Common Symptom with Rare Entity

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Citation

Dhillon HS, Gupta S. Common Symptom with Rare Entity. *Kathmandu Univ Med J.* 2025; 93(5): 106-8. (Special Issue)

ABSTRACT

Paragangliomas are extremely rare neuroendocrine neoplasms with an incidence of 2-8 per million. They mostly present as headache, hypertension, palpitations and diaphoresis. CT scan and MRI abdomen helps in the diagnosis and Positron Emission Tomography (PET) helps to rule out malignancy. Paragangliomas are diagnosed on clinical history, biochemical parameters and radiological imaging but rarely requires histopathology. Surgery is the gold standard treatment which should be performed as early as possible. Here we are reporting the case of young female patient at the age of 18 years presenting with atypical symptoms. Paragangliomas is rare with complex entity which requires a wide approach.

KEY WORDS

Metanephrines, Paraganglioma, Vanillylmandelic acid (VMA) level

INTRODUCTION

Chromaffin cell tumor are the tumor of chromaffin cells which develop from the embryonic neural crest and are commonly found in tissues such as the adrenal medulla, carotid and aortic bodies and organs of Zuckerkandl. Chromaffin cells can be divided in two groups; Pheochomocytomas located in the adrenal medulla and Paragangliomas (PGs) located in extra-adrenal chromaffin cells.[1] Only 5-10% of chromaffin cell tumor are extra-adrenal.[2] Thus, PGs are rare tumor.

Paragangliomas are sub classified into two more groups according to their distribution. The first group arises from parasympathetic ganglia and is mainly located in the skull and neck.[3] The most common extra-adrenal PGs occur as carotid bodies.[3] The second group arises from sympathetic ganglia of the thorax, abdomen and pelvis, usually in the para-aortic area. Out of these, mesenteric PGs are extremely rare.[4]

The 10% rule for Pheochromocytoma/paraganglioma is 10% malignant, 10% familial and 10% extra-adrenal. PGs represent 10% of catecholamine secreting tumors.[5] Due to its catecholamine properties, it presents as a mass with vague symptoms like a palpitation (60%), headache (50%) and diaphoresis (50%) that can lead to a paroxysmal hypertensive crisis due to increased catecholamine production. Therefore, the majority of extra-adrenal paraganglioma (75%) presents as an abdominal mass which is usually discovered incidentally.[5] Various literature review shows very few case reports of PGs.

Here we report a case of young female patient presented with the vague symptoms, later on diagnosed as a paraganglioma.

CASE REPORT

Eighteen years old unmarried female came to the Out Patient Department of Medicine with the complaint of diffuse abdominal pain and acid reflux for last 3 months (March 2025 to May 2025) which was more after eating spicy food. Patient was getting treatment on OPD basis from some local practitioner with diagnosis of gastritis and anxiety neurosis but did not get any relief. Patient and her family members were worried as the elder sister of the patient died at the age of 18 years due to hypertensive crisis. Patient was admitted in General Medicine In-Patient Department with same complaints for further evaluation. The complete general, physical and systemic examination

were normal. On routine workup of the patient, ultrasonography of whole abdomen shows well-defined heterogeneously isoechoic lesion measuring approximately 3 X 3 cms in left para-aortic area showing few tiny eccentric hypoechoic areas within it. Patient was advised for contrast CT abdomen for further work up of mass, CECT abdomen was done which showed a soft tissue mass of size 3.4 X 3.4 cms in mesenteric/preaortic area at L1-L2 level with suspicion of Paraganglioma, Gastrointestinal Stromal Tumor, Lymph node mass etc (Fig. 1).

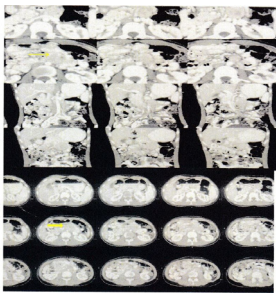

Figure 1. CECT abdomin showed a well defined enhancing soft tissue mass lesion about 3.4 cm X 3.4 cm seen at L1 to L2 level in preaortic location: s/o -? Extra-adrenal paraganglioma -? GIST -? lymph node mass

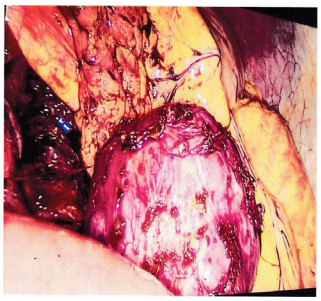

Figure 2. Intraoperative photo showing the tumor protruding from the lesser sac.

To rule out Paraganglioma, patient's 24 hr urine VMA was slightly raised. So, even after the radiological and biochemical investigations, the diagnosis could not be ascertained and excisional biopsy was planned for further evaluation and treatment. Laparoscopic excision of the mass was done (Fig. 2) which showed well defined globular mass protruding from the lesser sac. While handling the mass there was increase in blood pressure that was controlled by intravenous labetalol during surgery. The blood pressure had significantly reduced once the mass was extracted out and the sample (Fig. 3a, 3b, 3c) was sent for pathological evaluation which showed encapsulated lesion composed of cluster, nests and sheets of round to oval to polygonal chief cells separated by prominent fibro vascular stroma (Fig. 4, 5). Morphological finding was consistent with paraganglioma. Immunochemistry was found to be positive for Synaptophysin (granular cytoplasmic positivity in tumour cells) and Chromogranin (patchy cytoplasmic granular positivity in tumour cells) (Fig. 6, 7). Following Histopathology and IHC, a diagnosis of Paraganglioma was confirmed.

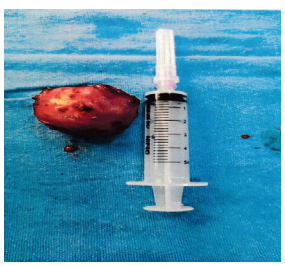

Figure 3a. Surgical specimen obtained

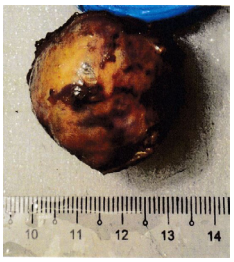

Figure 3b. Gross-Globular soft tissue piece measuring 3.5 am X 3 cm X 1.5 cm

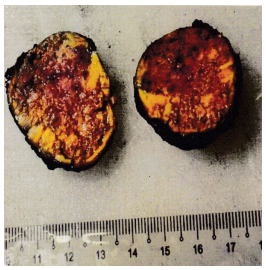

Figure 3c. Cut section friable yellowish areas

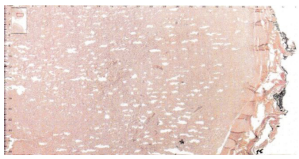

Figure 4. 2x Well encapsulated lesion composed of clusters, nests (zellballer pattern) and sheaths of round to oval to polygonal chief cells separated by prominent fibrovascular stroma.

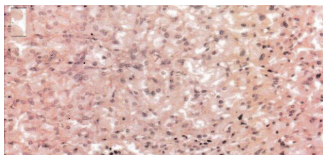

Figure 5. 4x cells are large with small round nuclei, having stippled chromatin, inconspicuous nucleoli and abundant granular eosinophilic cytoplasm with vacoulation.

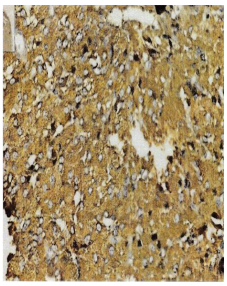

Figure 6. Chromogrannin staining showed cytoplasmic granular positivity.

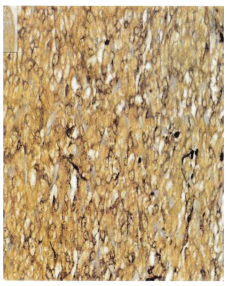

Figure 7. Strong S100 nuclear and cytoplasmic positivity.

The patient was kept under Intensive care unit care on ventilatory support due to fluctuations in blood pressure and was weaned off from ventilator support on the next day.

Following which patient recovered well and was discharged on post-operative day-4 with no complains at all. Patient is doing well on 6 months. A multigene panel that includes MAX, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127 was advised to rule out familial PGS, as she also had family medical history of PGs.

DISCUSSION

Paragangliomas cells can migrate to almost anywhere along the paravertebral and para-aortic axis from skull to pelvis. Literature search shows patient presenting with the involvement of various sites like supraglottic, retroperitoneum, duodenum, mesentery, vaginal, portocaval, para spinal, appendix, urinary bladder. The presenting symptoms of the PGs depends upon the site of involvement, functional and non-functional. The symptoms of functional paraganglioma are related to catecholamine release, including paroxysmal hypertension,

diaphoresis, headache, palpitations and tachycardia and even hypertensive crisis and the typical triad associated with Pheochomocytomas: palpitation, headache, and diaphoresis.[6] Non-functional PGs usually remains asymptomatic and diagnosed incidentally.

The present case is of a young female patient, who presented with the vague symptoms which were truly uncharacteristic for paraganglioma. PGs occur commonly in men and in the 3rd or 4th decade of life but in our case female patient presented in very early days of life with no functional symptoms.

The diagnosis of PGs can be made by clinically, biochemically and radiologically.[7] Elevated catecholamine's and their metabolites VMAs in serum and urine confirm the diagnosis.[8] But in our case, the VMAs were not so raised to give suspicion of PGs. CT and MRI scan is useful in localizing the tumor. On CT scan PGs usually appears as hyper vascular masses with areas of intralesional haemorrhages and necrosis.[9] CT scan have approximately 90% sensitivity for localization of extra-adrenal tumor, whereas on MRI scan lesion appear hyper intense on T2 weighted images and have sensitivity approximately 93–100%. Unfortunately, our case on CECT Abdomen could not confirm the diagnosis.

The definitive management of PGs is surgical resection for the localised mass, the same was in our case. Preoperative stabilization is important with fluid management, alpha blockers and beta blockers. Intraoperative hypertensive crisis is usual and can be treated with emergency anti-hypertensive drugs. Our patient was managed with the intra venous labetalol intra operatively. Successfully excision of the mass was done and histopathology and IHC confirmed the diagnosis of our case. Therefore, histopathology played very important role in the diagnosis and complete evaluation of the patient. 90% PGs are sporadic and 10-15% are hereditary. Hereditary PGs are multicentre and associated with multiple endocrine neoplasm type 2, von Hippel-Lindau disease, familial PGs and neurofibromatosis type 1. Our patient was young diagnosed at the age of 18 years with positive family history in elder sister suspicion of hereditary PGs. The patient was advised for the genetic testing which could not be done because of financial constraints and non- availability of test. Extra-adrenal PGs also have potential for malignancy. So early surgical resection of the mass and confirmation by histopathology is the cornerstone for the diagnosis and the management of the patient. Because of malignant potential and higher recurrence rate in PGs, lifelong follow-up is recommended.[10]

Paraganglioma is rare disease occur commonly in men, in the 3rd or 4th decade of life presented with specific symptoms and diagnosis can be made by clinically, biochemically and radiologically. Surgery is the mainstay treatment. Early presentation and young female sex is rare presentation along with positive family history makes it a unique case from others.

Each and every symptom, specific or non-specific should always be clinically evaluated. This case represents that even rare cases present with common symptoms which is seen in day-to-day life and hence no symptom should be overlooked. Surgical excision of the mass should be done as early as possible to diagnose the patient and to prevent the metastasis.

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