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PARAGANGLIOMA OF GALLBLADDER : A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Paragangliomas are rare endocrine tumours of neural crest origin. They occur along the paraganglia's pathway extending from the skull base to the pelvic floo. The common location of these neoplasms is the head and neck especially, carotid body, jugular foramen and along the course of the vagus nerve. Others locations can be seen included chest, mediastinum, abdomen retroperitoneum. The diagnosis is based on by histology andimmunocytochemistry. Primary gallbladder paragangliomas is extremely rare and only a small number of cases have been described. We report a case of a 66-year-old Moroccan woman with a paraganglioma of gallbladder found aincidentally during surgical removal of the gallbladder.

KEYWORDS: Paragangliomas, endocrine tumours, histopathological, immunohistochemical, gallblader.

INTRODUCTION

Paraganglioma is a unique neuroendocrine neoplasm, usually encapsulated and benign, arising in specialized neural crest cells associated with segmental or collateral autonomic ganglia (paraganglia).[1] It is rare extra-adrenal neoplasm that can associated with sympathetic or parasympathetic system. This tumour can occur in a variety of tissues, but location in gallblader is exceptional and a few case report have been published. The aim of this study is to discuss the clinical, histological, immunohistochemical, therapeutic features as well as the differential diagnosis of a paraganglioma of gallblader and compare them with literature data.

CASE PRESENTATION

We report the case of 61-year-old patient with no specific pathological history. She was consulted for a right upper quadrant abdominal pain evolving for 6 months. It often occur after a meal, particularly a large or fatty one, associated with nausea. The initial physical examination objectived obstructive jaundice and results of laboratory tests were unremarkable. Abdominal ultrasonography showed multiple gallstones**.** A abdominal pelvic computed tomographic scan was performed and shows a gallbladder distension in combination of a localised wall thickening and multiple cholelithiasis responsable of compression of an extrahepatic biliary duct. The IRM bilary was in favor of The Mirizzi syndrome responsible of dilatation of extrahepatic ducts which gradually taper to a normal common bile duct. with intrahepatic biliary duct dilatation. The cholecystectomy was performed. The pathological examination reported that macroscopically, the gallbladder dimensions were 6.2x2.5x1cm. She was totally settled by a circular mass, characterized by well circumscribed contours, firm consistancy with Haemorrhagic degeneration. There were many stones with a diameter of 1-2millimeters. Microscopically, the tumour was organoid 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. The mitotic activity was very low. There was no vascular or lymphatic invasion and the surgical resection limit was healthy.

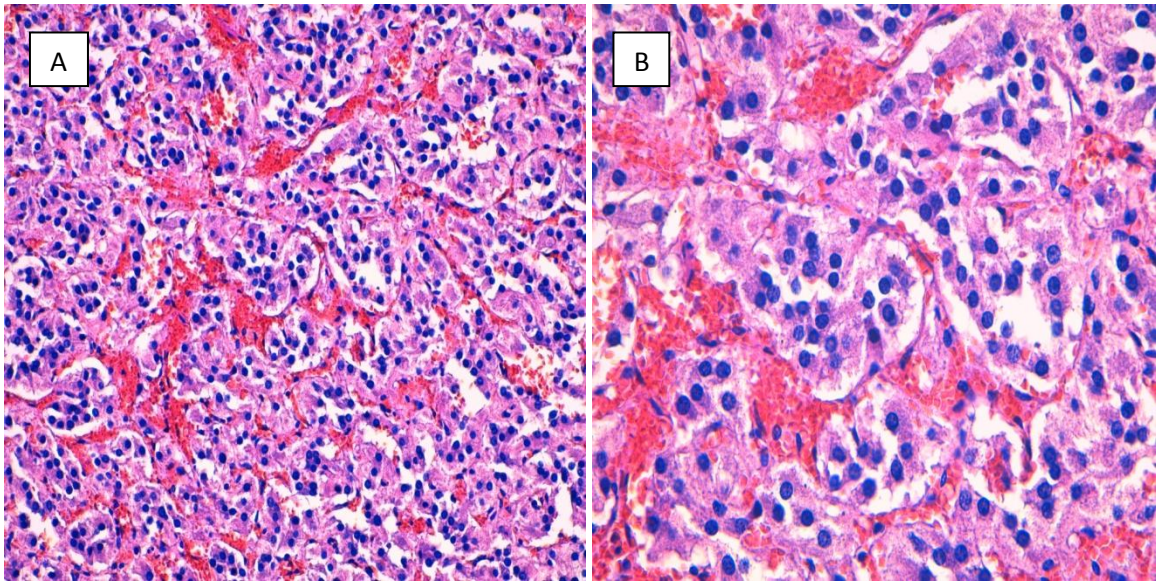

Fig. A: Organoid proliferation arranged in nests and lobules with prominent vascular network x10.
Fig. B: Presence of two cell types: Chief cells ans sustentacular cells x 20.

The chief cells showed expression of synaptophysin, chromogranin A, CD56 and were negative for cytokeratin. The sustentacular cells were immunoreactive for S100 protein. The KI-67 was estimated to 2%. Thus, the diagnosis paraganglioma of gallbladder was retained.

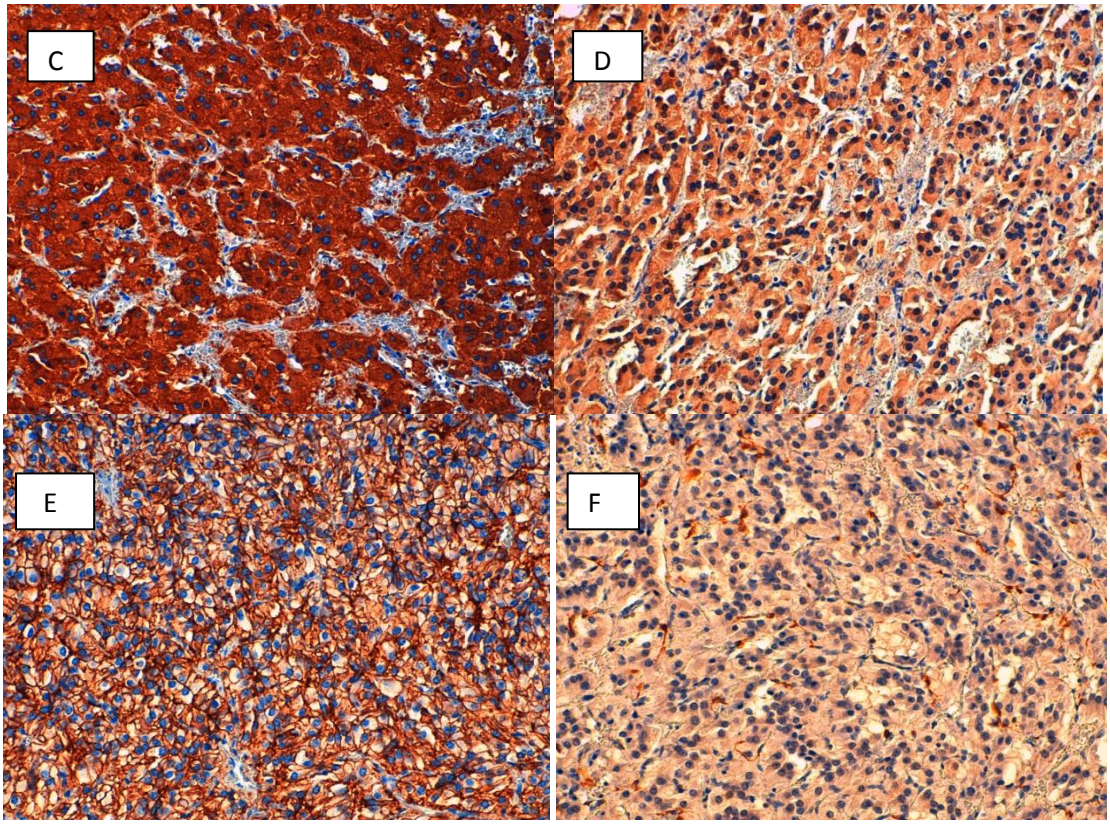

Fig C : Chief cells showing proeminent immunostaining for Synaptophysin X 20.
Fig D : Chief cells showing proeminent immunostaining for chromogranin A X 20.
Fig E : Chief cells showing proeminent immunostaining for CD56 X 20.
Fig F : Sustentacular cells were immunoreactive for S100 protein X 20.

DISCUSSION

Paragangliomas are non-epithelial tumours originating from neural crest-derived paraganglion cells situated in the region of the autonomic nervous system ganglia and accompanying nerves. There were usually benign but a malignant transformation can be seen in about 10% of cases.[2] The paraganglion system can be divided into the adrenal medulla and the extraadrenal paraganglion system. The latter can be further subdivided into the parasympathetic and sympathetic paraganglia.Head and neck paragangliomas arising from extra-adrenal paraganglia distributed along the parasympathetic nerves in the head and neck. These neuroendocrine neoplasms are named according to their anatomical sites of origin, which include the carotid body, jugulotympanicum (middle ear), vagus nerve, and larynx. There are generally non-functioning.[3,4] Sympathetic paraganglioma arising from extra-adrenal paraganglia distributed along the prevertebral and paravertebral sympathetic chains and the sympathetic nerve fibres innervating the retropentoneum, thorax, and pelvis. Location in the gallblader remains rare and only 9 cases have been reported in the literature. The average patient age is fourth and fifth decade with no gender predominance.[5] The majority of this neoplasm were non functional which explains the absence of specific functional signs of catecholamine hypersecretion, such as episodic or sustained hypertension, palpitations, diaphoresis, and headache. In general, the clinical features depends of location. In gallbladder location, the signs and symptoms was related to gallblader disorder. Several radiologic imaging techniques are currently available to evaluate extraadrenal paragangliomas of the body. Among these imaging methods, we dispose of CT and MRI, and functional imaging techniques with metaiodobenzylguanidine (MIBG) scintigraphy. Angiography is not currently used for diagnosis alone, but it is performed preoperatively for surgical planning and often for preoperative embolization.[6] The diagnosis is based on by histology and immunocytochemistry. Macroscopically, this tumours are firm, rubbery, delicately encapsulated, and well circumscribed, ranging from 2.0-6.0 cm in size. Haemorrhagic or cystic degeneration may be seen in larger tumours.[7] The tumours may firmly adhere to and occasionally invade adjacent tissues such as vessels and nerves. Microscopically, these tumors is well-differentiated resembling normal paraganglia. They are composed of chief (type I) cells arranged in nests or lobules (called Zellballen) surrounded by an inconspicuous single layer of sustentacular (type II) cells. The Zellballen are also surrounded by a delicate capillary network and a delicate supporting reticulin fibre network that may undergo sclerosis. The uniform round or polygonal chief cells have central, round to oval nuclei with finely stippled chromatin and inconspicuous nucleoli. Degenerative nuclear pleomorphism is typically mild. The cytoplasm is usually eosinophilic and finely granular. In some cases, it is amphophilic or clear.[8] Sustentacular cells are spindle-shaped; encompassing the lobules, their long processes are often so attenuated that they are not visible on routine light microscopy and can be detected only on immunostains for S100 protein. Consistent with their neuroendocrine differentiation, the chief cells of paragangliomas are immunoreactive for the commonly used neuroendocrine markers chromogranin-A, synaptophysin and CD56 and are usually negative for cytokeratin.[9] The KI-67 proliferation index is usually low. Paraganglioma can mimic neuroendocrine carcinoma or melanoma. Current thinking is that all paragangliomas have some metastatic potential. The most common sites of metastasis are the local lymph nodes, bone, liver, and lung. Metastases sometimes develop years or decades after resection of a primary tumour.[10] The treatment of paraganglioma usually involves a radical surgery. Radiotherapy provides short-term symptomatic relief and tumour growth retardation, but the long-term consequences are unclear. Recent literature suggests a molecular basis for the development of some paragangliomas. To date, autosomal dominant germline mutations of > 10 genes have been described in association with these tumours: VHL (associated with von Hippel-Lindau disease); RET (associated with multiple endocrine neoplasia type 2); NF1 (associated with neurofibromatosis type 1); genes coding for the subunits of the succinate dehydrogenase enzyme - SDHD (associated with inherited paraganglioma- 1), SDHA and SDHAF2 (associated with paraganglioma-2), SDHC (associated with paraganglioma-3), and SDHB (associated with paraganglioma-4) - which forms part of mitochondrial complex II.[11] In general, a single benign paraganglioma may not be indicative of any genetic predisposition, whereas multiple paragangliomas or an association of a paraganglioma with another neoplasia should prompt investigation of a possible genetic syndrome. In our case, there was no family history of genetic syndrome.

CONCLUSION

Paraganglioma of the gallbladder is rare. Positive diagnosis is based on histopathological and immunohistochemical approaches. The treatment of choice in this location is surgical resection. A careful clinical and genetic investigation most be carried out to search for an associated genetic syndrome.

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