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Case Report Open Access

Bi-Focal Retroperitoneal Paraganglioma in a Young Patient: A Case Report and Review of the Literature

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Abstract

Extra-adrenal paraganglioma of the retroperitoneum are rare neuroendocrine tumors arising from specialized neural crest cells, intimately associated with sympathetic nervous tissue and distributed along the aorta. Here we present a case of multiple extra-adrenal retroperitoneal paraganglioma in a 16-year-old boy. The clinical presentation, imaging characteristics, and surgical pathologic findings were reported. A comprehensive review of the medical literature concerning multiple extra-adrenal paraganglioma in the pediatric and adult population is also discussed.

Keywords: Paraganglioma; Retroperitoneum

Introduction

Extra-adrenal retroperitoneal paraganglioma are rare neuroendocrine tumors arising from specialized neural crest cells, intimately associated with sympathetic nervous tissue and distributed along the aorta [1]. They are rarely encountered in day to day surgical practice and affect mainly adults in the fourth or fifth decade of life [2]. The presentation of sporadic multiple extra-adrenal retroperitoneal paraganglioma within the pediatric population has rarely been reported. This rare presentation at a younger age causes considerable difficulty in diagnosis, treatment and long term prognosis. Here we report the clinical presentation, imaging characteristics, and surgical pathologic findings of a bifocal sporadic extra-adrenal retroperitoneal paraganglioma and review the related literature.

Case Report

A 16-year-old male was referred to our urology clinic for two retroperitoneal masses found on abdominal computed tomography scan. The patient complains of headache and sweating during physical exercises. He had no significant past surgical or medical history. Physical examination revealed high blood hypertension (140/80 mm Hg) with no other abnormalities. The heart rate was 72/min and he had a normal body mass index. Urinalysis, hematology and blood chemistry were all within normal range. The urinary concentration of norepinephrine was 1124 micrograms/24h (normal range: 15-80 micrograms/24h). To characterize these masses, a multiplanar MRI was performed. MRI confirmed the origin of the masses along each side of the aorta. The upper mass was located adjacent to the left side of the aorta at the level of the superior mesenteric artery just above the adrenal gland. The lower mass was found adjacent to the right side of the aorta at the level of the inferior mesenteric artery just beneath the lower pole of the right kidney (Figure 1). The upper lesion was well circumscribed, measured 25x26x30 mm and had a low intensity on T1 weighted images compared to the liver parenchyma and hyper intensity on T2 weighted images. After gadolinium injection, it showed a homogeneous early enhancement. The lower mass, also well circumscribed, measured 45×35×50 mm, had isointensity on T1 weighted images and intermediate intensity on T2 weighted images and showed a central area of low attenuation after gadolinium injection (Figure 1).

MIBG (metaiodobenzylguanidine) scintiscan labeled with ^{123}I showed intense fixation only of the upper left lesion.

The clinical presentation, biological and radiological findings confirmed the diagnosis of synchronous bifocal "alternate interior" extra-adrenal retroperitoneal paraganglioma with a functional secreting upper lesion and non-secreting lower lesion.

The patient subsequently underwent an open surgical resection of these two lesions after adequate preparation with alpha adrenergic blockade. The approach was performed through a midline incision and the two lesions removed without any peroperative complication. Postoperative recovery was uneventful with removal of the drain and the catheter on day 1. Patient was discharged 5 days after surgery. Gross pathology demonstrated well circumscribed encapsulated meaty to light tan appearance tumors measuring 28×30×40 mm for the upper lesion and 55×40×50 mm for the lower lesion. The cut surface of these tumors showed integrated amicula and abundant blood supply. Note multiple feeding vessels within tumor on cut section. The margins were negative (Figure 2). The microscopic findings can be seen in Figure 3

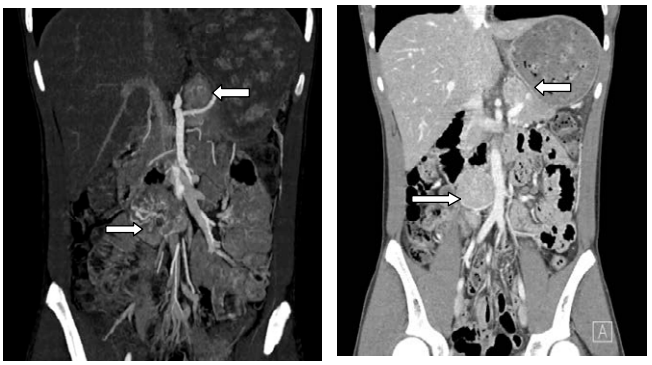

Figure 1: Coronal abdominal MRI showing well circumscribed upper and lower masses along each side of the aorta measuring 25x26x30 mm and 45x35x50 mm, respectively (arrows). The lower mass shows inner central hemorrhage and necrosis. The two masses show obvious intensification after injection of contrast medium.

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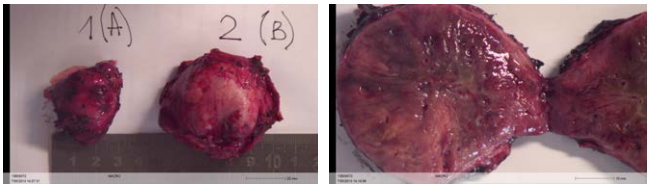

Figure 2: Gross pathology demonstrated a-) well circumscribed encapsulated meaty to light tan appearance tumors measuring 28x30x40 mm for the upper lesion and 55x40x50 mm for the lower lesion b-) the cut surface of these tumors showed multiple feeding.

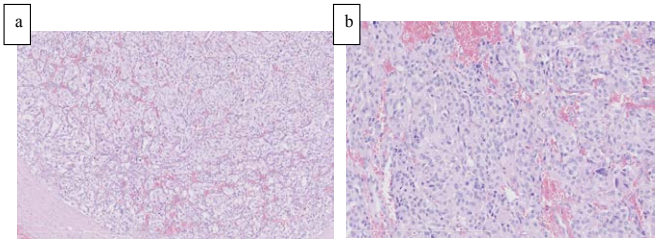

Figure 3: Microscopic findings: a-) the tumors presented a thick fibrous capsule and an arrangement of neoplastic chief cells surrounded by highly vascularized fibrous septa. b-) The nuclei were slightly ovoid surrounded by an eosinophilic cytoplasm (H and E, ×400).

and were the primary source of our diagnostic. The tumors presented a thick fibrous capsule and an arrangement of neoplastic chief cells surrounded by highly vascularized fibrous septa. (H and E, ×400) The tumor cells were same in size. The nuclei were slightly ovoid with an eosinophilic cytoplasm. There was no capsular or vascular invasion. The immune histochemical analysis shows a positive reaction for CgA, Syn, NSE and S-100.

Six weeks after the operation, the patient was doing well with resolution of all his symptoms, normal blood pressure without medication and the 24h urinary study of norepinephrine was within normal limit.

Discussion

The general designation "paraganglioma" applies to tumors arising from paraganglia regardless of location. The only exception is the paraganglioma of the adrenal medulla, which is universally known as pheochromocytoma. By extension, paraganglioma located outside the adrenal gland have been designated as extra-adrenal paraganglioma. Although these tumors can be found in any place from the cervical region to the pelvic cavity the majority are commonly seen in specific locations: the carotid body, jugular foramen, middle ear, aortic pulmonary region, posterior mediastinum, and abdominal paraaortic region including Zuckerkandl's body (like in our case). Paraganglioma can be derived from either parasympathetic or sympathetic neural origin, and it is only the latter that have capacity to secrete catecholamines [3]. Catecholamine secreting paraganglioma are most commonly found in the retroperitoneum. The non-secreting paraganglioma typically arise in the head and neck region, as well as the chest.

They are extremely rare in routine practice, accounting for 0.012% of all neoplasm [4]. The incidence of extra-adrenal retroperitoneal paraganglioma is even lower (2 per million of habitants) and affect mainly adults in the fourth or fifth decade of life, with no sex predilection [4]. The presentation of sporadic synchronous bifocal extra-adrenal retroperitoneal paraganglioma within the pediatric population has rarely been reported. This rare presentation at a younger age causes considerable difficulty in diagnosis, treatment and long term prognosis.

The clinical presentation in children varies from incidental findings on imaging till the classic triad of headache, palpitation and diaphoresis. The average age at presentation is 11 years, with a male to female ratio of 2:1 [5,6]. Weight loss, anxiety, and high blood pressure are also common findings [7]. Children more often present with signs and symptoms related to hypertension compared with adults. Sustained hypertension is found in more than 60-90% of pediatric paraganglioma cases whereas it is reported in only 50% of adult cases [8,9].

Pheochromocytoma and paraganglioma are estimated to be prevalent in approximately 1% of hypertensive pediatric patient and should be considered after exclusion of more common causes [6,10]. The intermittent complain of these adrenergic symptoms and the presence of normal blood pressure in 5% of cases (tumors secreting predominantly dopamine) render the diagnosis difficult in children [7].

The state-of-the-art diagnosis and localization of paraganglioma is based on measurement of plasma metanephrines and methoxytyramine and functional imaging studies [11]. However, normal plasma and urinary catecholamine concentrations are seen in nonsecreting paraganglioma even in the case of tumors of considerable size [12]. However, unlike head and neck paraganglioma, most extra-adrenal retroperitoneal paraganglioma are secreting tumors that's why hypertension and urinary catecholamine are usually elevated in extra-adrenal retroperitoneal paraganglioma. These tumors are functional in more than half of such cases in the pediatric population. Magnetic Resonance Imaging (MRI) is more sensitive than CT in detecting extra-adrenal tumors and should be preferred over CT in young patient. Although MRI has excellent sensitivity (90–100%) [13], its ability to specify a paraganglioma from other abdominal lesions can be insufficient. Metaiodo Benzyl Guanidine (MIBG) scintiscan is used to differentiate between functioning and nonfunctioning paraganglioma; however, its sensitivity is quite low when compared with that of CT and MRI. MIBG scintiscan could be reserved for children with small tumors (<1 cm) of extra-adrenal origin. Because they are known for their uptake of MIBG, neuroblastomas should be specifically considered in the differential diagnosis [14].

The final diagnosis is based on histological findings but there are no definitive arguments for malignancy. Local tissue invasion or pathological evidence of nuclear pleomorphism or mitotic activity does not necessarily imply malignancy. Distant metastasis and lymph nodes are the only reliable criteria for confirming malignancy. It has been reported that 10% to 40% of extra-adrenal paraganglioma are malignant in children [15].

The management of pediatric patients is similar to adults. Once the correct diagnosis is acquired, surgical treatment should be carry out after using alpha-adrenergic blockade for 2-4 weeks in order to prevent and treat a syndrome of possible intra-operative catecholamine release [16]. Minimal invasive approach should be favoured over open transabdominal route in children. Laparoscopic and robotic assisted laparoscopic removal of single lesion has been described but should be performed by experienced surgeon [17].

Extraadrenal paraganglioma represent 15-20% of the cases of pheochromocytoma. In about 15% multiple localizations were described essentially in head and neck paraganglioma and mainly in adults. To the best of our knowledge, there were no sporadic cases of multiple synchronous retroperitoneal paraganglioma described in children. These tumors are most often single sporadic lesion affecting adults.

Up to 20% of extra-adrenal paraganglioma are diagnosed in children and increasingly, some cases are diagnosed in children with genetic syndrome associated with paraganglioma [18]. Genetic counselling should be undertaken in all cases (refused by the patient in our case) especially in the case of multiple lesions, because up to 35% of multiple lesions are associated with a more complex hereditary syndrome [19]. The classical familial syndromes associated with paraganglioma are multiple endocrine neoplasia type 2 (RET mutations), von Hippel Lindau disease (VHL mutations), neurofibromatosis type 1 (NF1 mutations), and hereditary paraganglioma/pheochromocytoma syndromes (Succinate Dehydrogenase type A, B, C and D mutations) [19]. Although most pediatric paraganglioma are benign, these tumors can occasionally metastasize, a condition for which no curative treatment exists. Succinate Dehydrogenase B mutations mainly predispose to extra-adrenal retroperitoneal paraganglioma in children with a high malignant potential. The genetic mutation is often predictive of tumor activity, aggressiveness, and anatomic location. While overall malignancy rates are approximately 10%, the likelihood of malignant behaviour correlates fairly well with the patient's genotype.

Although extra-adrenal retroperitoneal paraganglioma are rarely diagnosed during childhood, the urologic surgeon should be able to diagnose and screen for such tumors, particularly in the context of multiple lesion or a known genetic predisposition. Optimal care of these children includes a multidisciplinary team approach at centres experienced in the evaluation and treatment of this uncommon neoplasm. Prolonged follow-up is necessary to rule out malignancy [20].

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