

Giant Pheochromocytoma: A Case Report and Review of the Literature

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Abstract: *Giant Pheochromocytoma are rare tumor and complete surgical resection is the only curative treatment. There are no definitive histological or cytological criteria of malignancy, as it is impossible to determine this condition in the absence of advanced local regional disease or metastases. This is a case report of 46 year old patient with giant retroperitoneal mass. The patient was a known case of hypertension. The USG-guided FNAC reported the case as- Malignant Neuroendocrine tumor-possibly pheochromocytoma/ paraganglioma. CECT reported the mass as retroperitoneal neoplasm. The VMA levels in urine were raised 3 folds. Surgery was performed and histopathological report suggested features of-Pheochromocytoma. Immunohistochemistry was performed for chromogranin A and NSE both were reported positive*

Keywords: Pheochromocytoma, paraganglioma, retroperitoneal tumor, adrenal medulla

1. Introduction

The extra-adrenal pheochromocytomas are known as paraganglioma. Pheochromocytomas are uncommon tumors of great clinical importance because they secrete catecholamines. Most pheochromocytomas are benign, and it is almost impossible to differentiate a benign from a malignant tumour only by its histological criteria. Many attempts have been made to find markers that would predict the future behaviour of a non-metastatic pheochromocytoma; these markers include immunohistochemical markers for growth capacity, angiogenesis and invasion markers (increased expression of Ki-67, p-53, VEGF, heparanase-1, Tenascin, COX-2; decreased expression of inhibin β B, S-100), different catecholamines values, necrosis, vascular and capsular invasion. However, to date, it is commonly accepted that no single feature is diagnostic of malignant pheochromocytoma without documented metastatic disease.¹

Radical surgery is the basis of therapy. Different treatment protocols have also been considered, such as chemotherapy, radiotherapy and hormone therapy, with poor results. The survival rate is unknown, due to the few cases reported.

2. Case Report

A 46-year-old male presented with complaints of dull, non radiating abdominal pain confined to right upper abdomen, left lower abdomen and left flank region since 2 months. Patient also complained of mass in abdomen involving umbilical and left flank region, gradually progressive in nature. Patient was a known case of Hypertension and was on treatment (amalong 5g) since 4 years.

The ULTRASONOGRAPHY showed mass around 10 cms in the retroperitoneal region which was displacing left kidney and stomach. Calcifications, necrosis and central collection were also seen. CECT was advised. Thyroid Function Test was done which showed normal range of T3

(1.63 nmol/L) and T4(111.7nmol/L) but raised TSH (6.33 uIU/ml) whereas normal range is 0.27 – 4.2 uIU/ml

CECT- contrast enhanced computer tomography was done of the abdomen which was reported as – Large well defined soft tissue mass measuring 21 x 12.8 cm arising from the retroperitoneum on the left side, the lesion was crossing the midline. It was having mass effect resulting in displacement of bowel loops and stomach in right side. The lesion was extending superior from left hypochondrium to left iliac region. Anteriorly it was extending upto anterior abdominal wall. There were areas of necrosis and calcification with extension. Impression- **Retroperitoneal Neoplasm**



Figure 1: Large 21 x 12.8 cm mass- **Retroperitoneal Neoplasm**

USG- guided FNAC was performed - which was reported as- Aspirate was cellular, smears studied showed haemorrhagic background with tumor cells predominantly distributed in singles and also in clusters. The cells were pleomorphic with abundant fragile vacuolated cytoplasm. Nuclei were vesicular with prominent nucleoli. The tumor cells showed peripheral endothelial cuffing with increased vasculature. Smears also showed areas of necrosis. Features suggested of –malignant neuroendocrine tumour possibly **Pheochromocytoma/ Paraganglioma** to be considered.

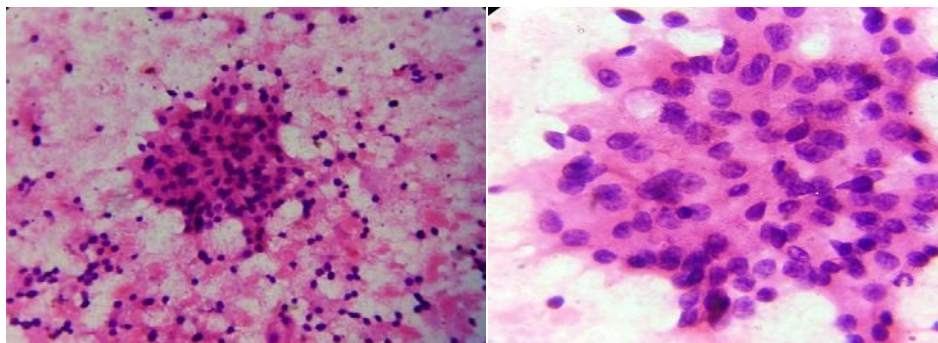


Figure 2: FNAC H&E - showed cellular aspirate, vesicular nucleus, salt and pepper chromatin and vacuolated cytoplasm

Urine was tested for VMA (vanil mandelic acid)- which revealed its increased level - **200.6mmol/24h** whereas the normal range is below 68.6 mmol/24hr. Patient underwent surgery which included – Exploratory laprotomy with

excision of retroperitoneal mass and splenectomy. The surgery was uneventful.



Histopathology- GROSS appearance was Specimen consisted of single globular mass measuring 26 cm in diameter.External-surface was congested, soft to firm in consistency. Cut- surface – drained haemorrhagic and necrotic material and showed predominantly solid areas with large areas of necrosis with focal areas of haemorrhage ; mucoid areas were also seen.

Histopathology Microscopic appearance – Multiple sections studied from mass showed tumor cells arranged in solid pattern and well-defined nests separated by delicate

fibrovascular stroma. These tumor cells were polygonal with moderate amount of granular eosinophilic cytoplasm. The nuclei were pleomorphic, round, hyperchromatic with coarse chromatin. Intracytoplasmic hyaline globules were present in some of the cells. Many mitotic figures and bizarre cells along with multinucleated giant cells were also seen. Large areas of haemorrhage and necrosis were also seen. Focal areas of spindling with cytoplasmic vacuolation was also seen.Features suggestive of - **Pheochromocytoma**

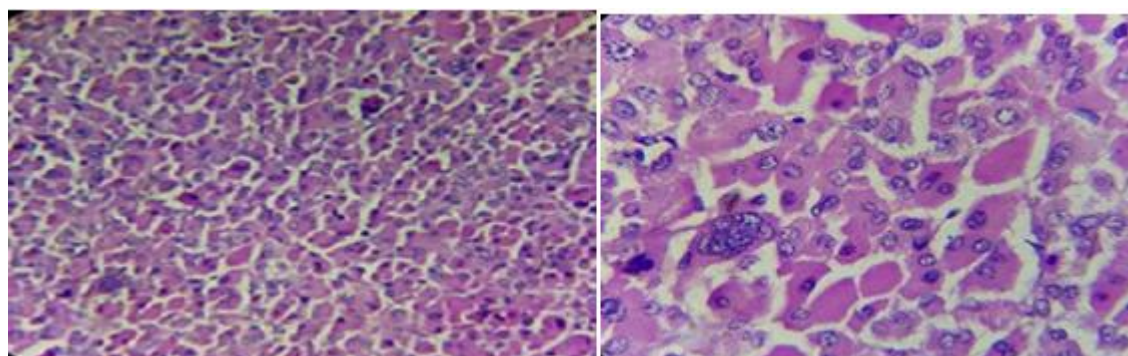


Figure- Histopathology microscopy- plump, irregular tumor cells with pink granular cytoplasm (due to high content of catecholamine-containing granules).Also many mitotic figures and multinucleated giant cells seen.

Immunohistochemistry- showed positivity for Chromogranin A and NSE

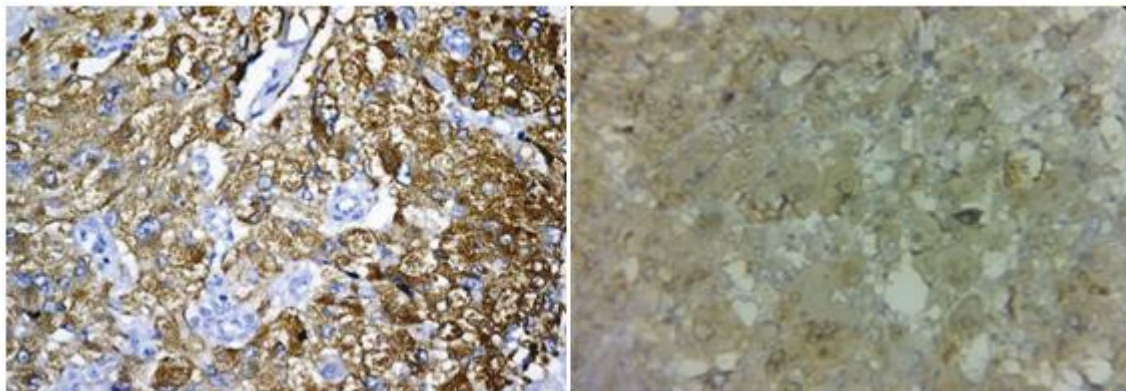


Figure: a) shows positivity for chromogranin A and b) shows positivity for NSE

3. Discussion

Pheochromocytoma is an infrequent tumour, originating from the adrenal medulla and sympathoadrenal neuroendocrine system chromaffin cells. They produce and secrete catecholamines; the triad of headache, sweating and palpitations in patients with hypertension is diagnostic, with a 94% specificity and 91% sensitivity.²

Preoperative diagnosis is usually made by the presence of clinical signs and the determination of catecholamines and their metabolites in blood and urine. Recent studies show a higher sensitivity for the determination of normetanephrine and platelet norepinephrine in 24-hour urine.³

Pheochromocytomas are traditionally known by “rule of 10” : 10% extra-adrenal, 10% bilateral (probably higher maybe upto 50%), 10% malignant (probably higher), traditional 10% familial is now been modified as 25% which harbours germline mutation. HIF-1alpha is the key oncogenic driver of pheochromocytoma Metastases is usually to lymph nodes, bone (ribs, spine), liver and lung; occasionally to brain, diaphragm, ileum, kidney, pancreas, peritoneum, pleura, spleen and stomach.

Computed tomography scan and magnetic resonance imaging (MRI) are the image techniques initially used in its localization, with a sensitivity between 75% and 100%,⁴ but a low specificity. In extra-adrenal pheochromocytoma, metastatic and recurrent pheochromocytoma MRI has a higher sensitivity than a CT scan. The 131I methaiodinebenzilguanidin (131-I-MIBG) gam-magrophy, despite its low image quality and definition, has a 83.5% sensitivity and, in combination with platelet normetanephrin, it reaches complete (100%) sensitivity.^{3,4} A PET scan has a better image resolution and, depending on the tracer (18-fluoro-dihydroxyphenylalanine), its sensitivity could reach 100%.⁵ Between 8% and 12.5% of pheochromocytomas are malignant,⁶ with a higher incidence of malignancy in the extra-adrenal location (from 29% to 40%). Preoperative diagnosis of malignancy is impossible in the absence of metastasis or local/regional invasion.

There are studies that try to define variables to determine malignant behaviour, such as the tumour size. According to Sturgeon and colleagues, sizes greater than 6 cm could be a predictor of malignancy.⁷ However, other authors disagree, such as Wilhelm and colleagues.⁸ There are few published

cases of pheochromocytomas larger than 20 cm; the biggest pheochromocytoma, with a size of 29 × 21 × 12 cm, was presented by Basso and colleagues.⁹

Currently, malignancy is defined by the existence of metastasis, local recurrence or invasion of adjacent structures. Histological diagnosis of malignancy might be determined by the proliferative activity and the presence of capsular and vascular invasion, although immunochemical techniques, such as such as expression levels of telomerase, are needed.⁶ These histological features compose the pheochromocytoma adrenal scaled score (PASS), designed by Thompson in 2002 to determine the prognosis of pheochromocytoma.⁶

Our case is a patient with a large-sized retroperitoneal mass measuring 26 cm in diameter which was reported on cytology as neuroendocrine tumor possibly pheochromocytoma/paraganglioma which was later confirmed on histopathological examination as well as on immunochemistry.

Once the pheochromocytoma is diagnosed, surgery is the treatment of choice. In the presence of metastases, resection can also improve survival and quality of life. Radiation therapy is also a useful option in these cases (mainly in bone metastases). Current chemotherapy combines cyclophosphamide, vincristine and dacarbazine, and it can achieve partial remission and improvement of clinical symptoms in more than half of all cases;⁵ some patients even experience complete remission. Hormonal blocking with 131-I-MIBG could be useful in residual or irresectable disease.¹⁰ Follow-up is also important and, with time, we can determine the malignant tumoural behaviour.

4. Conclusion

Pheochromocytoma has a good overall prognosis, with a 5-year survival greater than 95% in benign tumours and recurrences below 10%.¹⁰ For malignant tumours, due to their low incidence, only isolated cases are published rather than large series, so it is difficult to determine the outcomes.

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