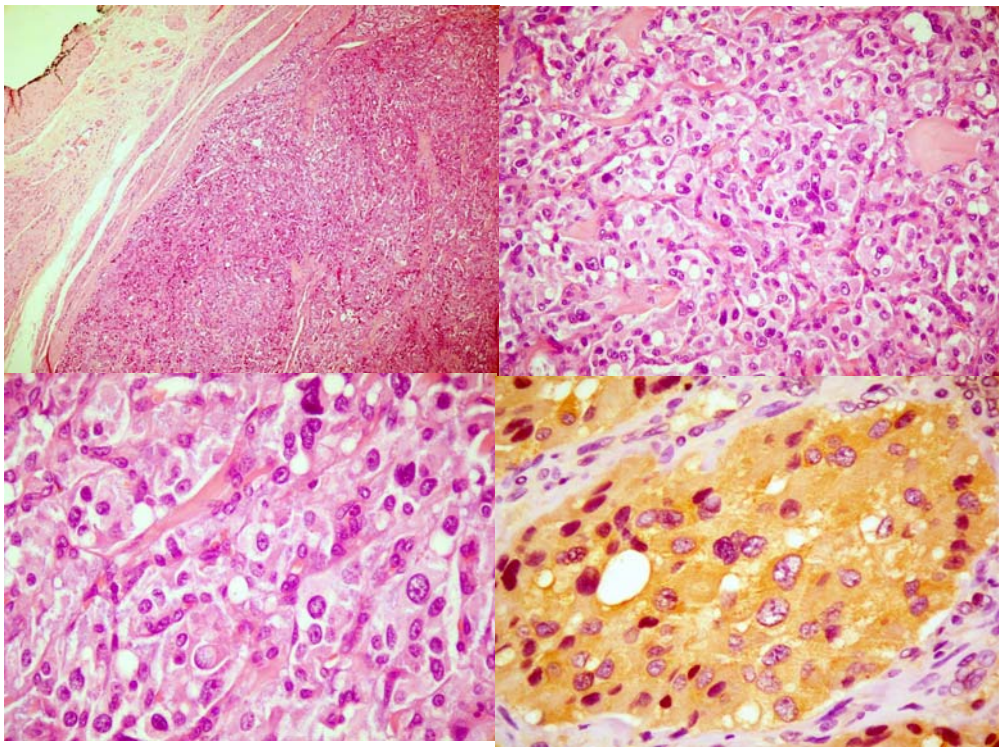

Figure 1 – A) Neoplasia with expansive growth pattern, located in the submucosal region and muscular HE 25x; B) neoplasia with grouped clusters, separated by vascularized connective septa, HE 100x; C) Cells with clear, acidophilic, granular cytoplasm, with discrete nuclear pleomorphism and evident nucleolus; D) Immunohistochemical reaction to chromogranin A.

clusters. A prominent vascular sinusoidal pattern observed on the surgical specimen was useful to establish diagnosis.[8,9]

Negativity of epithelial markers and positivity of neuroendocrine markers to immunohistochemistry corroborated histopathological findings.[10]

Treatment of these tumors is essentially surgical with complete resection with free margins, and one may consider pelvic lymphadenectomy as a complement.[7] This procedure may be performed via laparoscopy if the surgeon is experienced. In patients with functioning tumors, it is recommended to be very careful in the pre- and transoperatory period in order to prevent hypertensive crises. Radiotherapy role is only in cases of unresectable lesions, impaired margins if re-operation is not possible, or patients with no conditions to undergo surgery. There is controversy regarding indication of chemotherapy to treat these patients, with studies showing divergent results.[4,5] In selected cases only follow-up is recommended (elderly patients without major symptoms). In advanced cases, surgery may be possible after debulking chemotherapy, and in metastatic disease, chemotherapy should be used. The most used scheme is CVD (ciclophosphamide, vincristin and decarbazine).[11]

Prognosis directly depends on both presence of lymph node disease or metastases and size of lesion. Considering the risk of recurrence and metastases, a prolonged follow-up is recommended.[4]

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