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Case Report

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Unravelling the Unexpected: A Case Report of Adrenal Ganglioneuroma

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ABSTRACT

Background: Adrenal Ganglioneuromas (AGNs) are rare benign tumors originating from neural crest cells in the sympathetic nervous system. Due to their asymptomatic nature and radiological similarity to other adrenal masses, preoperative diagnosis remains challenging. Surgical excision followed by histopathological examination is the mainstay for definitive diagnosis and management. Ganglioneuromas have a very good prognosis with surgical removal.

Methods: We report a case of a 51-year-old male who presented with right lower quadrant abdominal pain and a single episode of hematuria. CT Urogram showed a well-defined, calcified lesion in the right adrenal gland, suggestive of an adrenal malignancy. The patient underwent a right adrenalectomy, and the excised tumor was sent for histopathological evaluation.

Results: Gross evaluation showed a well encapsulated mass which on microscopic analysis showed benign spindle cells interspersed with mature ganglion cells confirming the diagnosis of AGN. Immunohistochemical panel followed to rule out other differential diagnoses. The patient's postoperative course was uneventful, and no recurrence was observed on follow-up.

Conclusion: The report highlights the rarity of AGN, an adrenal neoplasm that is often diagnosed incidentally. Due to its overlapping radiological findings with malignant adrenal neoplasms, histopathological confirmation is crucial. Surgical excision remains the main treatment which offers an excellent prognosis.

Key-words: Ganglioneuroma, Adrenal gland tumours, Adrenalectomy, Schwannian stroma

INTRODUCTION

Adrenal tumours are mainly classified as 'Tumours of the adrenal cortex' and 'Tumours of the adrenal medulla and extra-adrenal paraganglia. [1] Adrenal medullary tumours include the tumours originating from the neural crest cells in the sympathetic ganglion.[2] They include Ganglioneuromas (GN), which are benign, ganglioneuroblastomas of intermediate differentiation, and neuroblastomas, poorly differentiated tumours.[1] GN is a rare benign tumour arising from the neural crest cells, most of which arise in the posterior mediastinum (39%-43%) followed by retroperitoneum (32%-52%), particularly the presacral space. However, Adrenal Ganglioneuromas (AGN) are rare, representing 0.3-2% of all adrenal tumours. [3-5]

AGNs occur most frequently in the fourth and fifth decades of life whereas GNs of the retroperitoneum and posterior mediastinum are usually encountered in children and younger adults. [6-10] Radiologically, AGNs have the potential to mimic other adrenal tumours like adrenocortical carcinoma (ACC) and pheochromocytoma. These are hormonally silent tumours and thus, can be asymptomatic, and large tumours can present with

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pressure symptoms. Despite the substantial size, they are usually detected incidentally, and are referred to as incidentalomas.[2] Therefore, a definitive pre-operative diagnosis of AGN is challenging and can be achieved on histopathological examination. Overall AGNs have a good prognosis following surgical resection. [11] On account of paucity of data on this entity, research publications are limited to case reports and series. Here we document a rare such case of AGN in a 51 year male who was treated adrenalectomy.

CASE REPORT

A 51-year-old male presented to the Urology outpatient department with complaints of abdominal discomfort for 2 months and a recent bout of haematuria. No significant personal or past history.

On general physical examination, there were no clinical signs of catecholaminergic, mineralocorticoid, or glucocorticoid hypersecretion. No lymphadenopathy was detected. Per abdominal examination, there was a vague lump of 10x10cm in the right hypochondrium that moved very little with respiration. The mass was not associated with tenderness.

All routine haematological and biochemical investigations including serum electrolytes were within normal limits. Ultrasonography abdomen showed a well-defined heteroechoic lesion with areas of calcification in the right suprarenal region. CT Urogram also showed a well-defined soft tissue density lesion with calcifications in the right suprarenal region measuring 14x11x10.7 cm, adrenal gland not visualized separately (Fig. 1 A-C). A radiological diagnosis of an adrenocortical tumour was offered.

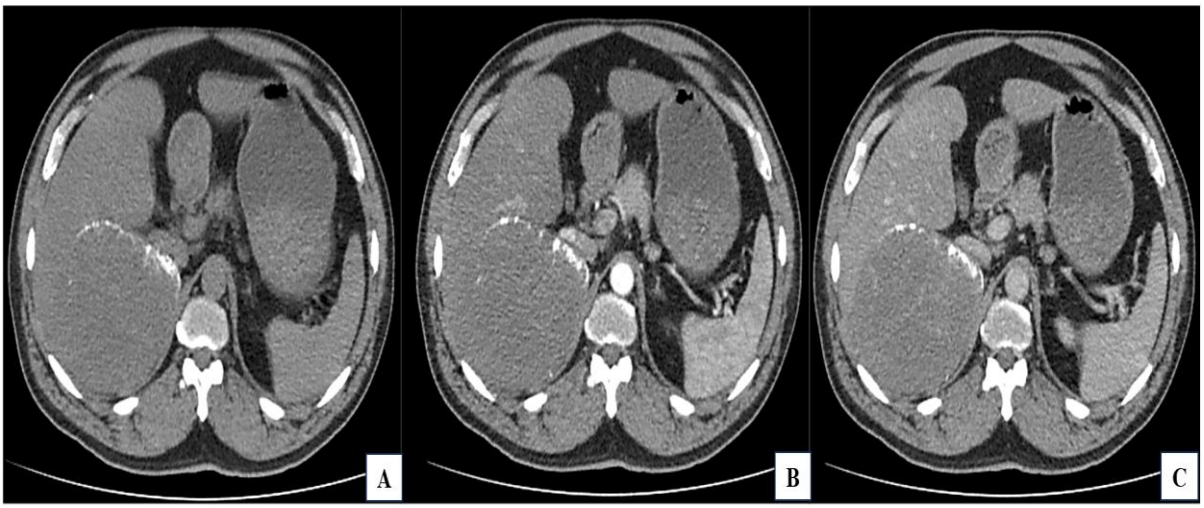

Fig. 1A-C: CT Urogram: Well-defined soft tissue density lesion measuring14x11x10.7cm with calcifications in the right adrenal gland

Subsequently, the patient underwent exploratory laparotomy which showed a large mass in the suprarenal region which was mobilised from all around and from the upper pole of the kidney. Adrenal gland was not visualized separately. The mass was excised in to and sent for histopathological examination. The postoperative period was uneventful.

Gross examination of the excised mass showed a well-encapsulated smooth globular firm mass measuring 14x11x10cm. The cut surface revealed a well-circumscribed firm, tan-white tumour with areas of punctate calcifications and focal pale yellow areas at the periphery (Fig. 2 A,B).

Microscopic examination showed a spindle cell neoplasm consisting of short interlacing fascicles and bundles. The tumour cells were spindle-shaped of the Schwannian type, exhibiting elongated nuclei with fine chromatin, with no detectable cytological atypia. Interspersed amidst were scattered small clusters of mature ganglion cells, large and round with abundant eosinophilic cytoplasm and eccentric rounded vesicular nuclei, a few showing prominent nucleoli. Mitotic figures were rarely seen. A few nerve bundles were also identified. Foci of calcifications seen. Focal areas of increased cellularity were seen. No tumour necrosis was identified. No immature/neuroblastic component was

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identified. A focus of thin and compressed normal adrenal parenchyma was identified at the periphery (Fig. 3 A-D).

A panel of immunohistochemical markers was performed further to confirm the diagnosis, which included S-100, Ki67, Desmin, and Smooth Muscle Actin (SMA). Tumour cells showed diffuse strong positivity for S-100 and were immunonegative for Desmin and SMA thus ruling out other close differentials. In view of focal increased cellularity, a low Ki-67 (<1%) ruled out a rare possibility of MPNST (Fig.4 A-D). With these findings, a diagnosis of Ganglioneuroma of the adrenal gland was established.

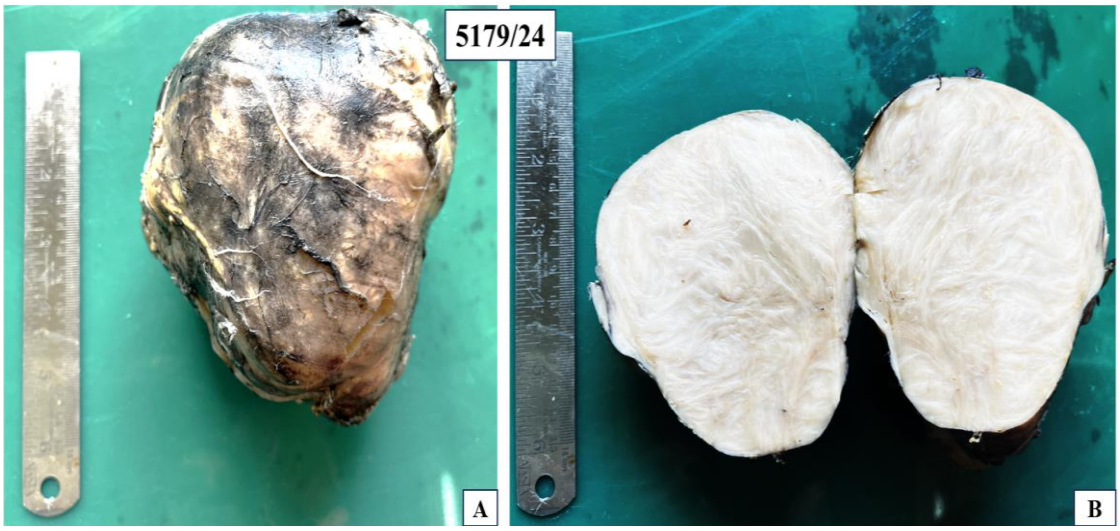

Fig. 2: A. Well-encapsulated adrenal mass; **B.** Cut surface is tan white, glistening & firm.

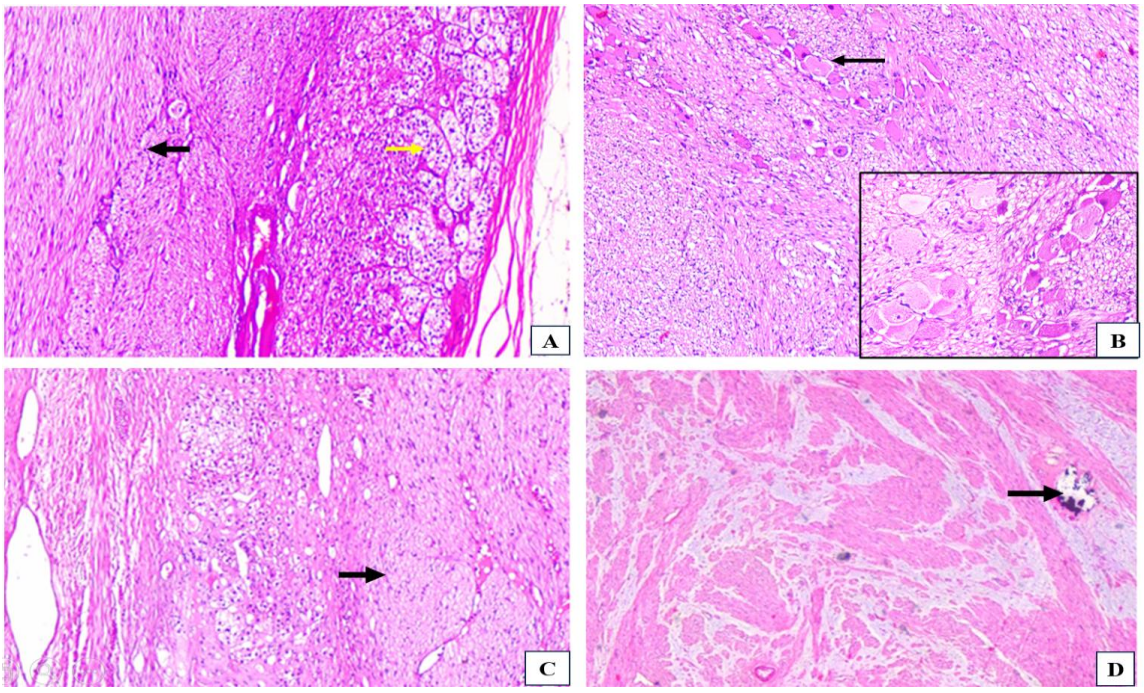

Fig. 3: A. Schwannian stroma (black arrow) and peripherally compressed adrenal parenchyma (yellow arrow); **B.** Mature-looking ganglion cells (inset): large cells with abundant cytoplasm and eccentric nuclei; **C.** Neural bundles amidst the tumour cells; **D.** Fibrous and myxoid stroma with calcification (arrow) {H&E: (200x)}.

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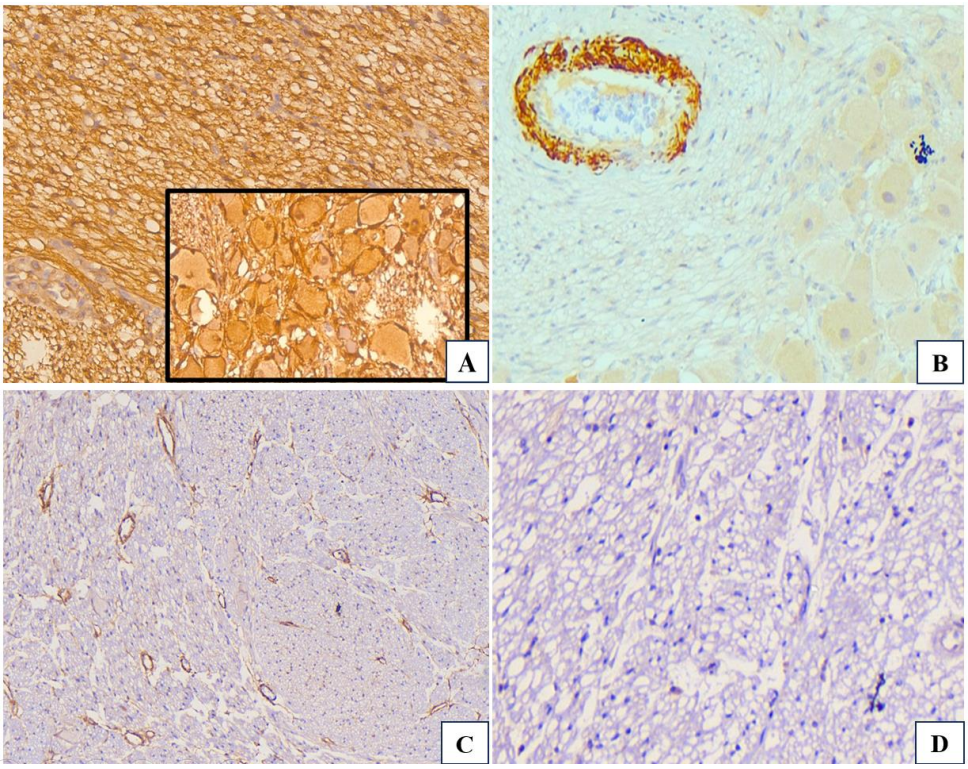

Fig. 4: A. S100-Diffuse strong nuclear and cytoplasmic staining in both ganglion cells and stroma; B. Desmin-Negative in tumour cells and ganglion cells with positive internal control (arrow); C. SMA-Negative in tumour cells highlighting the blood vessels; D. Ki-67- <1%. (100X Magnification) [IHC]

DISCUSSION

AGNs are rare benign tumours of neuroectodermal origin.[12] De Novo AGNs are extremely rare tumours representing 0.2-0.4% of all adrenal tumours. They are also known to arise from the maturation of pre-existent neuroblastoma in younger individuals spontaneously or after chemotherapy. [13,14]

Pre-operative diagnosis of AGN is challenging owing to the disease rarity, variable clinical presentation and lack of pathognomonic imaging findings. [15,16] Surgery continues to be the cornerstone of management and histopathological examination remains the mainstay of diagnosis. It is essential to rule out the other differential diagnoses, mainly retroperitoneal spindle cell neoplasms like Malignant Peripheral Nerve Sheath Tumour, especially in core needle biopsies. This necessitates the use of an appropriate panel of immunohistochemical markers to delineate various other spindle cell neoplasms. It is also noteworthy to keep in mind the heterogeneous nature of tumours, particularly the composite tumours of adrenals. Differentiation from other soft tissue tumours and gastrointestinal stromal tumour becomes imperative in view of diagnostic and definitive therapeutic implications.[17] Ganglioneuromas have very good prognosis following complete resection. However, some case reports mention the late recurrence or malignant transformation, especially after incomplete resection. [18]

In view of rarity of these tumours, the literature reviewed puts forward more case reports than case series. The clinicopathological parameters across various case reports and series are mentioned in Table 1. [19-23]

The age of presentation varied from a young age to middle age group. The majority of the patients presented with non-specific symptoms and were diagnosed incidentally similar to the present case. Radiologically, calcifications were seen in most of the cases except for the case reported by Kayastha et al. [20] In concordance with our case, radiological features across various studies mention overlapping variations making it challenging to differentiate AGNs from other adrenal neoplasms including adrenal adenoma, adrenocortical carcinoma and pheochromocytoma.[24] Microscopically, features comprised of a mature Schwannian stroma with intervening Ganglion cells (both mature and maturing). No necrosis or atypical mitosis was identified in any of the cases.

Therefore, histopathological examination has proven to be the current diagnostic gold standard. Surgery remained the backbone of management in all cases

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except the case reported by Aynao et al as it was a case of metastatic colorectal carcinoma. [20] Similar to our case, IHC was beneficial in arriving at a definitive diagnosis and ruling out malignant transformation and smooth muscle tumours.

Ganglioneuromas are not usually associated with genetic abnormalities, the role of RET and relationship with multiple endocrine neoplasia is uncertain.[25]

Table 1: Comparison of clinical presentation, radiological features, and pathological findings with other case reports

Parameters	**Present Study**	**Daghdagh *et al.*** [19]	**Aynao *et al.*** [20]	**Alqahtani *et al.*** [21]	**Kayastha *et al.*** [22]	**Adas *et al.*** [23]
Age/Gender	51 yr/male	22 yr/ female	40 yr/ male	41yr/ female	15yr/ female	18yr/female
Relevant history/ Familial history of tumours	Absent	Absent	Absent	Negative K/C/O SLE	Negative	Absent
Symptoms/ Presenting Complaints	Abdominal pain, hematuria	Incidentally detected in the follow up of Crohn's Disease	As a part of work up for metastatic Carcinoma Colon s/p chemotherapy C/F: abdominal pain, incidentally detected	Incidentally detected along with renal colic of renal calculi	Abdominal discomfort	Right Lower quadrant pain
Catecholaminergic /Mineralocorticoid signs	Absent	Absent	Absent	Absent	Absent	Absent
Laterality	Right	Right	Left	Left	Right	Left
Laboratory Investigations	WNL	WNL	WNL	WNL	WNL	WNL
Radiological Diagnosis Calcifications (if any)	Well-defined heteroechoic lesion with calcifications	Adrenal mass with calcifications	Adrenal mass D/Ds- Ganglioneuroblastoma neuroblastoma, pheochromocytoma, adenoma, adrenocortical carcinoma	Solid adrenal lesion with nephrolithiasis	Adrenal mass: Non adenoma without calcifications D/Ds-Adrenal lymphangioma, Ganglioneurom, Nerve Sheath tumours.	Adrenal mass: likely to be neoplastic
Intervention	Adrenalectomy	Adrenalectomy	In view of metastatic Ca, no surgery performed	Laparoscopic Adrenalectomy	Adrenalectomy	Exploratory Laparotomy
Pathology Biopsy/ Excision -Size -Microscopy Stroma Ganglion cells Calcifications Necrosis Mitosis	Excision 15x14x9 cm Mature Schwannian stroma Mature Present Absent Sparse	Excision 14x13x9cm Mature Schwannian stroma Mature Absent Absent No atypical mitosis	Biopsy Mature Schwannian stroma Mature Present Absent Sparse	Excision 8.5x6x4cm Mature Schwann cells Maturing Present Absent Sparse	Excision 11.4x11x10cm Schwannian stroma admixed with fibroblasts Mature Absent Absent Sparse	Excision 4.4x5.1x7.3cm Haphazardly arranged Schwann cells Mature Present Absent Sparse
Histopathological Differential diagnosis	Ganglioneuroma	Ganglioneuroma	Benign Spindle cell tumour	Ganglioneuroma	Ganglioneuroma	Ganglioneuroma
IHC Markers applied for final diagnosis	Positive for S-100, negative for Desmin, SMA, Ki-67 <	Not specified	Positive for S-100, Synaptophysin	Not specified/ used	Not specified/ used	Positive for S100, Vimentin, Synaptophysin
Follow up data	No complication identified	Regular monitoring done; no recurrence identified	No complications/ recurrence identified	No complication/ recurrence identified	residual adrenal SOL/Recurrence noted	No recurrence detected

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CONCLUSIONS

AGN is a rare benign neurogenic tumour that is difficult to diagnose preoperatively. Overlapping radiological features and non-functionality of such tumours explains the challenges in making a preoperative diagnosis. Hence, a complete pathological evaluation is required to differentiate AGNs from other solid adrenal masses. Adrenalectomy is therefore required to arrive at a diagnosis besides having an excellent prognosis post-complete resection. Additionally, prospective studies are desired to enable a better understanding of the pathogenesis, preoperative diagnosis, and management of AGNs.

CONTRIBUTION OF AUTHORS

Research concept- Shatarupa Das, Madan K
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Writing article- Madan K, Loretta Ann Pereira
Critical review- Malathi M, Siddhartha Biswas
Article editing- Shatarupa Das, Madan K
Final approval- Malathi M, Siddhartha Biswas

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