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Case Report

# Composite and Collision Tumours of the Adrenal are Rare Entities. We Present a Case Report of an Unusual Tri-Lineage Tumour

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## Abstract

A 39 year old female patient presented with a history of depression and anxiety, recurrent sore throats and mouth ulcers. She had also been experiencing palpitations for over two years, along with hot flushes, episodes of sweating (including night sweats), GI symptoms (diarrhoea, constipation and bloating), and dizzy spells. She had no significant weight loss. She had a family history of hypothyroidism and multiple sclerosis, but otherwise no significant past medical history.

**Keywords:** Depression; Anxiety; Sweating

An initial ultrasound to investigate abdominal symptoms revealed a right upper abdominal lesion, and a subsequent triple phase CT scan showed a 4.4cm adrenal mass. Plasma metanephrine and normetanephrines and urinary catecholamines were markedly elevated. ACTH was in the normal range, but cortisol levels were mildly elevated after overnight dexamethasone suppression. Subsequent nuclear medicine investigations characterised this lesion as a phaeochromocytoma with a separate adrenal adenoma adjacent (Figure 1A).

The adrenal lesion was excised laparoscopically and sent for histopathological examination.

Grossly the adrenal mass was composed of two separate lesions: a larger nodule with a pale-tan cut surface and variegated haemorrhage, and a smaller nodule with a pale orange cut surface (Figure 1B).

Histologically the larger nodule contained areas of nested large polygonal cell with eosinophilic cytoplasm, nuclear pleomorphism and hyperchromasia outlined by thin fibrovascular septae (Figure 1C). Intermixed with this were large mature ganglion cells, with areas of Schwannian and neural stroma. No immature elements were seen. There was noticeable nuclear atypia and hyperchromasia, but a low mitotic count (max. 2/10 high power fields). No definite spindle cell areas were seen within the phaeochromocytoma component. There were foci of haemorrhage but no necrosis. The lesion appeared encapsulated by a thin rim of compressed normal adrenal tissue with no extracapsular extension, no vascular invasion, and no involvement of the surrounding fat. This was regarded as a composite phaeochromocytoma-ganglioneuroma (PASS score 2).

The smaller nodule was well-circumscribed and composed of small nests of cells with abundant cytoplasm, with areas of clear cell morphology and oncocytic areas (Figure 1). There was surrounded by a rim of partly atrophic adrenal cortex. There was no high grade features and the modified Weiss score for this lesion was zero, favouring a cortical adenoma.

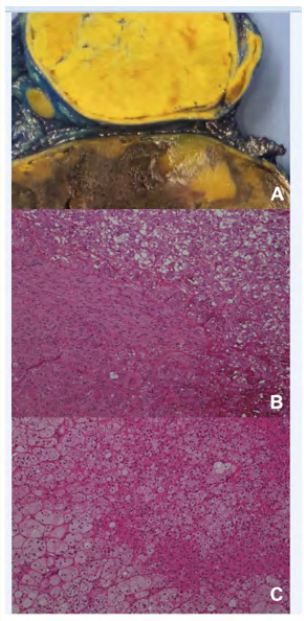


**Figure 1**

Immunohistochemistry on a representative section comprising both the nodules demonstrates the larger nodule to be highlighted by Chromogranin A, Synaptophysin and NSE, which also stains the ganglion cell rich foci. The neuromatous stroma component of the ganglioneuroma component stains for S100. This entire nodule is negative for Calretinin and AE 1/AE3. These morphological and immunohistochemical patterns would be consistent with a composite phaeochromocytoma and ganglioneuroma. The smaller nodule is positive staining for Melan A with patchy positivity for synaptophysin confirming an adenoma.

A recent review of composite phaeochromocytomas emphasises that these are rare lesions, with 94 cases described in the literature [1]. Composite tumours with three components are even less common. We performed a literature search on PubMed for "adrenal composite pheochromocytoma ganglioneuroma adenoma" and tracked citations for each case identified. 3 cases were identified in total, and are summarised in Table 1. A fourth case of phaeochromocytoma-corticomedullary tumour was also identified [5].

| Report | Patient age | Patient sex | Pathology | Genetic predisposition |
|---|---|---|---|---|
| Aiba., *et al.* 1988 [2] | 53 | Male | Composite phaeochromocytoma/ganglioneuroma and ipsilateral cortical adenoma | None |
| Bernini., *et al.* 2005 [3] | 69 | Female | Composite phaeochromocytoma/ganglioneuroma and contra-lateral cortical adenoma | Novel VHL mutation |
| Lau., *et al.* 2011 [4] | 64 | Male | Composite phaeochromocytoma/ganglioneuroma and ipsilateral cortical adenoma | History of neurofibromatosis type 1 |
| Lee., *et al.* 2007 [5] | 25 | Female | Phaeochromocytoma and mixed corticomedullary tumour | None |

**Table 1**

## Diagnostic considerations and differential diagnosis

A diagnostic consideration would be a corticomedullary mixed tumour, but these have admixed cortical and medullary elements rather than clearly demarcated nodules. A case of composite phaeochromocytoma and corticomedullary tumour has been reported [5].

The RCPath guidelines [6] suggest that for composite lesions the PASS score may not be a reliable predictor of behaviour (likewise with comparable scoring systems for the ganglioneuroma component). The PASS score for the Phaeochromocytoma component is 2/20 (with the literature suggesting that lesions

likely to metastasise scoring 4 and above), and the modified Weiss score of the adenomatous component is 0. The ganglioneuroma component is regarded as 'very low risk' histology according to the INRG staging schema. No fresh tissue was available for molecular analysis for MYCN amplifications or karyotyping.

## Conclusion

In conclusion, composite tri-lineage adrenal tumours are rare entities with only 4 cases previously reported. The clinical behaviour of these lesions may not be entirely captured by risk-scoring algorithms for the component parts. A referral to clinical genetics should be considered due to the association with inheritable conditions. In this case, her genetic screening showed no causative gene. On follow-up her plasma metanephrine levels have normalised.

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