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Case Study

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PARAGANGLIOMA OF URINARY BLADDER MASQUERADING AS UROTHELIAL CARCINOMA

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ABSTRACT

Paragangliomas are tumours arising from extra adrenal chromaffin tissue. Paraganglioma of urinary bladder are extremely rare. They are usually diagnosed on histopathology and confirmed on immunohistochemistry. They are frequently misdiagnosed as urothelial carcinoma, especially the nested variant. We reported a similar case which was diagnosed as urothelial carcinoma(nested variant) and came to our institution for review of diagnosis. The patient presented with only complaint of painless haematuria for past one month. Excluding all other possible differentials, the final diagnosis of paraganglioma was rendered. The treatment is different and prognosis of paraganglioma is much better than urothelial carcinoma, hence an accurate histopathological diagnosis is of prime importance.

KEYWORDS: paraganglioma, urinary bladder, urothelial carcinoma, IHC.

INTRODUCTION

Paragangliomas are also known as extra-adrenal pheochromocytoma as they arise from extra-adrenal chromaffin tissue. The first ever case of paraganglioma of urinary bladder was reported by Zimmerman in the year 1953.[1] They constitute 0.92% of all bladder tumours.[2] It is usually diagnosed on histopathological examination. It may be misdiagnosed as other tumours. Here we describe a case of paraganglioma in which the characteristic morphological features were patchy, hence leading to misdiagnosis of urothelial carcinoma. Immunohistochemistry(IHC) played an important role in reaching the final diagnosis.

CASE REPORT

A 32 year old female presented with complaints of painless haematuria for past 1 month. Urine routine showed 100-150 red blood cells/hpf. An abdominal ultrasound examination revealed a 5cm heterogenous mass along the dome of the bladder. Transurethral resection of bladder tumour(TURBT) was done outside and diagnosed as urothelial carcinoma (nested variant). We received 4 slides and 2 blocks at our institution for review before a definitive treatment could be offered to the patient.

Sections examined included bladder mucosa, submucosa and muscularis propria. The tumor cells were arranged in a diffuse, lobulated and nested patterns. Fibrovascular stroma was present focally in between the cell nests. The tumour cells were large polygonal with abundant eosinophilic granular cytoplasm, low nuclear/cytoplasmic ratio, oval nucleus with fine chromatin and inconspicous nucleoli. At places, the tumour cells showed clearing of the cytoplasm. The nucleus was vesicular at places. Atypia was mild and observed focally within the tumour cells. No necrosis or mitosis was observed. A part of the tumour also revealed cautery effects due to TURBT causing tissue distortion and blurred nuclei. The tumour was seen infiltrating and splaying the muscularis propria.[Figure-1] We kept the first differential diagnosis of paraganglioma and the second of urothelial carcinoma(nested variant).

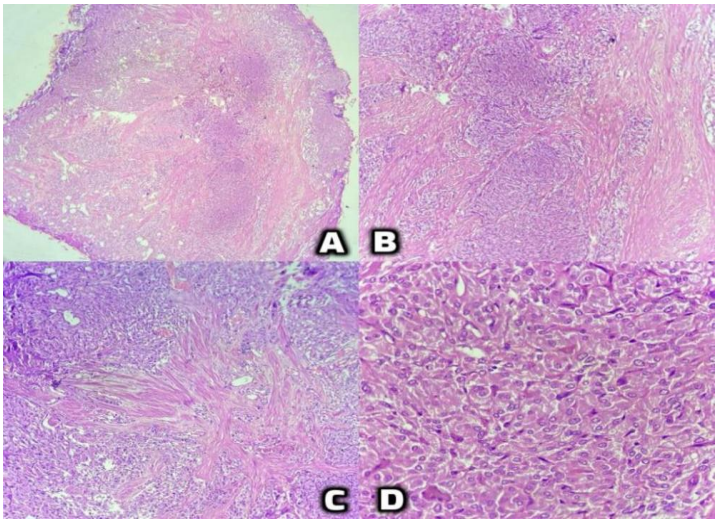

Figure-1: A- Scanner view of the tumor. B- Tumor as seen in 40x. C- Tumor splaying the muscularis propria. D- High-power view showing tumor cells in a nesting pattern.

Immunohistochemistry was done and was strongly positive for chromogranin. The tumour cells were also positive for synaptophysin and CD56. S-100 was patchy positive in the sustencular cells.[Figure-2] The tumour cells were negative for CK and Ki-67. Hence, on the basis of histomorphology and IHC, the final diagnosis of paraganglioma of the urinary bladder was given. The patient was advised to undergo complete resection of tumour and have regular radiological and biochemical follow up thereafter.

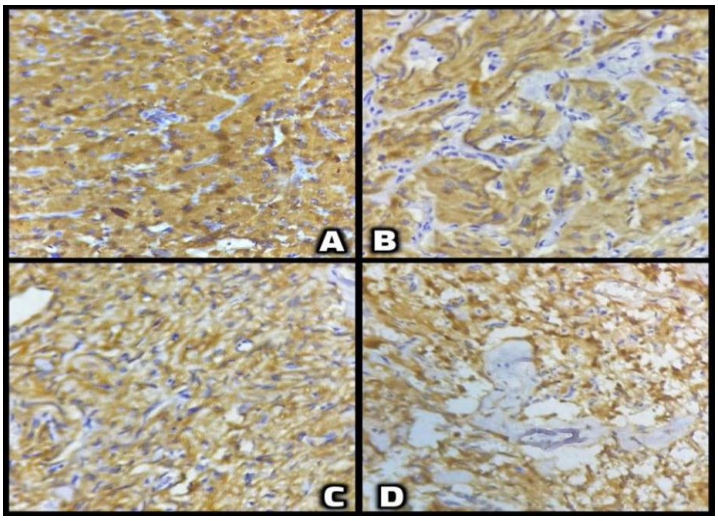

Figure-2: Immunohistochemistry- A- Chromogranin,B- Synaptophysin, C- CD56, D- S-100 positivity in sustencular cells.

DISCUSSION

Paragangliomas are tumours arising from extra-adrenal chromaffin tissue, hence they are also known as extra-adrenal pheochromocytomas. Of all the extra-adrenal pheochromocytomas, 6.7% arise from the genitourinary tract and of all the genitourinary paragangliomas, 83.3% arise in urinary bladder followed by kidney, urethra, renal pelvis and ureter.[3] They account for 0.92% of all bladder tumours.[2]These tumours exhibit an uncertain behaviour. Most of these are benign and the incidence of malignancy is reported to be around 10-15%.[4]

No specific site predilection has been found.[5] These tumours may be functional or non-functional depending on cathecholamine secretion. 63% of these tumours are functional. The functional tumours may present with hypertension, headaches, syncope, palpitations and micturition attacks. The non-functional tumours are usually silent and mostly presents with painless hematuria only.[2,4-6]

The definitive diagnosis of paraganglioma is given on histopathology. The tumor cells are arranged in a characteristic zellballen pattern with prominent fine fibrovascular network through the tumour nests. The cells are polygonal to round with abundant granular eosinophilic cytoplasm. Mild nuclear atypia may be there with very rare mitosis. However, the histology is not always characteristic and hence may lead to misdiagnosis, specially in TURBT specimens. The cells

may be arranged in diffuse pattern, pseudorossettes or irregular nests.[7]

According to Menon et al, the common factors leading to a misdiagnosis are – focal diffuse sheet like pattern, invasion of the muscularis propria, ribbon like growth pattern, focal necrosis, cautery effects, non functional tumors and failure to include this entity into the differential diagnosis. Some of the factors which could have lead to a misdiagnosis of urothelial carcinoma in our case are diffuse growth of the tumour cells with nesting pattern being focally present, a part of the tumour showing cautery effects which is common in TURBT specimens, invasion and splaying of the muscularis propria, the characteristic fibrovascular network in between the cells was present only focally and the patient did not have any symptoms of hormonal excess. Hence, a high index of suspicion and diligent search for characteristic features plays a vital role for the accurate diagnosis.[5]

The main differential diagnosis includes nested variant of urothelial carcinoma and metastatic large cell neuroendocrine carcinoma. Paragangliomas are strongly positive for neuroendocrine markers such as chromogranin, synaptophysin, CD56, NSE and S-100 is positive in sustencular cells. They are negative for CK which is positive in urothelial carcinoma and metastatic large cell neuroendocrine carcinoma. Metastatic large cell neuroendocrine carcinoma shows greater pleomorphism, necrosis and high mitotic activity. Another differential to be considered is granular cell tumour which shows polygonal cells with abundant eosinophilic cytoplasm and low N/C ratio arranged in cohesive lobules divided by fibrous septa. On IHC, they are diffusely positive for S-100 and negative for CK, synaptophysin and chromogranin, hence can be differentiated from paragangliomas which only show S-100 positivity in sustencular cells and strong positivity for synaptophysin and chromogranin. Hence, carefully searching for characteristic histological features of paraganglioma and IHC plays a vital role in excluding the differentials and reaching the final diagnosis.[8]

There is no reliable criteria to predict the behaviour or probability of metastasis.[8] The only criteria suggestive of malignancy are tumour invasion or metastasis. The most effective treatment is complete resection. It is safe and curative.[9] The tumour is either resected completely by TURBT or partial cystectomy is offered if it is invading the detrusor muscle. Tumour stage and complete resection are most important prognostic variables. Regular follow up through cathecholamine and metabolite testing combined with radiological investigations are required to avoid recurrences.[9,10]

CONCLUSION

Paraganglioma should be considered in the differential diagnosis of urinary bladder mass. They commonly present with painless hematuria with or without evidence of cathecholamine excess. High index of suspicion, searching for the characteristic histological features and supportive immunohistochemistry may prevent the misdiagnosis and change the therapy and prognosis.

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