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Case Report

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Unraveling the Unexpected: A Case Report of Adrenal Ganglioneuroma

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ABSTRACT

Background: This case report has discussed Adrenal Ganglioneuromas (AGNs) are rare, benign tumors invented from neural crest cells within the sympathetic nervous scheme. Due to their asymptomatic nature and radiological similarity to other adrenal masses, preoperative diagnosis remains challenging. Surgical excision followed by histopathological inspection is important for conclusive diagnosis and management.

Methods: We reported a case of a 51-year-old male who presented with right lower quadrant abdominal pain and a single episode of hematuria. Imaging naked a well-defined, calcified lesion in the right adrenal gland, expressive of an adrenal malignancy. The patient suffered a right adrenalectomy, and the excised tumor was exposed to histopathological and immunohistochemical analysis.

Results: Gross examination exposed a well-encapsulated, firm, tan-white mass. Microscopic analysis recognized Schwannian stroma with interspersed mature ganglion cells, confirming the diagnosis of AGN. Immunohistochemical staining presented diffuse positivity for S-100 and negativity for Desmin and SMA, ruling out other disparity diagnoses. The patient's postoperative course was ordinary, and no recurrence was observed on follow-up.

Conclusion: This study concluded that AGN is an infrequent, benign adrenal tumor that is frequently diagnosed incidentally. Due to its radiological mimicry of malignant adrenal neoplasms, histopathological confirmation is vital. Surgical excision remains the main treatment which offers an excellent prognosis. Increased documentation and study are essential to recover preoperative diagnostic strategies and management approaches.

Key-words: Adrenal gland tumours, Adrenalectomy, Ganglioneuroma, 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]

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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

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have the potential to mimic other adrenal tumours like adrenocortical carcinoma (ACC) and pheochromocytoma. These are hormonally silent tumours and as a result, can be asymptomatic, whilst large tumours can present with pressure symptoms. Hence despite having substantial size, are usually detected incidentally, and are referred to as incidentalomas.[2] Therefore, it is generally challenging to obtain a pre-operative diagnosis of AGN. A definitive diagnosis can be made by histopathological examination. AGNs have a good prognosis following resection. [11] On account of the paucity of data on this disease, research publications are limited to case reports and series. Here we document such a rare case of AGN in a 51-year-old male who required adrenalectomy.

CASE PRESENTATION

A 51-year-old male presented to Urology OPD with complaints of abdominal discomfort for 2 months with a recent bout of haematuria. The patient was not diabetic or hypertensive and did not have a history of any other systemic symptoms.

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 made.

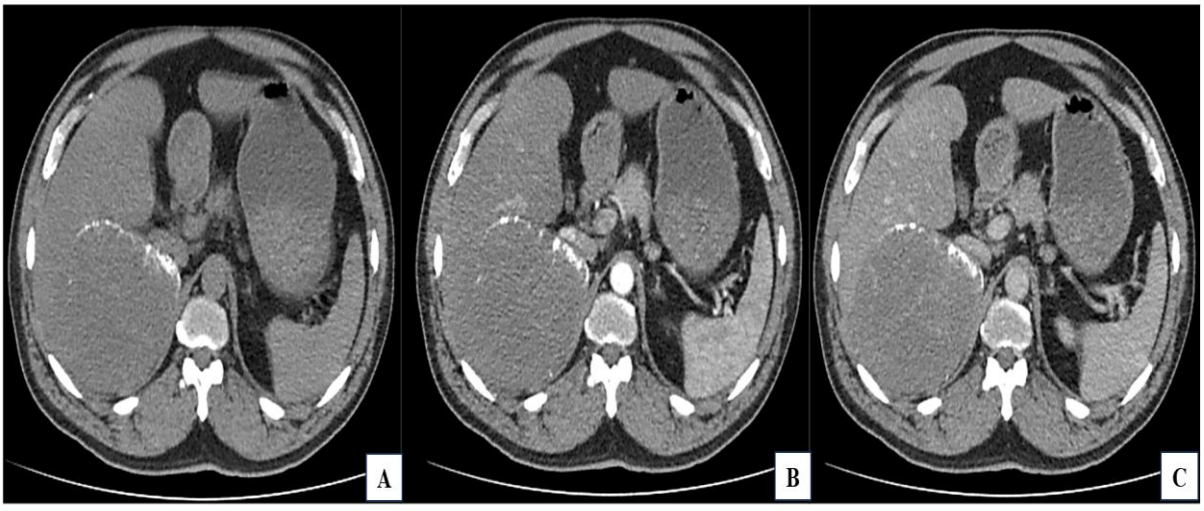

Fig. 1A-C: CT Urogram: Well-defined soft tissue density lesion measuring14x11x10.7cm with calcifications in the right adrenal gland

Subsequently, the patient underwent exploratory laparotomy. A large mass was noted in the suprarenal region which was mobilized from all around and from the upper pole of the kidney. The adrenal gland was not visualized separately. The mass was excised in toto and sent for histopathological examination. The post operative period was uneventful.

A 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

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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 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. Because 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.

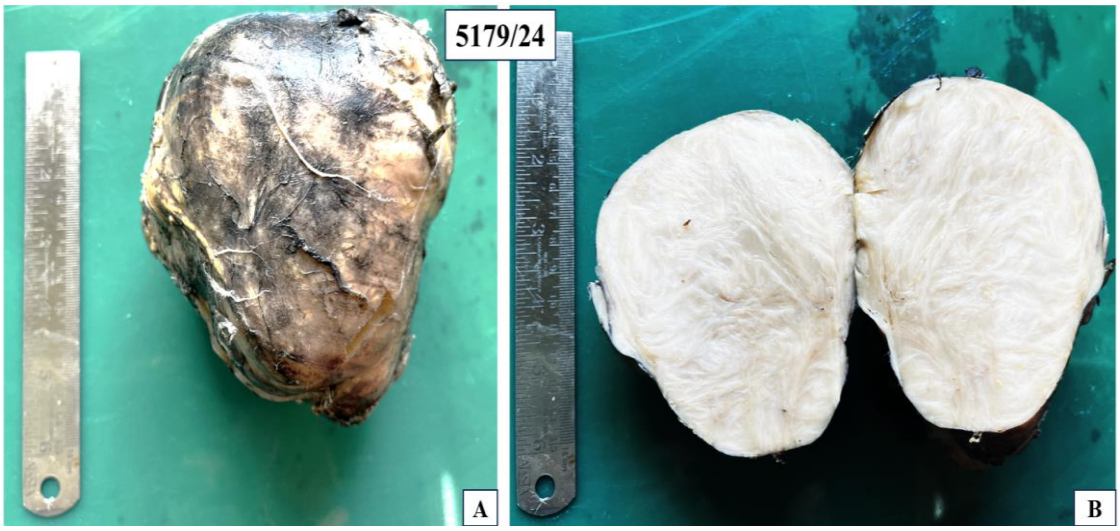

Fig. 2: A. Resected adrenal mass, well encapsulated; **B.** Cut surface-tan white, glistening and firm mass.

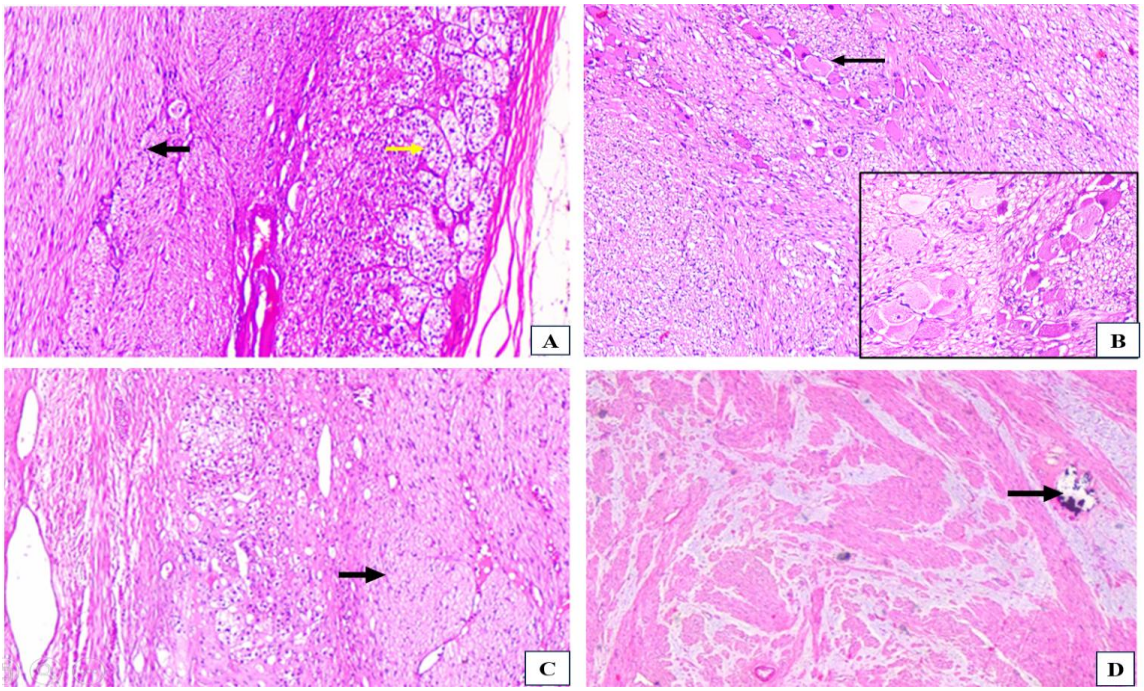

Fig. 3: A. Schwannian stroma (black arrow) and peripherally compressed adrenal parenchyma (yellow arrow); **B.** Mature-looking ganglion cells (inset): large cells with abundant cytoplasm and eccentric nuclei; **C.** Neural bundles amidst the tumour cells; **D.** Fibrous and myxoid stroma with calcification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

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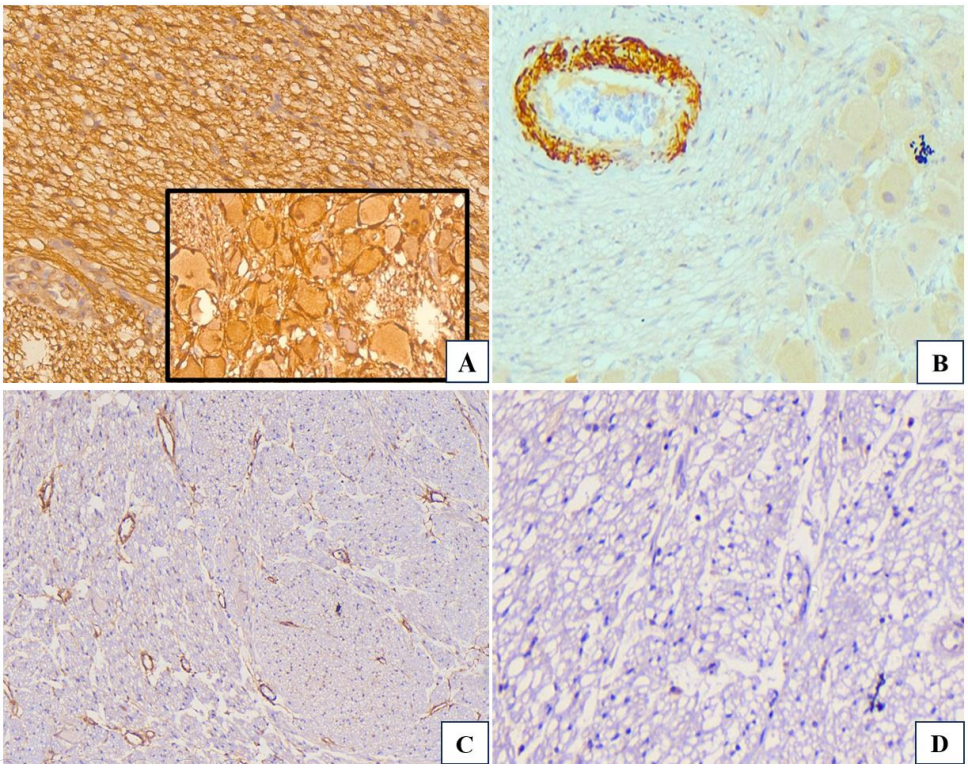

Fig. 4: A. S100-Diffuse strong nuclear and cytoplasmic staining in both ganglion cells and stroma; B. Desmin-Negative in tumour cells and ganglion cells with positive internal control (arrow); C. SMA-Negative in tumour cells highlighting the blood vessels; D. Ki-67- <1%. (100X Magnification)

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 can also 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's 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.[17,18] It is also noteworthy to keep in mind the heterogeneous nature of tumours in the case of composite tumours. Differentiation from other soft tissue tumours and gastrointestinal stromal tumour becomes imperative given diagnostic and definitive therapeutic implications.[20-22]

Ganglioneuromas have a very good prognosis with complete resection. However, some cases have reported late recurrence or malignant transformation, especially after incomplete resection. [23] Because of the 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. [17-20,22]

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.[21] 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

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remained the backbone of management in all cases except the case reported by Aynao et al as it was a case of metastatic colorectal carcinoma. [18] 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 its relationship with multiple endocrine neoplasia is uncertain.[24,25]

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

Parameters	**Present Study**	**Daghdagh *et al.*** [17]	**Aynao *et al.*** [18]	**Alqahtani *et al.*** [19]	**Kayastha *et al.*** [20]	**Adas *et al.*** [22]
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	Given 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 < 1%	Not specified	Positive for S-100, Synaptophysin	Not specified/ used	Nots 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. Owing to the imaging features and the non-functionality of such tumours which explains the difficulty in making a preoperative diagnosis, 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
Research design- Madan K, Loretta Ann Pereira
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Data analysis and Interpretation- Malathi M, Siddhartha Biswas
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Critical review- Malathi M, Siddhartha Biswas
Article editing- Shatarupa Das, Madan K
Final approval- Malathi M, Siddhartha Biswas

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