Case Report

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Extra-adrenal Mesenteric Pigmented Paraganglioma: A Rare Case Report

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ABSTRACT

Paragangliomas are rare neoplasms that arise from neural crest cells of the autonomous system. It has been estimated that 5% to 10% of paragangliomas occur in extra-adrenal sites, which can extend from the upper cervical region to the pelvis, parallel to the autonomic nervous system. This distribution corresponds to the embryologic development of the paraganglia from neural crest cells. Rarely, extra-adrenal paragangliomas can also occur outside this distribution. Herein, we present a case of a 70-year-old female with history of abdominal pain, in whom an abdominal mass was identified during ultrasonography. CT scan shows solid cystic mass arising from the right side of the pelvic cavity. Exploration laparotomy reveal well-circumscribed, encapsulated, ovoid and blackish mesenteric mass. After thorough microscopic and immunohistochemistry examination, the features were that of Pigmented Paraganglioma. This case report expands the morphologic spectrum of extra-adrenal paragangliomas and emphasizes the need to consider these tumors in the differential diagnosis of pigmented neoplasms.

Keywords: *Paraganglioma, Pigmented, Mesenteric, Extra-Adrenal, Melanin*

Introduction

Paraganglioma is the generic term used for nonepithelial tumours of paraganglion cells irrespective of anatomical site. Extra-adrenal paragangliomas, which account for 5-10% of these tumours, may arise from the parasympathetic or the sympathetic paraganglia.[1] The extra-adrenal paraganglioma occurs mainly in retroperitoneum but also in posterior thorax and neck. Other extra-adrenal locations include urinary bladder, gall bladder, kidney, prostate gland, prostatic urethra, pancreas, uterus, and spermatic cord.[2] The combined estimated annual incidence of pheochromocytoma/ paraganglioma is around 0.8 per 100,000 person years, and there are approximately 500 to 1600 cases in the United States per year. Mesenteric paragangliomas are exceedingly rare and only 12 cases of mesenteric paragangliomas have been published.[3] Although the microscopic features of paragangliomas are somewhat similar, regardless of the anatomic site, some differences have been noted according to the location of the tumour. [4] Occasionally melanin, neuromelanin, or lipofuscin pigment are also observed in adrenal or extra-adrenal paragangliomas.[5][6] Although the presence of melanin pigment is relatively common in adrenal gland paragangliomas but rare in extra-adrenal.[7] Pigmented paragangliomas are very rare and only a few cases have been reported. Here we are presenting a case of pigmented paraganglioma in mesenteric region.

Case Report

A 70-year-old, post-menopausal female having lower abdominal pain for 2 months, presented to a tertiary care center. On clinical examination, a mass was felt on the hypogastric and right lumbar region. Ultrasonography and CT scan showed approx. 12x10x8 cm3 sized large solid cystic lesion with solid component showing heterogenous post-contrast enhancement noted arising from a pelvic cavity on the right side and with its craniocaudal extent being L3 to L4 vertebra. Peritoneal deposit in sigmoid mesocolon was also seen. There was no evidence of lymph node involvement or liver metastasis. Routine laboratory examinations were within normal limits, including the serum tumour marker CA-125. As no clinical or imaging data suggested a paraganglioma, preoperative screening for catecholamines or metabolites was not performed. On exploration laparotomy, a large cystic mass was present in peritoneal cavity which arose from the mesenteric root, stalk had vascular communication with mesentery, the stalk was tied and cystic mesenteric mass was resected. Her vital signs were noted to be stable and consistent intraoperatively and postoperatively. The resected specimen was received in a histopathology laboratory and fixed in a 10% neutral formalin solution and processed routinely.

On gross examination, a mass was solid, cystic, well-circumscribed, encapsulated, ovoid and blackish in colour, measures 11x 7x 5.5 cm3 in size. (Fig.1) Multiple sections were routinely processed and stained with hematoxylin and eosin(H&E).

Microscopic examination revealed tumour cells predominantly arranged in diffuse pattern, at places forming vague nests separated by highly vascularized fibrous septa. (Fig.2) Cells showed mild to moderate pleomorphism. Cells were round/oval in shape, having round/oval nuclei, finely granular chromatin with variable amount of eosinophilic cytoplasm. (Fig.3) Intranuclear pseudo-inclusion and occasional multinucleated giant cells were seen. Extracellular melanin like pigment and areas of hemorrhage also seen. (Fig.4) Tumour was limited by capsule and mitosis and necrosis was not seen.

Immunohistochemistry was performed, tumour cells were immunoreactive for chromogranin, synaptophysin, NSE, Vimentin and immunonegative for HMB-45, CK, LCA, SMA, EMA, Inhibin, Desmin. (Fig.5, 6, 7, 8, 9)

Afterthoroughhistopathologicalandimmunohistochemistry examination, the diagnosis of Pigmented Paraganglioma was given.

Discussion

Paragangliomas are non-epithelial tumour originating from neural crest derived paraganglion cells situated in

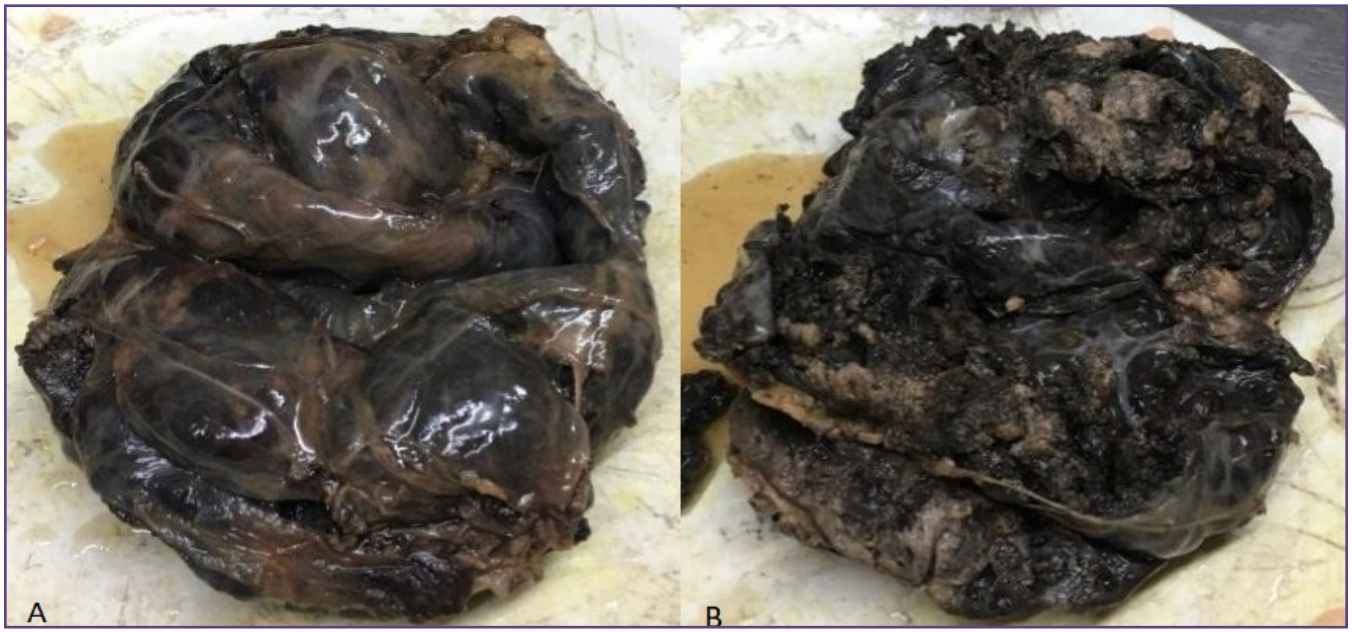


Fig. 1: A, B. (A) External Surface, (B) Cut surface. Grossly, mass was solid, cystic, well circumscribed, encapsulated, ovoid and blackish in colour.

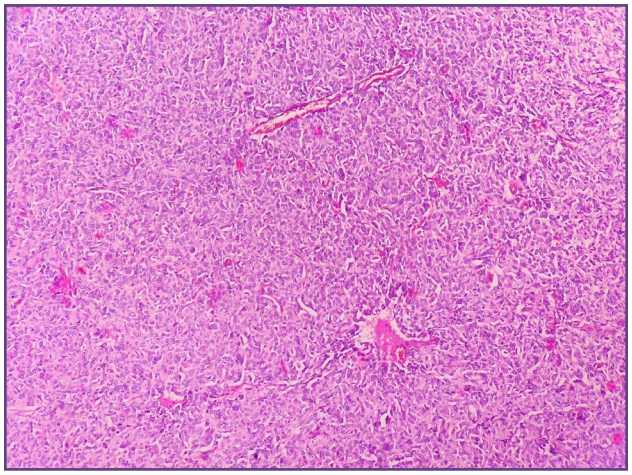


Fig. 2: Tumour cells arranged in diffuse pattern and at places forming vague nests separated by vascularized fibrous septa. (H&E, 10X).

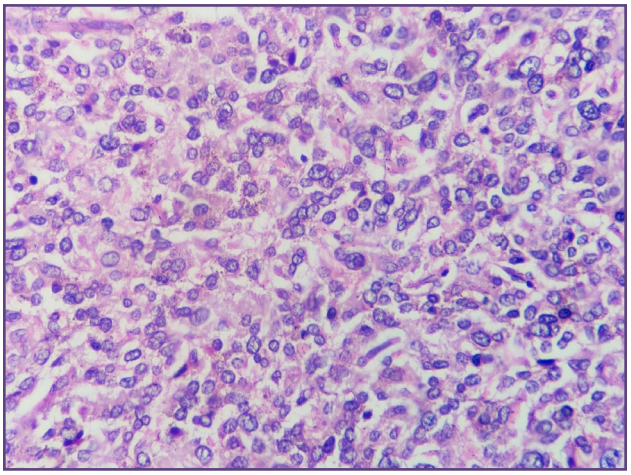


Fig. 3: Tumour cells were round/oval in shape, having round/oval nuclei, finely granular chromatin with variable amount of eosinophilic cytoplasm. (H&E, 40X)

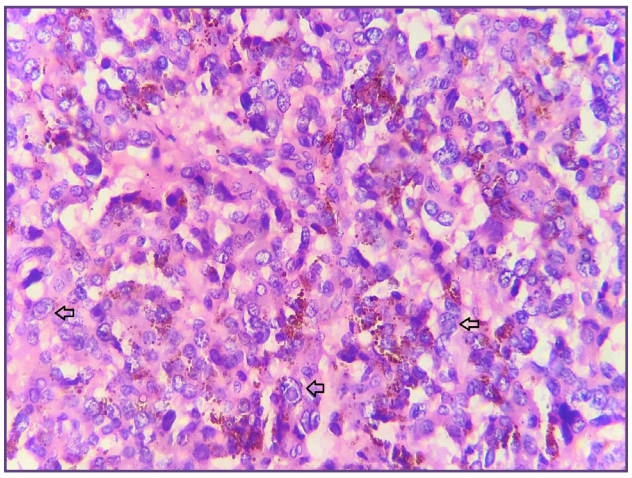


Fig. 4: Extracellular melanin like pigment and Intranuclear pseudo-inclusion (<---) were also seen. (H&E, 40X).

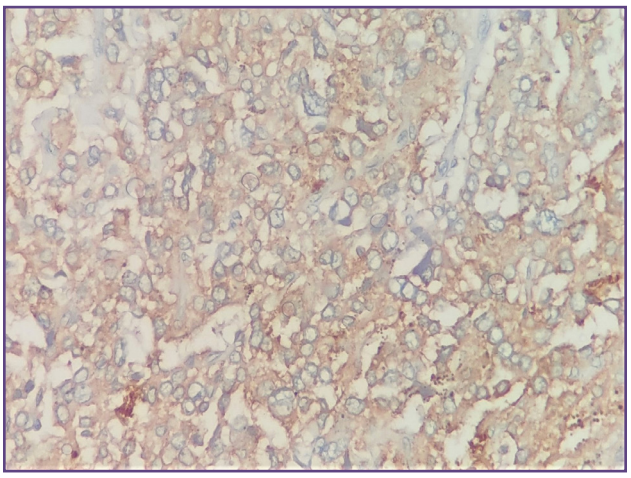


Fig. 5: Immunohistochemical staining for synaptophysin showed cytoplasmic positivity. (IHC, 40X).

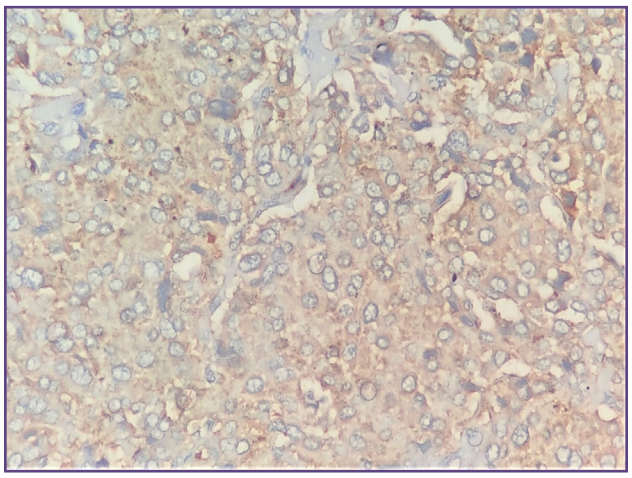


Fig. 6: Immunohistochemical staining for chromogranin showed cytoplasmic positivity. (IHC, 40X).

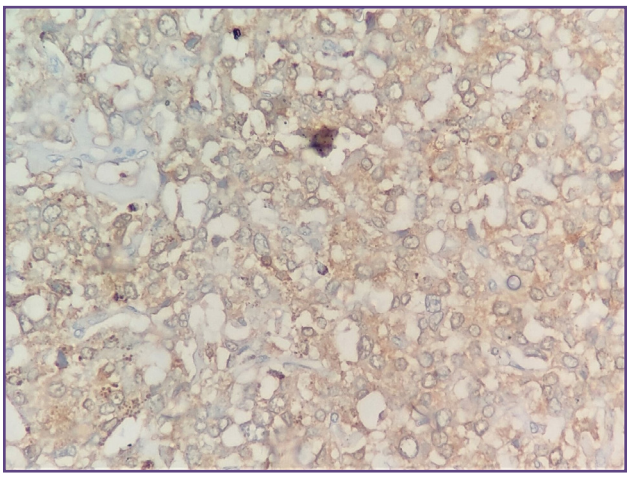


Fig.7: Immunohistochemistry for NSE showed cytoplasmic positivity. (IHC, 40X).

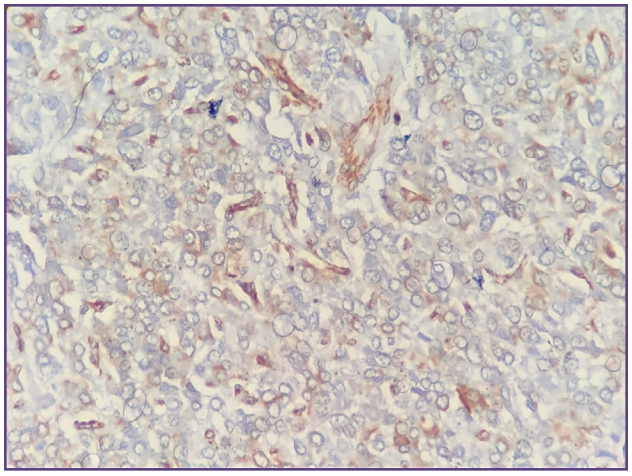
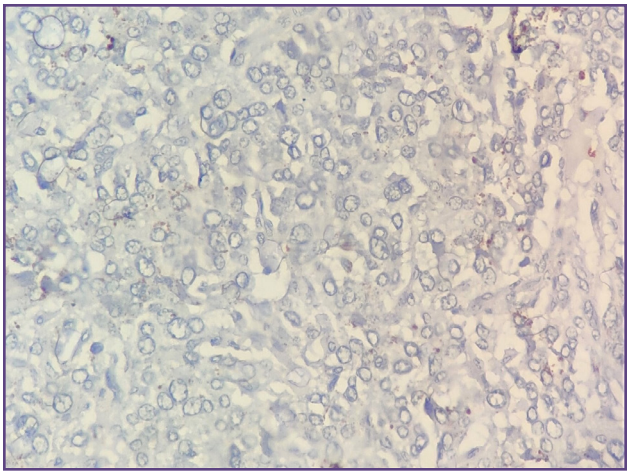
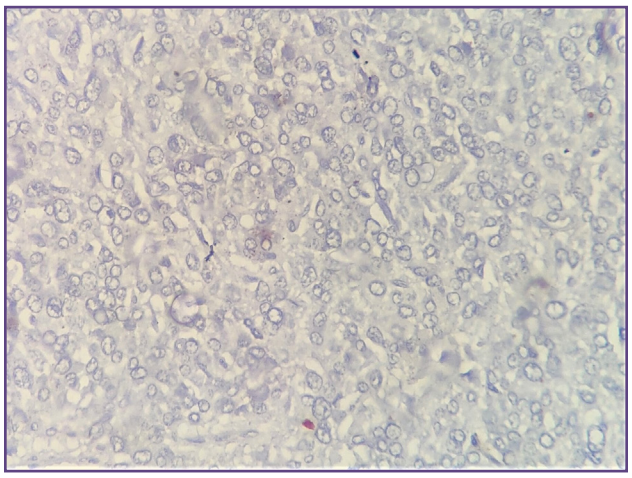


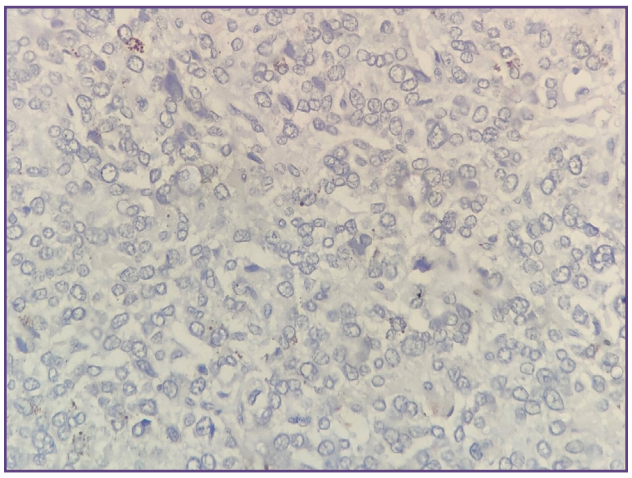
Fig. 8: Immunohistochemistry for vimentin showed immunopositivity. (IHC, 40X).



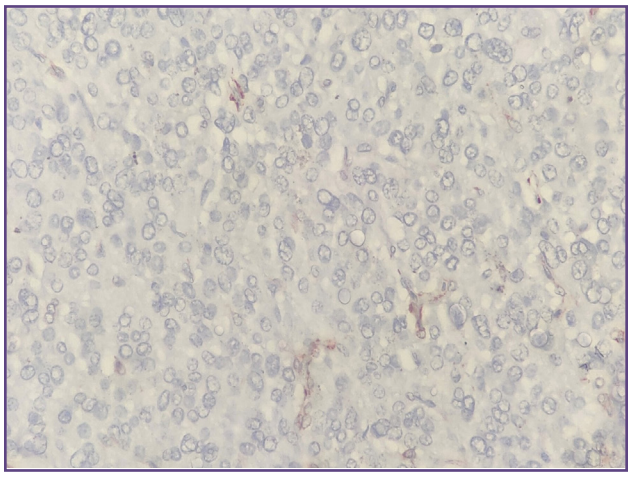
A. HMB-45



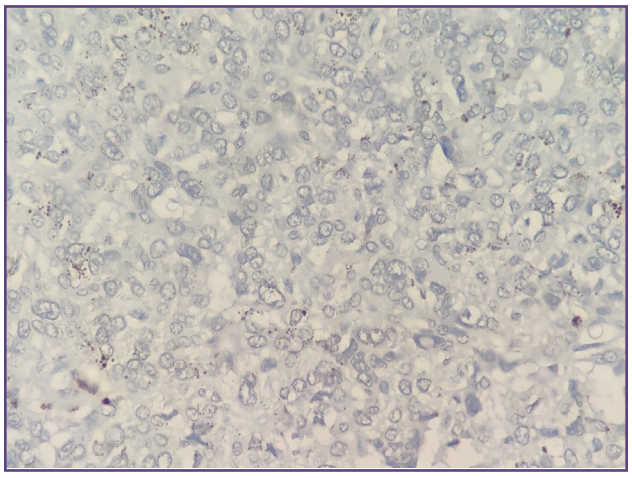
B. CK



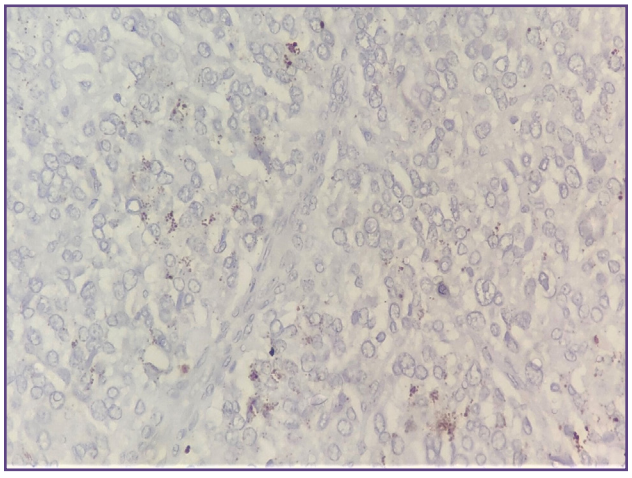
C. LCA



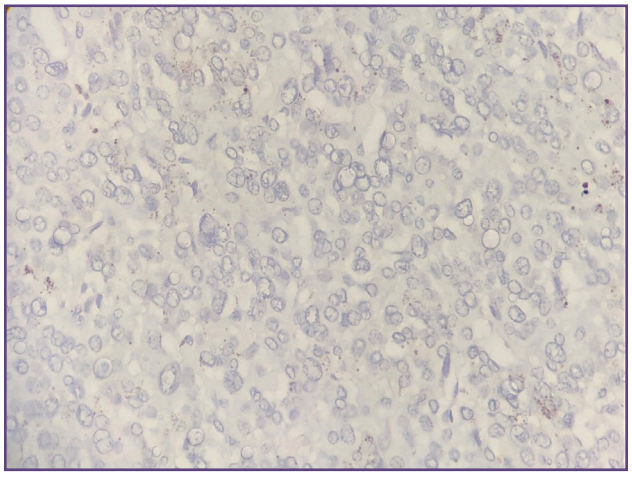
D. SMA



E. EMA



F. Inhibin



G. Desmin

Fig. 9: Immunohistochemistry was immunonegative for HMB-45 (A), CK (B), LCA (C), SMA (D), EMA (E), Inhibin (F), Desmin (G). (IHC, 40X).

the region of the autonomic nervous system ganglia and accompanying nerves. The paraganglion system can be divided into the adrenal medulla and the extra-adrenal.[8] Neoplasms derived from paraganglia of the adrenal medulla are known as pheochromocytoma while derived from extra-adrenal paraganglionic tissue are known as paragangliomas.[9] The extra-adrenal paraganglion system can be further subdivided into the parasympathetic and sympathetic paraganglia. The parasympathetic paraganglia are primarily located in the head and neck, which include the carotid body, jugulo-tympanicum, vagus nerve and larynx and are less frequently located in the thorax and pelvis. The sympathetic paraganglia are primarily distributed along the prevertebral and paravertebral sympathetic chains and the sympathetic nerve fibers innervating the retroperitoneum, thorax and pelvis.[10][11] Mesenteric origin of this tumour is very rare. The largest concentration of paraganglionic tissue present at a level extending from either the root of the inferior mesenteric artery or the renal artery to the aortic bifurcation, known as the organ(s) of Zuckerkandl. Mesenteric origin of these tumours theoretically arises from this region.[9]

Paragangliomas can occur at any age, with the highest incidence among individuals aged 40-50 years and approximately equal sex distribution. Compared with adult cases, pediatric pheochromocytomas and paragangliomas are more frequently familial, multifocal, and malignant. Familial paragangliomas show an autosomal dominant inheritance. Paragangliomas have a hereditary association in 10-50% of cases and also been associated with multiple endocrine neoplasia 2, von Hippel-Lidau disease, Carney triad and neurofibromatosis type 1; consequently, genetic testing should be considered for all patients diagnosed with paragangliomas. The risk of metastasis in paragangliomas overall is estimated to be 10-20%, the risk in extra-adrenal sympathetic paraganglioma is 2.5-50% depending on genotype.[12]

Extra-adrenal paragangliomas synthesize catecholamine, and most signs and symptoms are caused by excess catecholamine production and release. Patients with sympathetic paragangliomas usually have elevated norepinephrine only, or norepinephrine and dopamine, but not elevated epinephrine, as it is in the adrenal medulla.[8] However, most of the patients presented with mass effect symptoms or an incidental imaging finding; only 20% had documented catecholamine hypersecretion. In patients with catecholamine hypersecretion, most tumours were localized to the abdomen and pelvis.[13] We did not measures the level of catecholamine in our patient preoperatively, as it was incidental finding but the patient remained stable during and after the operation.

However, non-functional paragangliomas usually present with a palpable mass with or without abdominal pain, or even as incidental radiological findings. There are no specific radiological features for paragangliomas, and their CT and MRI scans features may overlap with other tumours. Further functional imaging such as I-meta-iodobenzylguanidine scintigraphy, 18F-fluoro-DOPA, 8F-fluorodeoxyglucose (18F-FDG/PET) or 68 Ga-DOTATATE PET/CT is considered essential during the primary investigation for metastatic disease in high risk patients based on their genetic profile.[14]

Microscopically, most common architectural pattern in pheochromocytomas and extra-adrenal paragangliomas is an anastomosing cell cord or trabecular arrangement, discrete, organoid (Zellballen) pattern and occasionally, solid or diffuse growth pattern or even a spindle cell component. The zellballen pattern is composed of two cell types: chief cells, which have abundant pale cytoplasm and hyperchromatic nuclei, and sustentacular cells, which are slender, spindle-shaped, and peripherally located around the nests. There is a prominent vascular network separating the tumour nests. Tumour cells have relatively abundant cytoplasm that is lightly acidophilic and finely granular. There may be marked pleomorphism and nuclear pseudoinclusion but mitosis are usually rare. Haemorrhage within the tumour can separate clusters of tumour cells and give a pseudopapillary or pseudo-glandular pattern.[2][8]

An unusual feature of this case was the presence of significant amounts of pigment. Based on histochemical staining or electron microscopy, pigments have been classified as neuromelanin, true melanin or lipofuscin. In addition, hemosiderin was also seen in some of tumour cells. It seems most likely that the iron deposition arose from prior haemorrhage within the tumour.[15]

Because benign and malignant paragangliomas have the same histological appearance, the distinction between benign and malignant is difficult. All pheochromocytomas and paragangliomas have metastatic potential. It can be analysed by histological pattern, cellularity, comedo necrosis, vascular or capsular invasion, Ki-67 labelling index and catecholamine type.[8][16]

Due to lack of specific morphological features like zellballan pattern and extensive melanin pigment we carefully approach the diagnosis. Most common differential diagnosis in our case was malignant melanoma. However, characteristic histological features and immunohistochemistry markers help to arrive diagnosis. Paragangliomas are comprised of chief cells and sustentacular cells that have a characteristic immunohistochemical profile. Chief cells are positive for chromogranin and synaptophysin, while sustentacular

cells are positive for S-100. Malignant melanomas show characteristic histological features, cellular pleomorphism and increased mitotic activity. It also shows positivity for HMB-45 and S-100. The second differential was a neuroendocrine tumour which was excluded by morphological features and negative for cytokeratin.

The treatment of choice for paraganglioma is surgical resection; most tumours are benign and can be excised totally, while chemotherapy and radiotherapy have both been proven ineffective. If the tumour is catecholamine secreting, the chronic and acute effects of excess circulating catecholamines should be reversed prior to the operation.[13]

Conclusion

In conclusion, pigmented paraganglioma is a very rare neoplasm. We have described a pigmented paraganglioma originating from the mesentery and expands the morphologic spectrum of these unusual tumours. This case highlights the wide distribution of these tumours and the importance of separating them from other more aggressive tumours such as malignant melanoma.

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Competing Interests

None declared

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