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Case report

Bladder paraganglioma — A report of two cases

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KEYWORDS
Bladder;
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Abstract
Introduction: Bladder paragangliomas (BP) are rare tumors, with clinical manifestations ranging from hypertension to hematuria to being asymptomatic. Histologically, they can mimic urothelial carcinomas. Around 200 cases of paragangliomas arising in the urinary bladder have been described in the world literature.
Observation: We report 2 new cases of BPs presenting with subtle clinical symptoms like increased urinary frequency. On routine cystoscopic examination of the bladder, bladder tumors were detected.
Conclusion: We would like to stress on the histomorphology and immunohistochemistry findings of this rare condition and its diagnosis on transurethral resection specimens.

Introduction

Paraganglioma (PGL) of the bladder is a rare neoplasm derived from paraganglion cells in the bladder wall. They account for about 0.06% of all bladder tumors. Since its first description by Zimmerman et al. in the year 1953 [1] around 200 cases have been described in the world literature [2]. Clinically, they generally present with micturition attacks, hematuria or paroxysmal hypertension [3]. We present 2 rare cases of paraganglioma of the bladder in an elderly patient, who was asymptomatic and another who had dysuria and increased frequency.

Case report

A 70 year old male, known case of ischemic heart disease (IHD) and hypertension was referred to our hospital with history of incidentally detected growth in the bladder. There was no history of hematuria, fever or dysuria. Examination revealed grade I prostatic enlarge-

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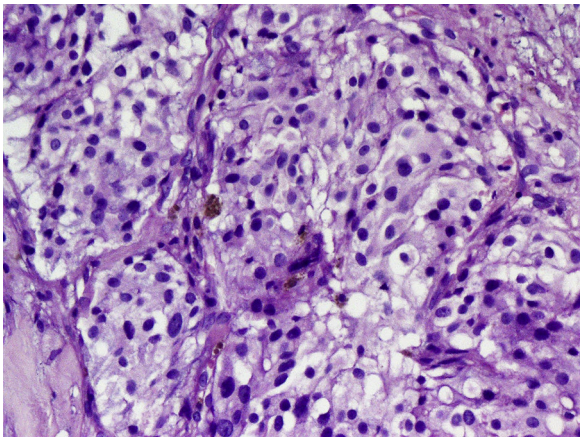

Figure 1 Section showing Zellballen pattern of tumor (H&E stain, 200×).

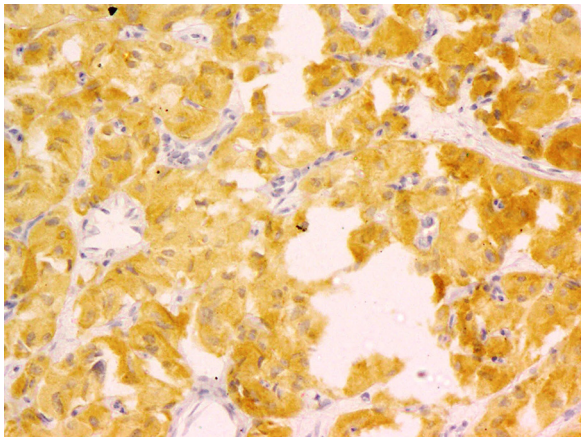

Figure 2 Strong immunoreactivity of synaptophysin in the tumor cells (DAB, 400×).

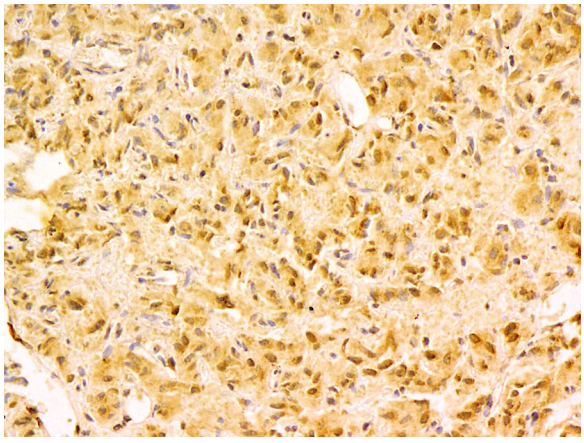

Figure 3 Strong immunoreactivity of chromogranin-A in the tumor cells (DAB, 200×).

ment. Cystoscopy revealed a 3 × 2 cm broad based solid growth in right lateral wall of bladder, well above the right ureteric orifice. Provisional diagnosis of papillary carcinoma was made. Transurethral resection (TUR) with complete excision of the tumor was performed and the specimen was sent for histopathological analysis.

The second case was a 42 year old male who presented with history of dysuria and increased frequency of micturition. Ultrasonography showed right hydroureteronephrosis with a 5 × 6 cm tumor arising from the right part of dome of bladder. Cystoscopy showed a 6 × 6 cm highly vascular broad based tumor arising from the dome of the bladder. Clinically carcinoma bladder or malignancy arising from urachal remnant was suspected. Transurethral resection of bladder tumor (TURBT) was done and specimen was subjected to histopathological examination. Patient developed hypotension during the procedure and had to be given hemodynamic support.

Pathological findings

Sections from the specimens showed a tumor composed of organized nests of cells with abundant granular eosinophilic cytoplasm with enlarged nucleus, anisonucleosis and occasional cells with intranuclear inclusions rimmed by spindle shaped sustentacular cells (Fig. 1). Focally hemorrhagic suffusion with wide separation of tumor nests was seen. No mitosis noted. Tumor islands were seen invading underlying muscular layer. On performing immunohistochemistry, the tumor cells showed diffuse positivity for synaptophysin (Fig. 2) and chromogranin A (Fig. 3), while Cytokeratin and CD68 were negative. S-100 showed artifactual background staining. Based on these findings the tumor was reported as paraganglioma of the bladder. The first patient has been on regular follow-up for the past 2 years, with no evidence of tumor recurrence. The second case was recovering on discharge.

Discussion

Paragangliomas (PGLs) are tumors arising from the paraganglia distributed along the parasympathetic nerves in the head, neck and mediastinum, along the sympathetic chain in the neck, thorax and pelviabdominal region, and in the supraneural gland and urinary bladder [4]. PGL's are classified as functioning or non-functioning depending on whether they secrete catecholamines. Malignant transformation has been reported in PGL's and account for 20% cases in urinary bladder. However, there are no reliable histological indicators of malignancy [4].

The importance of recognizing this entity is because of its frequent misdiagnosis as urothelial carcinoma especially on Transurethral Resection (TUR) Specimens. Since the follow-up treatment is different, proper diagnosis becomes all the more necessary [5].

The presence of classical nesting or Zellballen pattern with delicate fibrovascular cores when recognized helps in identifying the lesion. On the other hand, the presence of diffuse growth pattern, invasion of muscularis propria and extensive cautery artefacts may lead to improper diagnosis as urothelial carcinoma.

Clinically, the patients affected are one or two decades younger than those of urothelial carcinoma [5]. If symptomatic, patients may present with episodic or sustained hypertension or headache associated with voiding. Grossly, PGLs are usually lobulated and well circumscribed unlike the infiltrative pattern of urothelial carcinoma. However, this is not identifiable in initial TUR specimens. The Zellballen pattern of growth should raise the suspicion on histology followed by confirmation with immunohistochemistry (IHC). Infiltration into the muscle is not associated with desmoplasia. Also the neuroendocrine atypia that is frequently seen as bizarre forms is not associated with increased mitoses as expected in case of

urothelial carcinoma. Though sustentacular cells were not stained prominently in both the cases, it has been reported to be of weak staining especially in malignant cases [5,6].

Apart from urothelial carcinoma, the other differentials include nested variant of urothelial carcinoma, which can be distinguished by IHC with cytokeratin or epithelial membrane antigen. PGLs are positive for neuroendocrine markers and sustencular cells stain with S-100 protein. Metastatic tumors including renal cell carcinoma, melanoma and prostatic carcinoma are to be differentiated. Cytokeratins and EMA can be used to rule out metastatic renal cell and prostatic carcinoma. Melanoma will stain positive with S-100 which is seen only in sustentacular cells in PGLs. The second case showed the presence of pigment which can be seen in pigmented PGLs [7]. Carcinoid tumors may mimic Zellballen pattern, but IHC will show positivity for cytokeratin in contrast to PGLs. Granular cell tumor is another differential [8] which again stains positive with S-100 and CD68. In tru-cut or small biopsies, it has to be distinguished from normal paraganglia of the bladder wall, wherein the bland cytology and pattern helps in the diagnosis.

Surgery is the mainstay in all suspected cases of PGLs [8]. Surgical resection with partial or complete cystectomy with pelvic lymph node dissection is ideal, especially when malignancy is suspected. However, based on the size and location, partial cystectomy or TURBT may be done. TURBT results in incomplete excision, as most of the tumors extend beyond the detrusor muscle. Pre-operative medical treatment is advised in functioning tumors [9].

In conclusion, we would like to stress on the recognition and diagnosis of this rare entity whenever TURBT bits show Zellballen pattern rather than the usual features of urothelial carcinoma. IHC should be performed for confirmation of the same.

Authors' contributions

Concepts, design, definition of intellectual content, literature search, data acquisition, manuscript preparation, manuscript editing — Dr. Vidya Monappa, Dr. Padmapriya Jaiprakash.

Clinical studies, and manuscript review — Dr. Joseph Thomas, Dr. Padmaraj Hegde.

Consent from the patient

Obtained.

Conflict of interest

None of the authors report any conflicts of interest, including personal or financial interests.

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