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Case Report

Pathology Section

A Rare Presentation of Adrenal Leiomyoma Arising in a Ganglioneuroma: A Case Report

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ABSTRACT

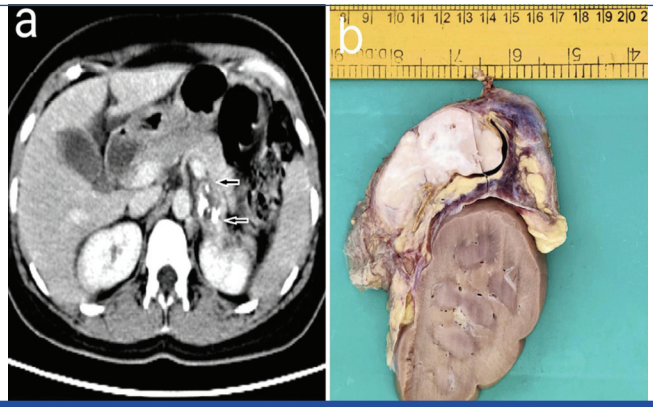
Leiomyomas are benign tumours of smooth muscle origin and can occur in any part of the body with adrenal gland being an uncommon site. Ganglioneuromas of adrenal gland are benign neural crest-derived tumours. Both of these tumours are usually detected incidentally. Hereby, the authors report an unusual case of a 31-year-old woman, who presented with paroxysmal attacks of headache, palpitations and flushing pointing towards a hormone secreting adrenal tumour. However, functional adrenal markers were normal. Radiological investigations revealed 8×3 cm heterogeneously enhancing left suprarenal mass with calcification and extension to left renal vein. Patient underwent left nephrectomy and adrenalectomy with a high clinical suspicion of malignancy because of tumour extension to the renal vein. The histopathological examination revealed a leiomyoma arising in a background of ganglioneuroma which was later on confirmed using immunohistochemistry. Authors have presented the present case because of atypical presentation as a hormone secreting adrenal tumour with radiological features of malignancy and the unique histomorphology of the combined occurrence of leiomyoma and ganglioneuromatous area in the adrenal gland. To the best of author's knowledge, this is the first case report of such an occurrence in the adrenal gland.

Keywords: Benign tumour, Neural crest-derived, Smooth muscle tumour, Suprarenal mass

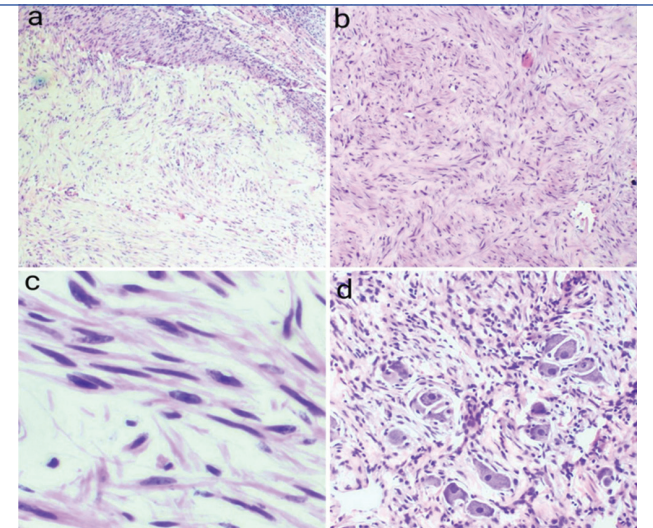
CASE REPORT

A 31-year-old female with no known co-morbidities presented with complaints of paroxysmal attacks of headache, palpitations and flushing since the past one year. She described a bilateral throbbing type of headache lasting for 20 minutes to one hour which was precipitated by stress. There was no history of photophobia or nausea or vomiting. There was a history of weight loss of 6 kg over the past two months. Her physical examination and routine investigations were normal. Urine metanephrines and, catecholamines, and serum cortisol was normal. Contrast Enhanced (CT) showed heterogeneously enhancing 8×3 cm lesion in the left adrenal gland with necrosis and coarse calcification, bulging into and with possible extension along the left adrenal vein [Table/Fig-1a]. Gallium-68-Dodecanetetraacetic acid Tyr3-octreotide (DOTATATE) PET/CT done showed no Significant Somatostatin Receptor (SSTR) expression and no metastasis.

The CT guided biopsy was inconclusive. Based on the clinical and imaging findings, the possible diagnosis considered were adrenocortical carcinoma and pheochromocytoma. Intraoperatively, there was a hard mass in the left adrenal gland with extension along left renal vein, renal vein thrombus and possible adhesion to left kidney and diaphragm; therefore, left adrenalectomy with nephrectomy was done with the clinical and radiological suspicion of malignancy. Grossly, the specimen consisted of adrenal gland with a well-demarcated unencapsulated grey white firm lesion centered in the adrenal medulla measuring 7.5×3×2.6 cm [Table/Fig-1b]. The adjacent upper pole of kidney and perirenal fat showed areas of haemorrhage and fat necrosis. Microscopy revealed a circumscribed neoplasm composed of fascicles and sheets of long spindly cells with bland cigar shaped nucleus (leiomyoma) [Table/Fig-2a-c]. No significant nuclear pleomorphism, increased mitotic activity or necrosis was seen. Focal areas showed ganglion cells, Schwann cells and nerve fibres in the background (ganglioneuromatous area) [Table/Fig-2d]. Stromal and perivascular hyalinisation and calcification was present. Normal adrenal tissue seen compressed along the periphery of the lesion was normal. Adjacent kidney and perirenal fat showed haemorrhage and collection of foamy macrophages. The morphological differential



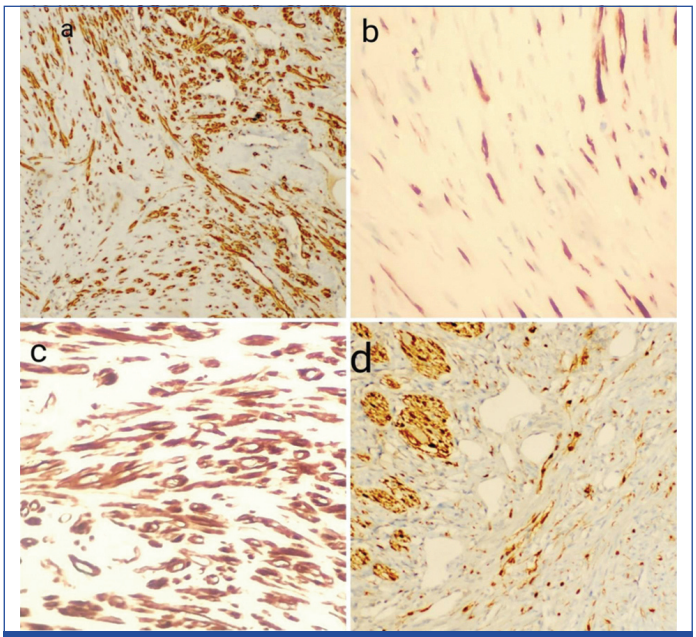
[Table/Fig-1]: a) CECT abdomen axial cut showing heterogenous enhancing left suprarenal mass with calcification and possible extension into left renal vein (black arrow with white outline); b) Gross image of adrenal leiomyoma showing a circumscribed lobulated grey white lesion.



[Table/Fig-2]: a) Photomicrograph showing adrenal tissue with leiomyoma comprising of spindle cells and hyalinised stroma (Haematoxylin and Eosin [H&E, 4X]); b) 10X showing sheets and fascicles of spindle cells; c) 40X showing bland spindle cells with cigar shaped nucleus; d) 10X showing ganglioneuromatous area with ganglion cells and Schwann cells.

diagnosis considered was leiomyoma, schwannoma, and spindle cell predominant ganglioneuroma.

Immunohistochemistry (IHC) showed that the long spindle cells were positive for smooth muscle markers-Smooth Muscle Actin (SMA), desmin and h-caldesmon [Table/Fig-3a-c]; S100 and Human Melanoma Black (HMB) 45 negative with a MIB labelling index of 5-6%. S100 stain highlighted the ganglion cells and Schwann cells in the ganglioneuromatous area [Table/Fig-3d]. Because of the presence of proliferation of smooth muscle marker positive spindle cells closely admixed with the neural marker positive ganglion cells and Schwann cells, the diagnosis of adrenal leiomyoma arising in a background ganglioneuroma was made. The postoperative period was uneventful and the patient is doing well and symptom free.



[Table/Fig-3]: a) Immunohistochemistry showed strong cytoplasmic positivity for SMA in the neoplastic smooth muscle cells. 10X; b) Desmin positivity, 40X; c) Strong diffuse cytoplasmic positivity for h-caldesmon, 40X; d) S100 highlighting the ganglion cells and Schwann cells, 10X.

DISCUSSION

Leiomyomas of the adrenal gland are extremely rare benign tumours with less than 30 cases reported in literature till date [1]. They have a wide age range of presentation (2-72 years) with a median age of 34.5 years and female preponderance [2]. Ganglioneuromas are benign peripheral neuroblastic tumours derived from neural crest cells and can occur in the adrenal medulla. The spectrum of peripheral neuroblastic tumours comprise of neuroblastoma, ganglioneuroblastoma and ganglioneuroma with ganglioneuroma forming the differentiated end of the spectrum. Clinically, both these tumours are hormonally inactive and mostly detected incidentally. Hormone secretion including catecholamines and dopamine has been rarely reported in few cases of ganglioneuromas arising in adrenals [1]. Adrenal leiomyomas when symptomatic, present with non specific symptoms, abdominal discomfort, anorexia, weight loss and malaise. About 50% cases have associated immunodeficiency either acquired or congenital. About 5% cases have Epstein-Barr Virus (EBV) association [2]. The patient was not immunocompromised and although she had symptoms pointing towards a functioning adrenal tumour, biochemical tests were normal.

The incidence of adrenal tumours is increasing due to the advancements in the field of radiology and higher rate of detection of small clinically silent so-called “incidentalomas”. Radiologically, adrenal leiomyomas are homogeneously or heterogeneously enhancing lesions and can have hypo attenuated low density areas simulating necrosis and less commonly calcifications [2,3]. Calcifications are more frequently seen in neuroblastomas, pheochromocytomas and ganglioneuromas of the adrenal gland [4]. Leiomyomas of adrenal gland although benign can mimic malignancy clinically and radiologically as is seen in the present case [5]. Therefore, histopathological examination is the gold standard for establishing diagnosis. The histopathological features of adrenal leiomyomas are similar to those of leiomyomas elsewhere. The differential diagnosis includes spindle cell lesions of the adrenal gland with bland cytomorphology like schwannomas, cellular spindle areas of ganglioneuroma, spindle cell predominant areas of pheochromocytoma and other rarer mesenchymal tumours like solitary fibrous tumour, gastrointestinal stromal tumour. Pleomorphic spindle cell lesions include sarcomatoid areas of adrenocortical carcinoma, metastatic malignant melanoma, primary and metastatic sarcomas with spindle cells. A panel of IHC markers including but not limited to SMA, desmin, S100, CD34, HMB45, MelanA, STAT6 and CD117 in the appropriate clinical set-up and morphology helps in arriving at the diagnosis [6].

The interesting morphological feature in our case is the presence of scattered ganglion cells and Schwann cells in a fibrous stroma in addition to the areas of a conventional leiomyoma. The ganglioneuromatous area was positive for S100 and negative for SMA and these areas were closely admixed with the neoplastic SMA positive and S100 negative smooth muscle cells of leiomyoma. Adrenal leiomyoma arising in a background of ganglioneuroma has not been reported till date, to the best of our knowledge. However, aberrant differentiation in the form of adipose tissue has been documented in ganglioneuromas termed as lipomatous ganglioneuroma or lipoganglioneuroma. They can occur in retroperitoneum, as well as, adrenal [7,8]. Ganglioneuromas being derived from neural crest cells are capable of ectomesenchymal differentiation, embryologically contributing to the smooth muscle cells of the vascular system including major blood vessels of heart [9]. Smooth muscle differentiation have been reported in other neural crest-derived tumours like schwannoma and primitive neuroectodermal tumour [10,11]. Neuroblastoma derived cell lines also show smooth muscle differentiation [12]. This phenomenon can explain the unique occurrence of this smooth muscle derived neoplasm arising in the background of ganglioneuroma.

CONCLUSION(S)

Adrenal leiomyoma presenting with symptoms of hormone secretion and radiological features of malignancy poses a diagnostic challenge. Leiomyoma should be considered in the differential diagnosis of adrenal mass with atypical presentation. The unusual finding of ganglioneuroma in the background of leiomyoma throws new light into yet another aberrant differentiation pathway, possible for ganglioneuroma, apart from the already described lipomatous differentiation. More studies are needed in this direction for better understanding of these tumours.

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