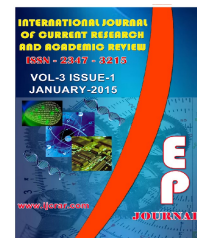




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Two Cases of Unusual Presentation of Asymptomatic Retroperitoneal Paraganglioma

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KEYWORDS

Paragangliomas, neuroendocrine cells, norepinephrine and nor-metanephrine

A B S T R A C T

Paragangliomas are rare tumors which arise from neuroendocrine cells and extra-adrenal paragangliomas account for only 10 to 15% of all paragangliomas and may present incidentally as a symptomless mass. Typical triad of fluctuating hypertension, headache, and sweating if not present makes preoperative diagnosis difficult. Definitive diagnosis is usually made with histologic findings and surgery is the treatment of choice. We report two cases of paraganglioma in male patients who presented with retroperitoneal tumor without any symptoms. In the present case, tumor size >10 cm was a high risk depicting malignancy.

Introduction

Paragangliomas are rare tumors arising from the neural crest tissue that develops into sympathetic and parasympathetic paraganglia throughout the body. Paraganglioma of adrenal medulla is known as pheochromocytoma while paragangliomas located outside of adrenal gland are broadly classified as extra-adrenal paragangliomas. Paragangliomas are also further divided into functioning and nonfunctioning based on their ability to secrete hormones. Functional paragangliomas have shown to secrete norepinephrine and nor-metanephrine resulting in clinical manifestations such as fluctuating or episodic hypertension,

headache, and sweating. On the contrary, nonfunctioning paragangliomas are mostly asymptomatic and found incidentally as a mass. When nonfunctioning paraganglioma gets enlarged it presents as abdominal pain secondary to compression of surrounding organs.

Case report

My patients 55 yrs and 53 year-old male with no significant past medical history was brought to the hospital for evaluation for abdominal lump which was felt by the patient.

Physical examination was within normal limits. Patients' blood work was unremarkable including negative cardiac biomarkers. Ultrasound of RUQ was performed which showed mass located adjacent to gallbladder without any gallstone or common bile duct (CBD) dilation. Preliminary findings of fine-needle aspirates done during the EUS were consistent with low grade neoplasm, possibly vascular in origin with carcinoid tumor as a differential.

CT scan of abdomen and pelvis with contrast was performed to further evaluate the mass which showed in the two patients well-defined 12 and 10 cm enhancing retroperitoneal mass. It also showed several small cystic foci within the mass.

Open laparotomy through right paramedian incision was done. Preoperatively, 12X5.7 cm and 10X 3.8 cm mass was found in the two patients within the C-loop just inferior to stomach, medial to duodenum, and on top of pancreas without involvement of any structure. Pathology revealed that tumor was comprised of a relatively uniform population of cells arranged in the clusters and these clusters were surrounded by reticulin fibrosis. This appearance is known as Zellballen arrangement, which is typical of paraganglioma (Figure 1). The tumor was highly vascular in nature as highlighted by the CD34 immunostain. Tumor cells were negative for epithelial AE1/AE3 cytokeratin and strongly immunoreactive for neuroendocrine markers CD56, chromogranin A, and synaptophysin. Positron emission tomography (PET) scan was performed for staging purpose which did not show any evidence of malignancy. Because of very close surgical margins of tumor cells, patient also received adjuvant radiotherapy. As there was no metastatic disease, chemotherapy was not provided.

Patient is currently symptom free after 6-month follow up and is closely followed by physicians.

Discussion

Paragangliomas can develop anywhere along the midline of the retroperitoneum. The exact incidence of retroperitoneal paragangliomas is unknown, although males are typically affected more frequently than females. In addition, most patients are diagnosed between 30 and 45 years of age (Andersen *et al.*, 2011). Clinically, patients with a retroperitoneal paraganglioma often present with back pain or a palpable mass (Moslemi *et al.*, 2012). Only a subset of paragangliomas is clinically functional and often exhibit signs and symptoms consistent with active secretion of catecholamine, including headaches, sweating, palpitation, and hypertension (Andersen *et al.*, 2011). The present cases represent a rare symptomless normotensive malignant paraganglioma that developed in relatively aged men.

Conventional treatment for paragangliomas typically involves complete surgical excision, while surgical debulking is considered a mainstay of palliative therapy for malignant paragangliomas. In some cases, complete excision is difficult due to the highly vascular nature of paragangliomas and their proximity to major blood vessels.

Although paragangliomas are usually benign, 30–50% of all retroperitoneal paragangliomas are malignant. No definitive tests are currently available to differentiate between benign and malignant paragangliomas. Malignancy can often only be confirmed by detecting local invasion of surrounding structures upon examination at the time of resection, or by detecting the

presence of metastases (Arrabal-Polo *et al.*, 2010). Furthermore, although histological and immunohistochemical findings do not permit a definitive diagnosis of malignancy, several factors have been associated with malignancy. These include a tumor weight ≥ 80 g, high concentration of dopamine proximal to the tumor, tumor size ≥ 5 cm, presence of confluent tumor necrosis, and a younger patient age. In the present case, tumor size >10 cm was a high risk depicting malignancy.

Extra-adrenal paragangliomas account for 10 to 15% of all adult paragangliomas with an incidence rate of 2–8 cases per million people/year (Arrabal-Polo *et al.*, 2010). Age of onset is between 30 and 45 years with some literature suggesting male predominance, while other literatures suggest equal incidence between men and women (Arrabal-Polo *et al.*, 2010). Genetic mutation within the succinate dehydrogenase B unit (SDHB) and succinate dehydrogenase D unit (SDHD) are associated with increased risk for extra-adrenal paragangliomas. It has also been reported that incidence and prevalence of malignant paragangliomas are higher in patients with SDHB mutation (van Hulsteijn *et al.*, 2012). There is also an association between extra-adrenal paraganglioma, gastrointestinal stromal tumor (GIST), and pulmonary chondroma which is known as the Carney's triad (Lee *et al.*, 2007). Abdominal paragangliomas are mostly retroperitoneal in location, accounting for 85% of all extra adrenal paragangliomas. The most common site for retroperitoneal paragangliomas is between the origin of inferior mesenteric artery and the aortic bifurcation known as organ of Zuckerkandl. Paragangliomas arising from jugulotympanic body are called chemodectomas, whereas paragangliomas originating from the carotid body are known as carotid body tumors. Paragangliomas

located in the second part of duodenum are called gangliocytic paraganglioma (Disick and Palese, 2007). Functional paragangliomas can be diagnosed based on presentation and subsequent laboratory investigation revealing elevated catecholamines and their metabolites in the blood and urine. Nonfunctional paragangliomas are mostly found incidentally or present as a mass with symptoms of surrounding organ compression. On CT scan these tumors appear as soft-tissue masses with either homogenous enhancement or central areas of low attenuation. It appears as highly vascular structure with areas of intralesional hemorrhage and necrosis (Sangster *et al.*, 2010).

Extra-adrenal paragangliomas also have potential to be malignant, although previously reported incidence of 10% is not accurate. It has been reported in the literature that around 20% of paragangliomas could be malignant with poor survival (Andersen *et al.*, 2011). While histopathological findings are not much useful to differentiate between benign and malignant paragangliomas, extensive local invasion and distant metastasis to liver, bone, and lymph nodes have been used as indicators for malignancy (Arrabal-Polo *et al.*, 2010; Sangster *et al.*, 2010; Moslemi *et al.*, 2012).

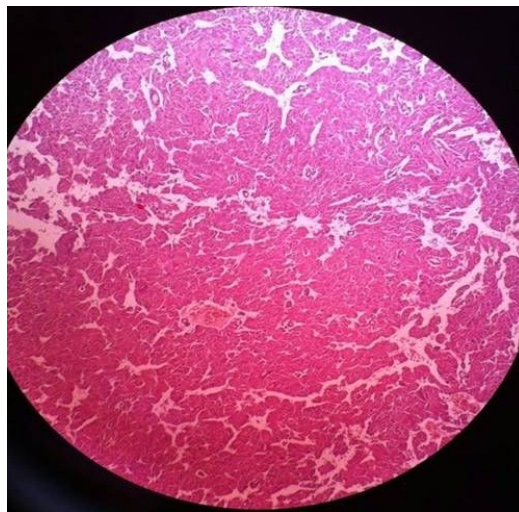
Surgery with complete removal of mass either via laparoscopy or via traditional laparotomy is the treatment of choice for retroperitoneal paragangliomas owing to its malignant potential. Patient with metastatic disease will require adjuvant radiotherapy while chemotherapy is restricted to patients not accessible for surgery and resistant to radionuclide therapy (Andersen *et al.*, 2011). Because of malignant potential and higher recurrence rate in paragangliomas, lifelong

follow up is usually recommended (Shah *et al.*, 2012).

Fig.1 Gross photograph of the paraganglioma



Fig.2 Microphotograph of the paraganglioma with typical zellballen pattern



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