

Primary retroperitoneal paraganglioma simulating pancreatic neoplasm

A. Bhagya Lakshmi¹, N. Subba Rao², P. A. Ramani³, O. Sirisha⁴

¹Professor and Head, ²Professor, ³Assistant Professor, ⁴Post-graduate Student, Department of Pathology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India

ABSTRACT

Retroperitoneal paragangliomas deriving from the neural crest cells of the sympathetic system are relatively rare. They can be either functional if they secrete the catecholamine or non-functional. If the tumor is functional, the diagnosis of paragangliomas can be made easily even before surgery. We present a case of retroperitoneal paraganglioma in a 40-year-old female diagnosed initially as pancreatic lesion on imaging techniques. However, sudden fluctuations in blood pressure levels upon manipulation of the mass were noticed intra-operatively. Then, paraganglioma was suspected, and it was confirmed as retroperitoneal paraganglioma on histopathological examination.

Key words: Abdominal pain, Retroperitoneum, Primary paraganglioma

INTRODUCTION

Paragangliomas are rare neuroendocrine tumors that arise from the extra-adrenal autonomic paraganglia, consisting mainly of neuroendocrine cells that are derived from the embryonic neural crest. Retroperitoneal paragangliomas are very rare usually occurring in middle age and are mostly benign tumors, but with increased risk of malignancy.^[1] They can present with abdominal pain, palpable mass or hypertensive episodes associated with catecholamine production. Surgical excision remains the mainstay of treatment.^[2] Here, we report a case of retroperitoneal paraganglioma, which was preoperatively mistaken for a pancreatic tumor and later discovered to be a retroperitoneal paraganglioma with histopathological diagnosis.

CASE REPORT

A 40-year-old female presented with pain lower and mid abdomen and persistent vomiting for 1 month. Pain was insidious in onset, dull in nature, not increasing in severity, and there were no aggravating or relieving factors. Vomiting were non-bilious, vomitus consisted of food material. On routine examination, she was diagnosed as having diabetes and mild hypertension. She was started on Insulin and antihypertensives. She was a known case of hypothyroidism for past 5-6 years and was on the levothyroxine supplementation. Ultrasound abdomen revealed a mass in the pancreas at the junction of body and tail, which was further confirmed by computed tomography (CT) abdomen. Routine hematological and biochemical investigations were within normal limits.

Catecholamine levels were not estimated in our case as there was no suspicion of paraganglioma. In view of the imaging findings, distal pancreatectomy was planned. Intra-operatively, a circumscribed mass was noted in the para-aortic region with its vasculature directly arising from the aorta (Figure 1a). On manipulation of the mass, there were sudden fluctuations in blood pressure levels that necessitated rapid removal of the mass. The blood pressure levels normalized after its excision. The pancreas was normal grossly. There were no adhesions or pelvic or omental deposits. The liver and adrenals were normal. Post-operative blood pressure returned to within normal limits. Post-operative recovery was uneventful. We followed up the case for 2 years and found the patient to be symptom free. Grossly, the tumor was a circumscribed mass measuring 7 cm × 5 cm × 4 cm (Figure 1b). On cut section, it was yellow to brown in color, predominantly solid with a few cystic and hemorrhagic areas (Figure 2). Specimen was thoroughly grossed, processed and stained with standard hematoxylin and eosin stain. On histopathological examination, the tumor cells were arranged in characteristic zellballen pattern with nests of tumor cells surrounded by thin fibro-vascular septa. Individual tumor cells had moderate amount of eosinophilic granular cytoplasm with round to oval nucleus with coarse chromatin and prominent nucleoli (Figure 3a and b). Occasional cytoplasmic hyaline globules were seen within the tumor cells. There were occasional mitotic figures. Spindle shaped cells were also seen within the fibro-vascular septa. Histopathological features were consistent with paraganglioma.

Address for Correspondence:

Dr. A. Bhagya Lakshmi, Department of Pathology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India. E-mail: dr.a.bhagyalaxmi@gmail.com

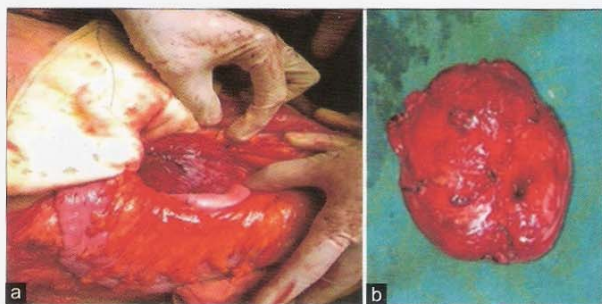


Figure 1: (a) Intra-operative photograph showing a circumscribed mass noted in the para-aortic region, (b) gross specimen showing the total mass after excision measuring 7 cm x 5 cm x 4 cm and was richly vascular



Figure 2: Cut section of the specimen with predominant yellow to brown solid areas with foci of cystic spaces

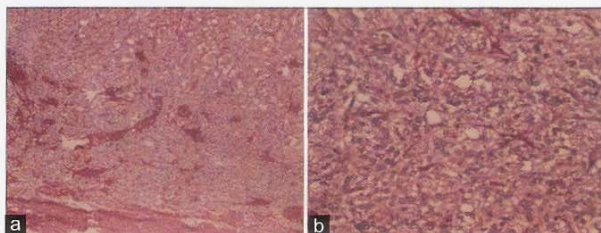


Figure 3: (a) Photomicrograph showing tumor cells arranged in characteristic Zellballen pattern with nests of tumor cells surrounded by thin fibro-vascular septa (H and E, 40), (b) Photomicrograph showing tumor cells with granular eosinophilic cytoplasm surrounded by thin fibro-vascular septa (H and E, 100)

DISCUSSION

Extra-adrenal paragangliomas can arise from those related to either the parasympathetic system or with the sympathetic system. The former are usually non-chromaffin, are concentrated in the head, neck, and mediastinum. The latter is chromaffin, predominate in the retroperitoneum along the thoraco-lumbar para-aortic region.^[3] Intra-abdominal paragangliomas account for about 70% of sympathetic paragangliomas.^[4] Approximately 10-20% of paragangliomas of the retroperitoneum are extra adrenal that lie along the

aortic axis in close association with the sympathetic chain. Most extra-adrenal paragangliomas arise from the organ of Zuckerkandl, whereas a smaller number are derived from the paraganglia lying at other points along the aortic or iliac vessels.^[5]

Retroperitoneal paragangliomas occur at a relatively earlier age than those of the head and neck. Most of the cases present in between 30 and 45 years of age, although the malignant forms may have an even younger median age. Males and females have almost equal preponderance. The two most common presenting symptoms are back pain and a palpable mass. About 10% of patients present initially with metastatic disease.^[3]

These tumors are grossly lobular, red brown, well circumscribed masses. Histologically characterized by trabecular or organoid arrangement of round to polygonal cells (Zellballen) with central nuclei and eosinophilic, faintly granular cytoplasm, extensive delicate vascular network and variable nuclear hyperchromasia and pleomorphism. Malignant retroperitoneal paragangliomas range from 30% to 50%.^[4] There are no reliable histological criteria that can predict malignancy. Aggressive behaviour has been associated with tumor necrosis, vascular invasion, and increased mitotic activity. Metastatic spread is the only reliable criterion for malignancy.^[6]

Functional paragangliomas account for 30-60% of the tumors. They secrete nor-epinephrine. Resultantly, the patients experience paroxysmal episodic hypertension, as well as the typical triad of symptoms associated with pheochromocytomas, i.e., palpitations, headache, and profuse sweating. A large proportion of non-secretory (non-functional) tumors are incidentally discovered in normotensive patients during imaging and most commonly presents as abdominal pain or mass.^[4] Our case presented with abdominal pain not responding to therapy and with mild hypertension. However, post-operative blood pressure returned to normal limits range.

Extra-adrenal paragangliomas are difficult to diagnose pre-operatively unless the lesion is functional. In the latter instance, the diagnosis can be established by measuring total urinary catecholamines, and the localization of the mass by means of angiography. Extra-adrenal paragangliomas when located in the para-aortic region may be confused with other retroperitoneal tumors, especially pancreatic tumors as seen in the present case. Scintigraphy with ¹²³I labeled meta-iodo-benzyl-guanidine (MIBG) offers superior specificity than CT and magnetic resonance imaging.^[4]

Compared to pheochromocytomas, extra adrenal paragangliomas are more aggressive and tend to metastasize more frequently which mandates a long period of follow-up. Cytogenetic studies revealed 'vhl' gene mutations in sporadic paragangliomas and succinate dehydrogenase B and succinate dehydrogenase C mutations in familial paragangliomas.^[7,8]

If a retroperitoneal paraganglioma is suspected clinically, appropriate steps to document, functional activity should be undertaken before surgery. Pre-operative premedication with β -adrenergic blocking agents is essential to prevent intraoperative hypertensive crises or tachyarrhythmia during surgical manipulation of the tumor. Adjunctive therapies including, MIBG, radiotherapy and chemotherapy can only be considered palliative. Hence, Surgery should be aimed at complete removal.^[3]

CONCLUSION

Retroperitoneal paragangliomas are rare and often misdiagnosed as pancreatic lesions especially when located close to the pancreas.

While dealing with retroperitoneal tumors, a thorough clinical evaluation with a differential diagnosis of retroperitoneal paraganglioma should be carried out especially in patients with a history of hypertension.

REFERENCES

1. Kimura N, Lam KY, Capella C, Komminoth P, De Krijger RR, Tischler AS, *et al.* Extra-adrenal sympathetic paraganglioma: Superior and inferior paraaortic. In: DeLellis R, editor. WHO Classification of Tumours Pathology and Genetics Tumours of Endocrine Organs. 3rd ed. Lyon: IARC Press; 2004. p. 164-5.
2. He J, Wang X, Zheng W, Zhao Y. Retroperitoneal paraganglioma with metastasis to the abdominal vertebra: A case report. *Diagn Pathol* 2013;8:52.
3. Weiss SW, Goldblum JR. Paraganglioma. In: Weiss SW, Goldblum JR, editors. *Enzinger and Weiss's Soft Tissue Tumors*. 5th ed. Philadelphia: Elsevier Publishers; 2008. p. 989-1015.
4. Sangster G, Do D, Previgliano C, Li B, LaFrance D, Heldmann M. Primary retroperitoneal paraganglioma simulating a pancreatic mass: A case report and review of the literature. *HPB Surg* 2010;2010:645728.
5. Rosai J. Peritoneum, retroperitoneum, and related structures. In: Rosai and Ackerman's *Surgical Pathology*. 9th ed. Edinburgh: Mosby; 2004. p. 2400.
6. Rha SE, Byun JY, Jung SE, Chun HJ, Lee HG, Lee JM. Neurogenic tumors in the abdomen: Tumor types and imaging characteristics. *Radiographics* 2003;23:29-43.
7. Srirangalingam U, Khoo B, Walker L, MacDonald F, Skelly RH, George E, *et al.* Contrasting clinical manifestations of SDHB and VHL associated chromaffin tumours. *Endocr Relat Cancer* 2009;16:515-25.
8. Neumann HP, Pawlu C, Peczkowska M, Bausch B, McWhinney SR, Muresan M, *et al.* Distinct clinical features of paraganglioma syndromes associated with SDHB and SDHD gene mutations. *JAMA* 2004;292:943-51.

Received: 02.09.2013; Revised: 08.06.2014; Accepted: 13.10.2014