



Composite Pheochromocytoma- A Case Report

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Abstract

Pheochromocytoma originates from primitive neuroectodermal cell rest in adrenals and other paraganglion structures. The term composite pheochromocytoma is used in reference to pheochromocytoma where there are other components resembling neuroblastoma, ganglioneuroblastoma, ganglioneuroma and spindle cell sarcomatous tumour coexist. Here a 61 year old man with pheochromocytoma of right adrenal gland along with tumour component of MPNST-malignant peripheral nerve sheath tumour co-exist (Composite pheochromocytoma) is being presented. The patient presented with left flank pain of one month duration along with complaints of Insomnia, anxiety, palpitation and persistent constipation of short duration.

Keywords: Pheochromocytoma, Composite Pheochromocytoma, Adrenal gland tumor.

Introduction

The adrenal medulla is made up of polyhedral cells arranged in cords or clumps. The adrenal medullary cells derive from neural crest cells. Medullary cells are innervated by cholinergic preganglionic nerve fibres that reach the gland via splanchnic nerves. Medullary parenchymal cells accumulate and store their hormone products in

prominent dense secretory granules 150-350nm in diameter.¹

Histologically these cells and granules have a high affinity for chromium salts (chromaffin reaction) and thus are called chromaffin cells and contain chromaffin granules.

Adrenal Pheochromocytoma arises from the chromaffin cells of adrenal medulla. Peak

incidence seen in the 5th decade. 10% of the cases are familial.

Pheochromocytoma are functional tumors with presentation that varies both morphologically and clinically.

The familial cases can be of the following types:

MEN2A & 2B (40%cases) - Multiple endocrine neoplasia

MEN 2A

- Parathyroid hyperplasia
- Medullary thyroid carcinoma
- Pheochromocytoma

MEN 2B

- Mucosal neuromas
- Marfanoid body
- Medullary thyroid carcinoma
- Pheochromocytoma

Von Recklinghausen disease (1%-5%)

Neurofibromatosis-1

Von Hippel-Lindau disease (10%-20%)

Familial cerebello retinal angiomas

As the cell of origin is the primitive neuroectodermal cell, they can differentiate in to various morphological pattern. These lesions can also have tissue pattern of other neurological tumours.

More rarely complex tumors where pheochromocytoma with foci of neuroblastoma, ganglioblastoma, ganglioneuroma or malignant peripheral nerve sheath sarcoma exist.³

Case Report

A 61 year old man presented to the hospital with the complaints of left flank pain of one month duration. Patient also had complaints insomnia, anxiety and palpitation. There was a past history of difficulty in passing stools and vomiting for past one week. Being a diabetic for past 4 years, he was on regular treatment and follow up.

The general examination did not reveal any evidence of either any café au lait spots or neurofibromatosis.

Serum cortisol was 43.290µg/dl, the reference being 10-20 µg/dl. All other parameters are within normal limits.

The CT imaging showed multiple enlarged, enhancing soft tissue lesions noted along the walls of left renal pelvis with extrarenal extension.

Macroscopy

Two containers were received; container-1 has an already partially cut open nephrectomy specimen measuring 12x12x4 cm. On C/S grey/white areas measuring 7x5cm are identified.

At one end cystic area measuring 5x2x2cm is identified.

Container-2 labelled as left suprarenal mass has a single grey/white grey/black soft tissue mass measuring 5x3x2cm. On C/S grey/yellow, grey/white areas are identified.



Fig. 1(a,b) Nephrectomy Specimen & cut section



Fig. 2 Suprenal Mass

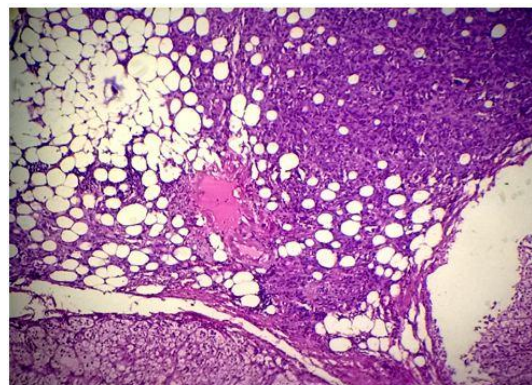


Fig 3: Tumour cells infiltrating the neighbouring areas. Portion of pheochromocytoma is also present.

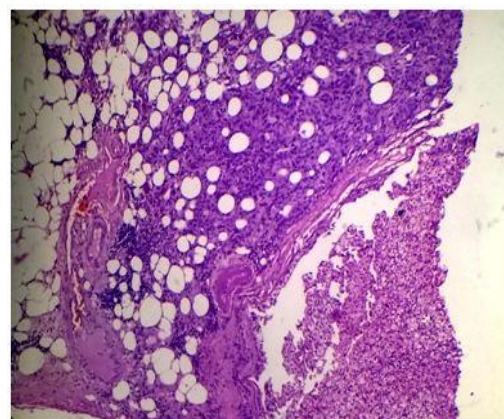


Fig 4: Tumour cells infiltrating the neighboring areas. Portion of pheochromocytoma is also present

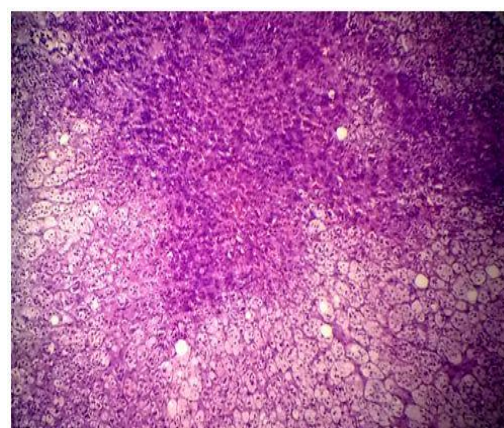


Fig 5: Tumour composed of clear cells cells arranged in sheets; there are also areas, where hyperchromatic tumour cells arranged closely, where vague trabecular pattern is noticed.

Microscopy: (Fig-3 to 15)

The suprenal mass had remnants of adnexal cortex along with a tumor-Fig4. The tumour cells are markedly pleomorphic and anaplastic in nature. The cells are arranged in a resting pattern (zellballen appearance namely polygonal cells arranged in small nests) -fig 5-8 and vague trabecular pattern-fig5. Individual cells appear larger with eosinophilic inclusions. Also seen are elongated spindle shaped cells with prominent hyperchromatic plump nuclei with scanty cytoplasm arranged in sweeping bundles. There are frequent mitotic figures and tumour giant cells. Also seen are elongated spindle shaped cells with wavy nuclei and tapering cytoplasmic membrane. Vascular invasion and embolization are present Fig16. Areas of haemorrhage is also seen. Capsular invasion is present.

Multiple sections studied from the kidney reveal spindle celled neoplasm similar to that seen in adrenal gland along with extensive areas of hemorrhagic necrosis. The rest of the kidney exhibits features of end stage renal disease Fig19.

Histological Features are Consistent with the Diagnosis of Pheochromocytoma with Malignant Peripheral Nerve Sheath Tumor (Composite Pheochromocytoma)

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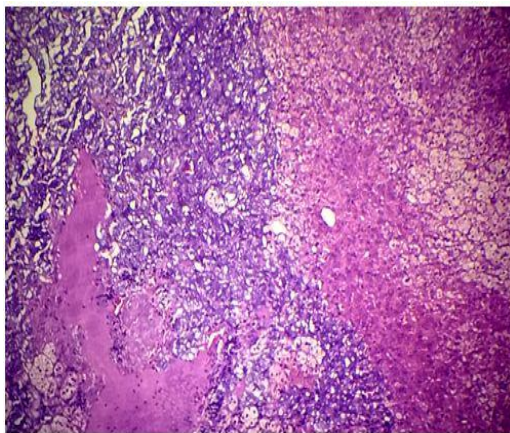


Fig 6: Pheochromocytoma, where part of the tumour contain clear cells and the rest of the areas showing trabecular pattern

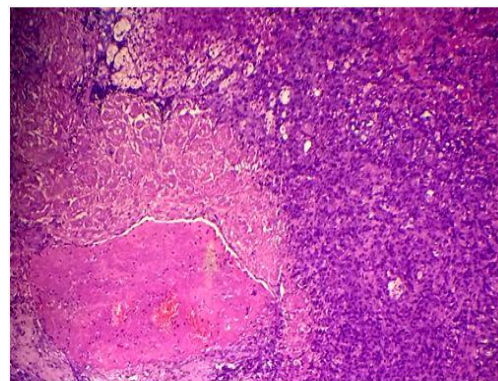


Fig 9: Primitive tumour cells arranged in sheets, with an occasional area exhibiting pseudo rosettes; areas of coagulation necrosis are also present.

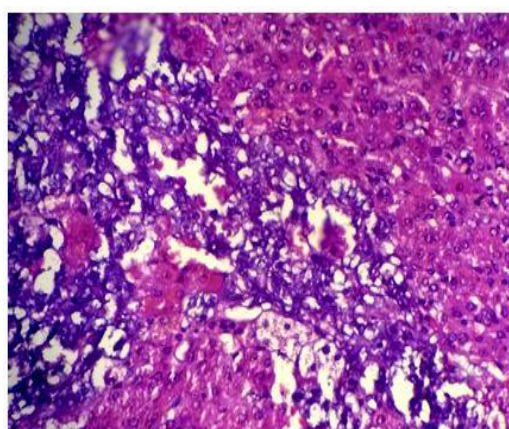


Fig 7: Tumour cells arranged in trabecular pattern .Clear tumour cells with necrotic areas

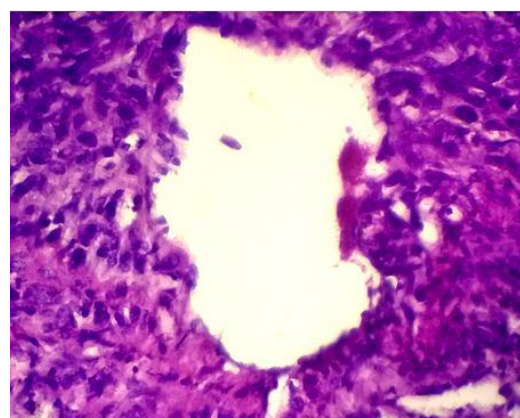


Fig10: Pseudorosette formation

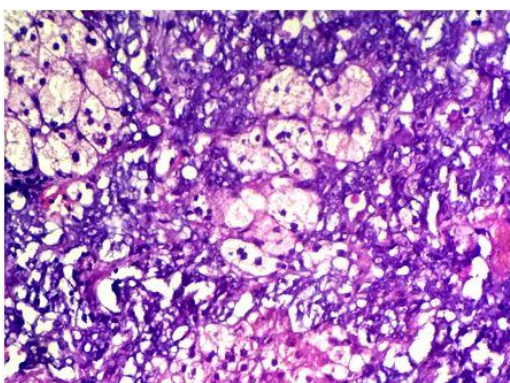


Fig 8: Anaplastic tumour cells along with clear cells containing hyaline globules Clear tumour cells with, some of which contain eosinophilichyaline globules

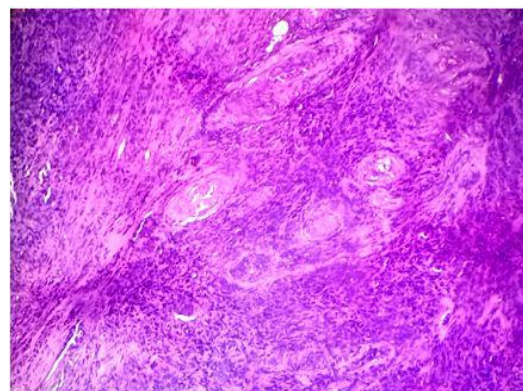


Fig 11: Tumour cells with neural differentiation

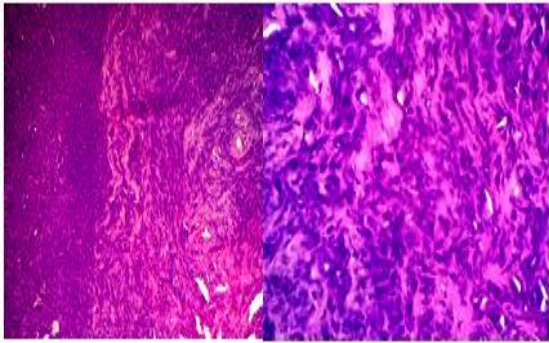


Fig 12: A portion of the tumour, where closely packed, primitive hyperchromatic cells along with a partially differentiated spindle shaped cells with an elongated spindle shaped cells with wavy nucleus and tapering cytoplasmic membrane arranged as sweeping bundles.

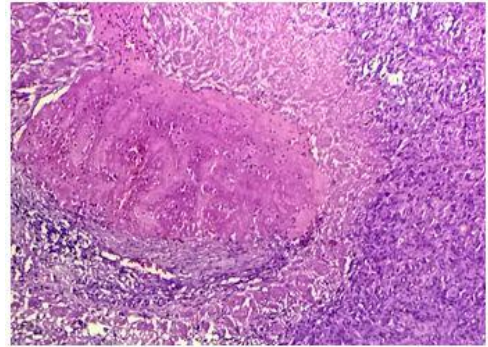


Fig 15: A blood vessel with an organized thrombus; thrombus contain tumour cells

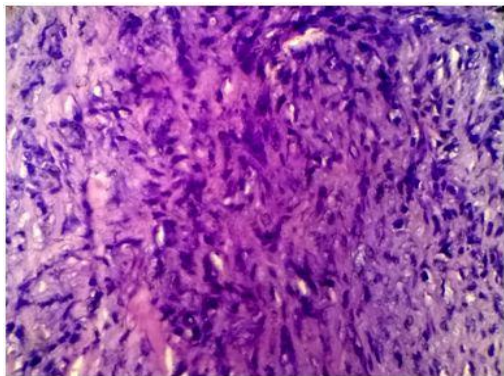
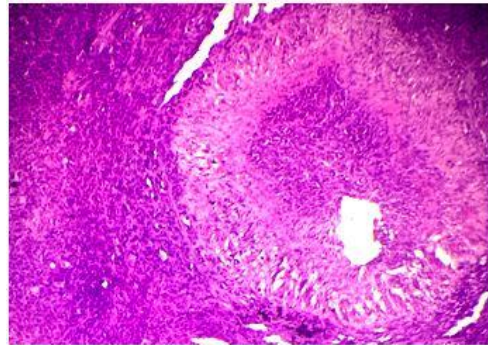


Fig 13: Markedly anaplastic tumour cells

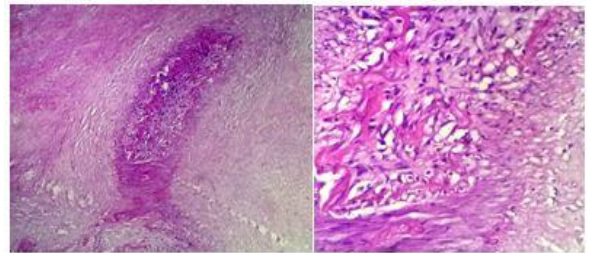


Fig 16: Kidney –Extensive fibrosis, where a vessel is filled with thrombus along with tumour cells.

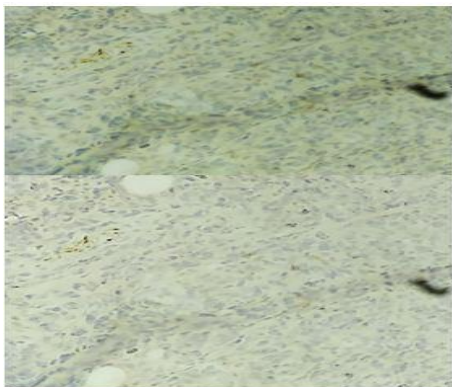


Fig-14: IHC-Neurofilament-Positivity

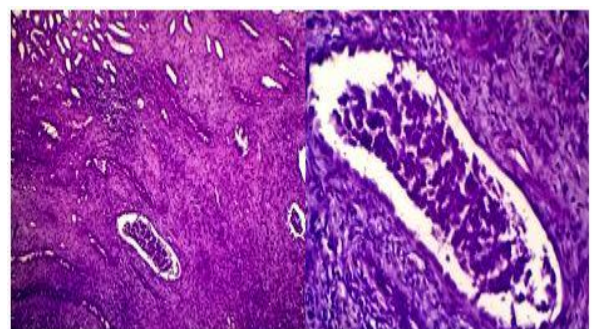


Fig 17: Kidney- a blood vessel with tumour emboli. A blood vessel filled with thrombus containing tumour cell

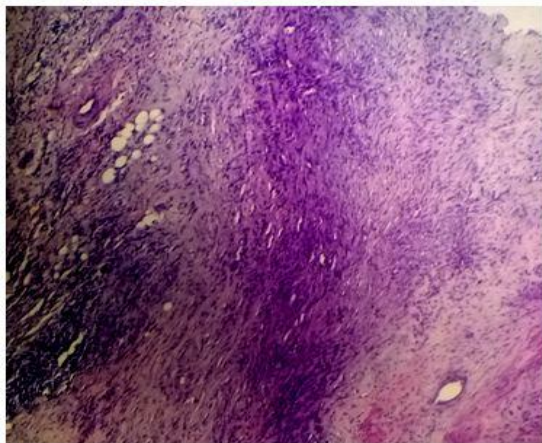


Fig 18: Anaplastic tumour cells in the kidney

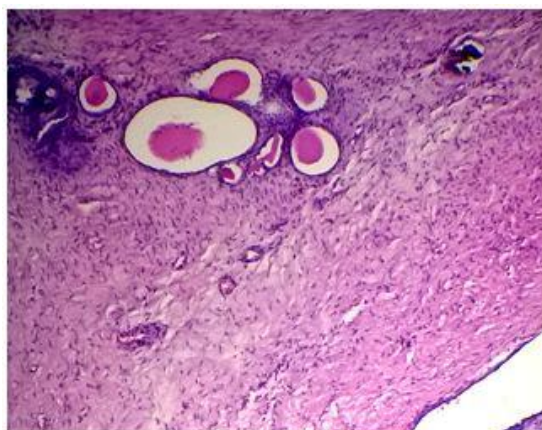


Fig 19: Thyroidization seen in End Stage Renal Failure

Discussion

Composite pheochromocytoma refers to a pheochromocytoma that has a component resembling neuroblastoma, ganglioneuroblastoma, ganglioneuroma or even rarely a malignant peripheral nerve sheath tumour (MPNST; malignant schwannoma). A case of bilateral pheochromocytoma–MPNST has been reported in a patient with von Recklinghausen disease.²Based on the relatively few cases reported to date, the presence of areas resembling neuroblastoma or ganglioneuroblastoma does not necessarily indicate a poorer prognosis and the biologic behavior of these tumours may be as difficult to predict as that of more traditional pheochromocytomas. A recent study compared composite pheochromocytoma with cases of ordinary pheochromocytoma and neuroblastoma and found the composite tumors to have features

(recurrence, N-myc amplification, mortality) closer to those of ordinary pheochromocytoma than neuroblastoma. Therefore it is suggested that composite pheochromocytoma may be regarded as a histologic variant of classic pheochromocytoma. Immunohistochemistry done for identification of neural elements in pheochromocytoma which showed focal positivity. Fig-14.

Conclusion

A 61 year male presented with constipation and mass on the left flank on surgery found to be a renal and suprarenal mass. Histologically a composite pheochromocytoma with infiltration in the kidney was identified. The post-operative follow up is uneventful.

Acknowledgement

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