

## Case Report

# Retroperitoneal composite pheochromocytoma/paraganglioma complicating pregnancy: a rare case report

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## ABSTRACT

Pheochromocytoma is a tumor of adrenal medulla. Pheochromocytoma arising outside the adrenal medulla is commonly called paraganglioma. These tumours arise from paraganglia of the autonomic nervous system, most commonly occurring in head and neck region, and much less frequently in the retroperitoneum. But when they occur below the diaphragm in the organ of zuckerkandl or retroperitoneum, they are also called as extra adrenal pheochromocytoma. Composite pheochromocytoma/paraganglioma is a tumor composed of pheochromocytoma/paraganglioma along with another tumor of neural crest origin composed of either a ganglio-neuroma/ ganglio-neuroblastoma /neuroblastoma or schwannoma. They are mostly located in the adrenal gland, while extra adrenal composite pheochromocytoma is extremely rare. Only 4 cases in the retroperitoneum have been described in the literature. Composite tumors of the adrenal medulla are rare tumors accounting for less than 3% of all sympatho-adrenal tumors. We report a rare case of retroperitoneal extra adrenal composite pheochromocytoma in a 19 year old female with a history of 3 months amenorrhoea.

**Keywords:** Extra-adrenal pheochromocytoma, Composite paraganglioma, Retroperitoneum, IHC

## INTRODUCTION

Extra adrenal composite pheochromocytoma is a very rare tumor. The term composite is used when an additional component of non-pheochromocytoma is present, theoretically arising from a common embryonic progenitor i.e. neural crest. Non-pheochromocytoma elements can be ganglioneuroma, ganglioneuroblastoma, neuroblastoma and more rarely schwannoma. Although pheochromocytoma can occur at multiple sites and in association with number of other tumors, the presence of both pheochromocytoma and ganglioneuroma within a single tumor is extremely rare.<sup>1</sup> It is apparent that composite tumors may display symptoms referable to

hormonal hypersecretion by either component of the tumor. We diagnosed a rare case of retroperitoneal extra adrenal composite pheochromocytoma in a normotensive patient.

## CASE REPORT

A 19 years old female presented with complaints of 3 months of amenorrhoea. She had no other co-morbidities. Past history nil significant. She had undergone routine antenatal scan in Gandhi hospital, Secunderabad. It was a surprise to her and her obstetrician, that along with a live fetus, there was a large heterogeneous mass in the retroperitoneum. Ultrasonogram of abdomen showed a

large well defined mass lesion in the left supra-renal area measuring about 16.7×11.2×8.1 cm in size, causing inferior and medial displacement of left kidney. Spleen was displaced superiorly. Pancreas was compressed and displaced anteromedially, bowel loops were displaced medially. An impression of large left adrenal mass was considered with probability of adrenocortical carcinoma/pheochromocytoma/neurofibroma. Vital data were within normal limits. Case was referred to surgical department for further management. Special investigations were done which included VMA spot test, which was negative. 24 hour urinary protein was within normal limits. 24 hour urinary metanephrines levels were increased to 20 mg/day. Other routine investigations including biochemical, haematological, electrocardiogram & X-ray chest were within normal limits. During admission in hospital, patient complained of spotting per vaginum. Per vaginal examination revealed cervical os opened, indicating threatened abortion. She was referred to department of Obstetrics for termination of pregnancy.

Pregnancy was terminated and patient was posted for exploration, which revealed a large retroperitoneal mass. Mass was removed through trans-peritoneal/anterior abdominal approach. The operative findings showed a highly vascular tumour occupying the retroperitoneum, lying superomedial to the left kidney.

### **Gross examination**

Received two masses. First one was a large, well circumscribed encapsulated mass measuring 20×10×6 cm. Cut section showed gray white mass along with mucoid, gelatinous areas with spotty foci of haemorrhages. No native tissue at the periphery was made out. Second specimen sent as para aortic lymph node was irregular mass measuring 4×3×1 cm.

Cut section showed solid gray white areas, looking like lymph node. Sections were given from the representative areas from both masses and submitted for routine processing.

### **Microscopic examination**

Multiple sections revealed well encapsulated tumour tissue arranged in a Zell-Ballen pattern, composed of nests of oval to polygonal cells surrounded by a delicate spindle shaped cells. Individual tumour cells had moderate to abundant amount of granular eosinophilic to amphophilic cytoplasm, round to oval nuclei and single prominent nucleoli. Intermixed with these cells were areas showing sheets of mature ganglion cells surrounded by fascicles of elongated, spindle shaped neural/Schwann like cells. Spotty areas of hemorrhages were also seen. At places polygonal cells showed multinucleation, intranuclear inclusions and hyaline globules. Ganglion cells were uni or multinucleate with brownish Nissl granules in some of them. Intervening stroma showed

prominent neural differentiation and patchy lymphocytic infiltration. No marked cellular atypia, necrosis or abnormal mitosis seen. No native tissue was seen.

Sections studied from second mass revealed fibro-collagenous capsule, pericapsular adipose tissue of lymph node, which was almost replaced by the tumor deposit, having similar histological features as described above.

### **IHC**

A panel of IHC markers was ordered for both the masses with chromogranin, S100, NSE & Ki-67. IHC with chromogranin was diffusely positive in all components with intense positivity in the Zell-Ballen clusters, S100 was positive in sustentacular cells and ganglion cells. NSE showed positivity in the Zell-Ballen nests and in the neuronal component. Ki67 was very low, <0.5%. After surgery patient underwent whole body scan which showed intact bilateral adrenal glands, with no other deposits elsewhere in the body.

### **Diagnosis**

A final diagnosis of non-functioning retroperitoneal extra-adrenal composite pheochromocytoma was made.

### **DISCUSSION**

Extra adrenal composite pheochromocytoma in the retroperitoneum is a rare tumor,<sup>2</sup> typically having features of pheochromocytoma/paraganglioma with those of ganglioneuroma, ganglioneuroblastoma, neuroblastoma, neuroblastomatosis, peripheral nerve sheath tumour like schwannoma or neuroendocrine carcinoma.<sup>3</sup> In our case the non-pheochromocytoma component was ganglioneuroma,<sup>4</sup> constituting for about 20-25%. Only 11 extra adrenal composite pheochromocytoma cases have been reported, with 6 cases located in the urinary bladder,<sup>5</sup> 4 cases in retro-peritoneum<sup>6</sup> and one case in cauda equina.<sup>7</sup> The patients ages ranged from 5 to 82 years with majority in the age group of 40- 60 years. Males and females were equally affected.

Embryologically both chromaffin and ganglion cells are derived from neural crest cells and migrate to somatic areas.<sup>8</sup> Any disturbance in migration or maldevelopment of the neural crest might result in the development of composite tumours.<sup>9</sup> These cells have potential to produce many peptide hormones and biogenic amines. Because these cell populations have similar derivation, one might expect these tumors to be more common than what is apparent from the literature, and this finding may represent under reporting or under recognition of this condition. It is apparent that a composite tumor of pheochromocytoma and ganglioneuroma may display symptoms referable to hormonal hypersecretion by either components of the tumor. Watery diarrhoea has been described in some cases attributable to increased secretion of vasoactive intestinal peptides.<sup>10</sup> Both the

pheochromocytoma and non-pheochromocytoma components were capable of secreting VIP. This further supported its common origin. In our case the patient had no hypertension or any classical symptoms of pheochromocytoma. The composite tumors were often associated with familial syndromes such as NF-1<sup>11</sup> and MEN-2A.<sup>12</sup> Grossly the composite pheochromocytoma were usually similar to pure pheochromocytoma and thus composite phenotypes are generally detected on histopathological examination. In our case the tumor tissue was traversed by bundles of spindle cells that showed Schwann cells and axons. No genetic abnormalities were found to distinguish composite tumors from pure pheochromocytoma/paraganglioma.

Comstock et al.<sup>13</sup> reported that neither composite pheochromocytoma nor classic pheochromocytoma demonstrated N-myc amplifications. It was difficult to predict the biologic behaviour of composite tumors. The prognosis is variable. In our case para aortic lymph node showed metastatic tumor deposit, probably implying malignant potential. Composite pheochromocytoma-ganglioneuroma were treated principally by surgical resection, and adequate clinical follow up was advised for potentially malignant neoplasms.

## CONCLUSION

Composite pheochromocytoma/paragangliomas are rare tumors mostly located in the adrenal gland, while extra adrenal composite pheochromocytoma/paraganglioma are extremely rare. The clinical features were similar to pure pheochromocytomas, but little is known about the biological behaviour, outcome and molecular genetic profiles.

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