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Case Report with Literature Review

Paraganglioma of the Paravesicle Region –A Case Report and Review of Literature

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Abstract
The generic term paraganglioma is applied to tumours arising from paraganglia regardless of the location. The only exception is the tumours of the adrenal medulla which is known as pheochromocytoma. [1] *The tumours can be found practically every site in which paraganglia are located. The most commonly seen locations include: the carotid body, jugular foramen, middle ear, aorticopulmonary region, posterior mediastinum and abdominal para aortic region.*
Extra-adrenal paragangliomas are neoplasms arising from cells of neural crest origin anywhere along the distribution of the sympathoadrenal neuroendocrine system. Nearly 85% are intra-abdominal, 12% are intrathoracic, and 3% are cervical. [2]
This report describes a 66-year-old male presenting with difficulty into micturition with increased frequency and decreased flow. MRI showed a well-defined paravesicular soft tissue mass measuring 33x35mm in the lateral aspect of the left seminal vesicle. The complete biochemical work-up and haematological investigations were within normal limits. The patient underwent surgical exploration with complete excision of the right seminal vesicle. Gross examination revealed a well-defined yellow brown tumour with a rim of seminal vesicle. Microscopy revealed characteristic Zellballen pattern of arrangement of the tumour, with neoplastic cells having abundant granular cytoplasm. The cells uniformly expressed synaptophysin and chromogranin. S100 positivity was noted in the sustentacular cells and tumour cells. Ki67 index was less than 2%.
The patient is on follow-up and is healthy till date.
Keywords: *seminal vesicle, paraganglioma, paravesicle.*

Introduction

Extra-adrenal paragangliomas is a tumour arising from the neural crest cells or organs, with the organ of Zuckerkandl being the most frequent site. The other sites been anywhere along the sympathetic chain. They are rarely encountered in routine practise. To the best of our knowledge, there have been three reported cases of primary seminal vesicle paragangliomas in the medical literature, ours being the fourth. We hereby present this case to stress on the rarity and the importance to diagnose accurately with timely intervention.

Materials and Methods

A 66 year old male patient with unremarkable past medical history and surgical history, presented with urgency and difficulty in micturition with decreased flow. The vitals were within normal limits.Biochemical parameters, including routine hematologic assessment were unremarkable. Serum and urine biochemical markers were within normal limits.

Magnetic resonance imaging of pelvis showed an enhancing soft tissue mass arising from the seminal vesicle measuring 35x 33mm, which showed heterogenous post contrast enhancement.

With a pre-operative diagnosis of leiomyoma, the patient underwent surgical exploration and laproscopic excision of the left seminal vesicle and Vas deferens.

On gross examination the seminal vesicle and the mass in-total measured 4 x 3 x 2.5 cm, and attached vas deferens measuring 3 cm. On cut section a well-defined, circumscribed yellow to pale brown tumour was noted measuring 3 x 3 x 2.5 cm, separate and distinct from the adjoining and unremarkable seminal vesicle.

Results

On microscopy the tumour was circumscribed and encapsulated and showed ‘Zellballen’ pattern composed of tumour nests separated by thin fibrovascular septae having cuboidal cells with central oval nucleus and small nucleoli. Occasional typical mitoses were seen. The tumour was distinct from the adjoining seminal vesicle. Our provisional primary diagnosis was an extra-adrenal paraganglioma, with a second distant possibility of a poorly differentiated metastatic carcinoma.

Immunohistochemical study showed tumour cells to be diffusely strong positive for chromogranin and synaptophysin. S100 showed positivity in sustentacular cells and tumourcells. The Ki 67 was reported to be less than 2%. There was absence of immunoreactivity for cytokeratin.

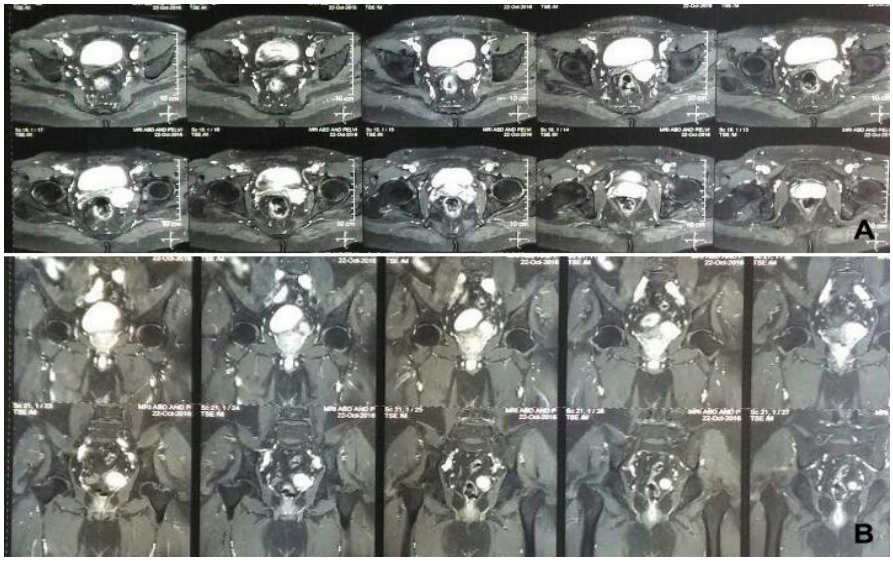

Figure 1: Magnetic resonance imaging shows coronal images with and without fat saturation and axial plane images with fat saturation showing hyperintense well defined lesion in the left seminal vesicle.

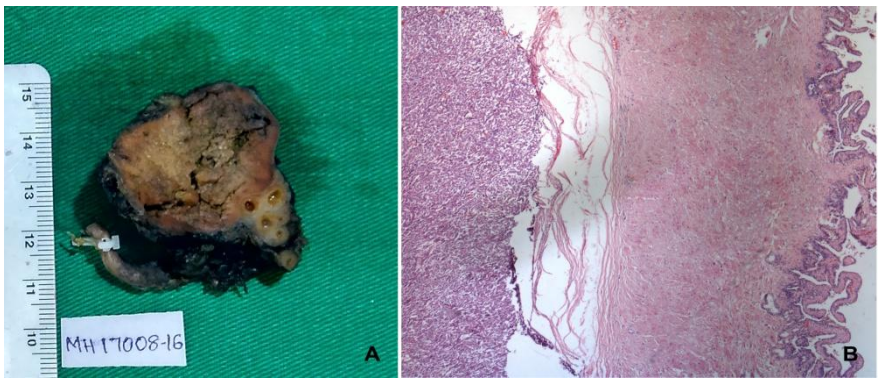

Figure 2

A- Excised mahogany brown tumor with adjacent seminal vesicle
B-Photomicrograph showing sharp demarcation of the tumor and seminal vesicle (40x)

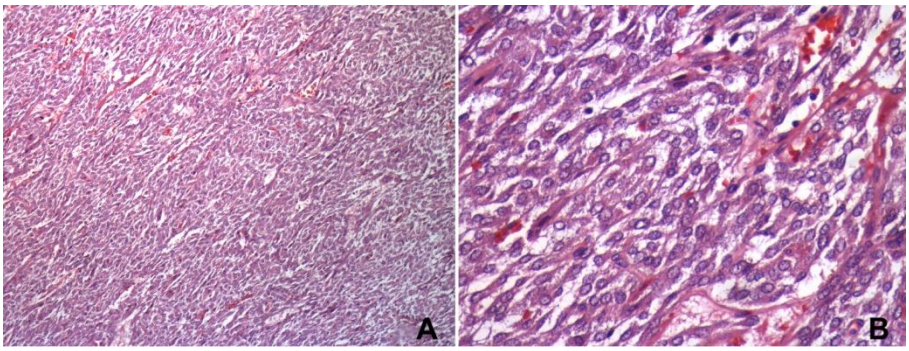

Figure 3

A- Photomicrograph showing nested pattern of arrangement of tumor(10x)
B-Photomicrograph shows elongated tumor cells with eosinophilic granular cytoplasm and round nuclei.(40x)

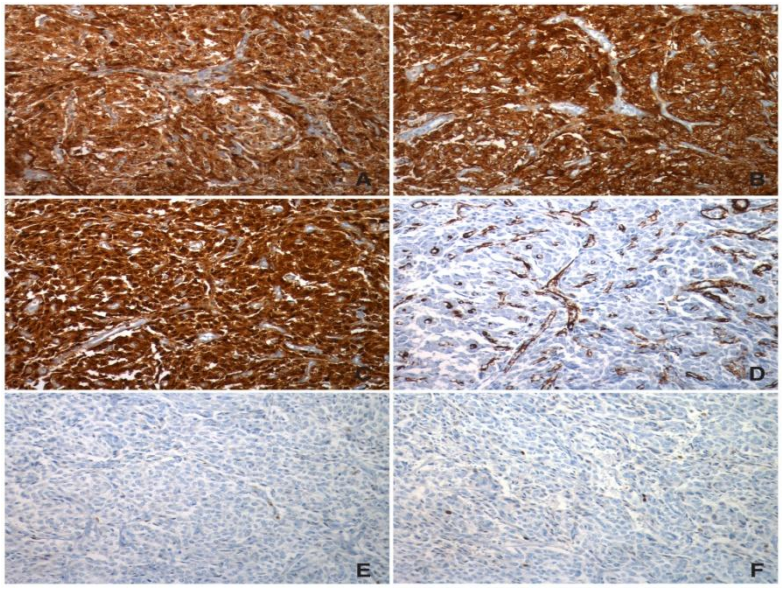

Figure 4

A- Intense cytoplasmic positivity of synaptophysin in the tumor(x100)
B-Intense cytoplasmic positivity of chromogranin in the tumor(x100)
C-Positive staining of smooth muscle actin in the tumor(x100)
D-Sustentacular cells highlighted by S100 stain(x100)
E-Tumor cells negative for cytokeratin(x100)
F-Ki67 index is very low(x100)

Discussion

Seminal vesicles (SV) are a pair of accessory glandular structures of the male reproductive system, which are extra-peritoneal in location, interposed between the bladder and the rectum. The vas deferens (VD), which are contiguous with the epididymal tail, terminate and form bilateral outpouchings. These lateral outpouchings are termed the SVs. The development of male accessory glandular tissue, SVs, prostate gland, and bulbourethral glands is stimulated by the androgens produced in the 10^{th}-12^{th} weeks of fetal life.

Primary neoplasms of the SV, are extremely rare, which usually are of epithelial or mesenchymal origin[3]. The malignant neoplasms are more common than benign. The reported benign tumors are cystadenomas, fibromas, schwannomas, and paragangliomas . The most common malignant neoplasm is adenocarcinoma[4]. The other malignant tumours such as sarcomas and seminomas have been reported in the literature[3]. Metastasis to the SV is most commonly secondary to carcinomas of the urogenital system[4]

Primary paraganglioma of the seminal vesicle are extremely rare, with only 4 reported cases in English literature.

The first case was reported in by Alvarenga et al (2012) an elderly male presented with arterial hypertension and a past history of chromophobe RCC diagnosed 12 months prior. This case was a classic example of 4 functional paraganglioma with return of BP within normal limits post-surgical excision. Another case reported by Chang Lui et al (2016) also showed arterial hypertension and elevated serum and urinary catecholamines. The BP and biochemical parameters returned to normal values following surgical excision. Another case reported was by Alharbi and Al-Ghamdi (2013) in which the patient was incidentally detected following imaging for an acute abdomen due to appendicitis.

Comparison with other reported cases

Study	Patient characteristics	Symptoms	Treatment	Follow-up
Alvarenga et al(2012)	61 years,arterial hypertension, withpast history of Chromophobe RCC (1 yr ago)	Incidental	Surgical excision	Healthy at 14 months follow-up (blood pressure under control)
Alharbi and Al-Ghamdi (2013)	26 years, unremarkable past medical and surgical history	Patient presented with acute appendicitis ; incidentally detected seminal vesicle neoplasm	Surgical excision	Healthy at 12 months follow-up with CT imaging
Chang Lui et al (2016)	41 years, family history of hypertension	Complaints of chest distress of 2 years duration. Diagnosed of hypertension. Elevated urinary VMA and blood catecholamine was confirmed.	Surgical excision	Healthy at 3 months follow-up. Postoperative BP within normal limits.
Tosev et al(2016)	36 years	Intermittent hypertensive derailments	Surgical excision-Robotic assisted method	Healthy till date
Our study(2017)	66 years	Urgency and difficulty in micturition	Surgical excision	Healthy till date

The most common location for paragangliomas are abdominal, followed by intrathoracic and cervical, however in the genitourinary tract, biliary bladder is the most common site for paraganglioma (79.2%), followed by the Ureter (12.7%), pelvis (4.9%), and ureter (3.2%).[5, 6]

The histogenesis is unknown, speculation has it that it arises from paraganglion nests that occur secondary to dysgenesis during embryogenesis, which is the postulated hypothesis of paragangliomas arising in spermatic cord. As the histogenesis of spermatic cord and seminal vesicle

is from the wolffian duct, it can be explained with similar histogenesis.[7,8]

Paragangliomas that are hormonally active with excess catecholamine secretion are considered functional, such tumours are usually uncommon in the head and neck region with a greater predilection for the thorax and abdomen.[9]

The commonest clinical presentations related to catecholamine excess include headache, palpitations and sweating[10]. The cardiovascular effects can be sudden, particularly heart attack, cerebral haemorrhage, malignant hypertension that can be life threatening. The non-functional tumours classically present as incidentalomas, that present during evaluation of patients with unrelated symptoms and or an enlarging palpable mass/pain related to local growth of the tumour. [11,12]

Paraganglioma may occur sporadically or in association with hereditary syndromes. The classical familial syndromes is associated are multiple endocrine neoplasia type 2 (RET mutations), von Hippel Lindau disease (VHL mutations), hereditary PGL/pheochromocytoma syndromes (SDHx mutations) and rarely neurofibromatosis type 1 (NF1 mutations).[13]

Conclusion

The challenge lies in distinguishing benign from malignant paragangliomas. The only accepted differentiating point is the presence of metastatic deposits at non-chromaffin sites.[14] Molecular markers have been reported as markers of malignancy in pheochromocytomas.[15,16] These include heat shock protein 90, human telomerase reverse transcriptase, vascular endothelial growth factor, vascular endothelial growth factor receptor hypoxia inducible factor 2-α, cyclooxygenase 2, tenascin C, N cadherin- and secretogranin II-derived peptide EM66. The practical application of these markers will require more studies.

The treatment modalities include catecholamine blocking, surgery, radiation therapy and surgery being the primary modality of treatment for localized paraganglioma. Palliative therapy is opted for unresectable or metastatic tumours.[17]

Declaration of Conflicting Interests

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