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Case report

Diagnostic imaging of a rare case of incidental adrenal ganglioneuroma

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Abstract. A 53-year-old man complaining of pain in the right hypochondrium underwent an abdominal ultrasound that showed a left adrenal lesion. Further instrumental investigations (CT and MRI, both with contrast medium) were performed which diagnosed an adrenal ganglioneuroma, confirmed by the histological examination. The patient also underwent an endocrinological examination. The treatment was surgical and consisted of an adrenalectomy through video-laparoscopic access. Adrenal ganglioneuromas are rare tumors but well described and known in the literature. For this reason, this case report has primarily an educational purpose: the totality of the data collected (clinical, laboratoristic, instrumental, and histopathological) constituted a multidisciplinary case, with the focus on imaging. (www.actabiomedica.it)

Key words: adrenal ganglioneuroma, adrenal adenoma, ganglioneuroma, incidentaloma, MRI

Introduction

Adrenal ganglioneuromas (AGNs) are benign sympathetic tumors originating from neural crest cells. It is a rare tumor, therefore its prevalence ranges from 0.3% to 4% across all adrenal masses and is roughly 1 per million in the general population (1).

Ganglioneuromas (GN) mostly affect the posterior mediastinum or retroperitoneum, but they can also develop in the neck and the adrenal glands (2). These lesions are clinically and hormonally silent, hence they are frequently detected occasionally on imaging (3). In most cases GNs are asymptomatic, and the presence of signs or symptoms is due to the mass effect (2).

The definitive diagnosis is histopathological; hence the preoperative diagnosis remains difficult. The gold-standard treatment is adrenalectomy, with a good prognosis after surgery without recurrence (4).

Case presentation

We report the case of a 53-year-old male patient who went to our clinic complaining of pain in the right hypochondrium and epigastrium that did not respond to conservative treatment.

He underwent an abdominal ultrasound that described an occasional finding of a nodule in the left adrenal gland. The finding required further instrumental investigations: an abdominal CT and MRI, both with contrast medium administration, were performed.

The abdomen CT was performed before and after the administration of intravenous iodinated contrast medium (100 mL of Omnipaque 350). It showed a nodular formation with a diameter of 53 mm (anteroposterior) x 40 mm (transverse) x 47 mm (craniocaudal), with thin parietal calcifications in the left adrenal gland. The lesion appeared hypodense in the pre-contrast phase (28 HU). After

the medium contrast administration, in the arterial phase, the lesion didn't present contrast enhancement, while it had a modest enhancement in the portal phase (Figure 1).

Unfortunately, a late-delayed-phase CT sequence (10-15 min.) was not performed for this patient.

Following the CT features the first diagnostic hypothesis was a lipid-poor adrenal adenoma, worthy of

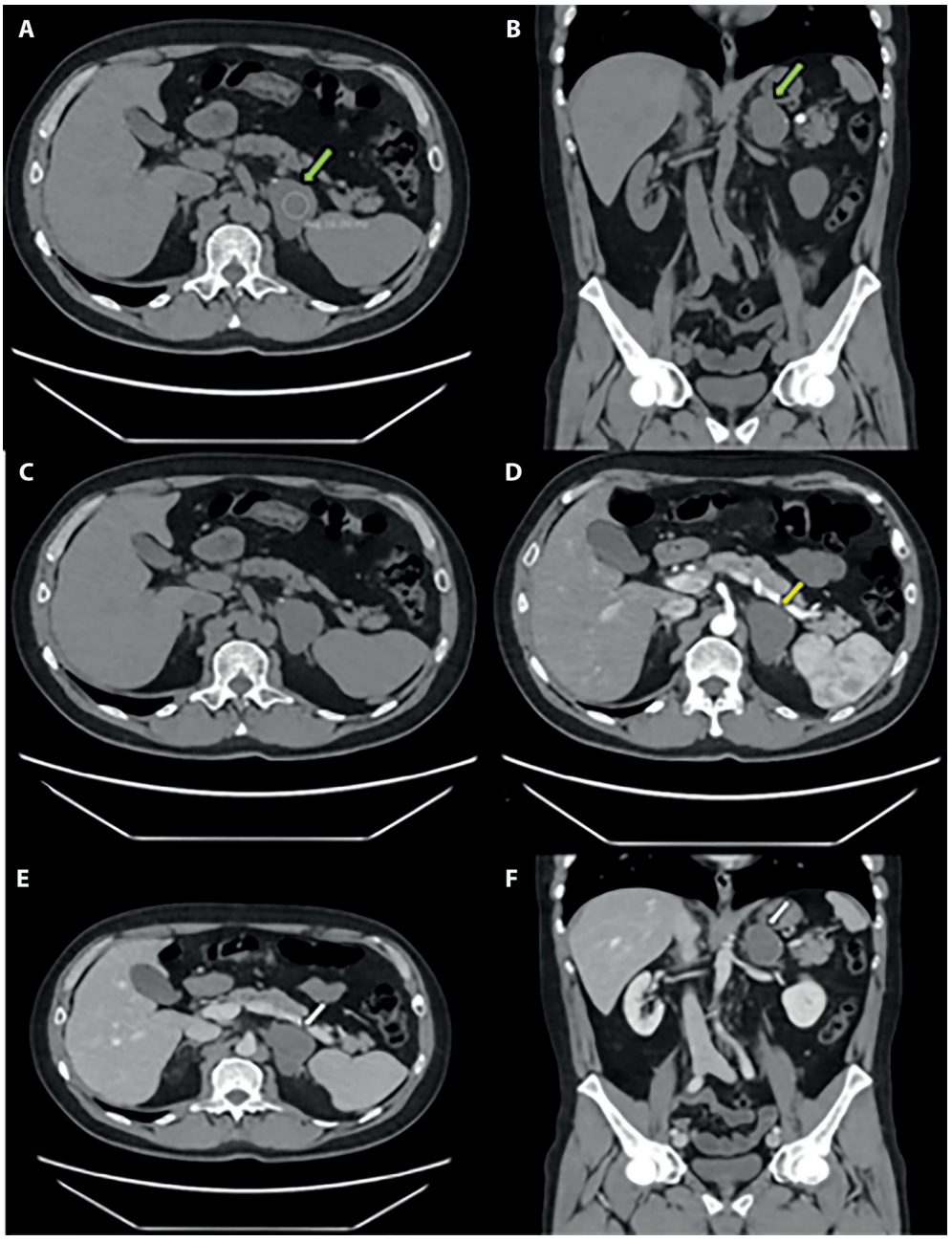

Figure 1. Axial (A) and coronal (B) plane of the pre-contrast CT showed the nodular formation in the left adrenal gland (green arrows) with thin parietal calcifications. (*) In the pre-contrast phase, in the axial plane, the nodule appeared hypodense (C). In the arterial phase, in the axial plane (D), the lesion did not present contrast enhancement (D). In the portal phase, in the axial (E) and coronal plane (F), the nodule had a modest contrast enhancement (white arrows).

further diagnostic investigation by MRI examination with contrast medium administration.

After 30 days, the patient underwent an MRI with high-field equipment (1.5 Tesla) before and after contrast medium administration (16 ml ProHance). The MRI protocol included T1-Weighted (T1-W) and T2-Weighted (T2-W) images in three planes, diffusion-weighted images (DWI), and Dynamic Contrast Enhanced (DCE) images in the axial plane.

The MRI examination showed in the left adrenal gland, an oval-shaped area with clear and regular margins, approximately 50 mm (anteroposterior) x 35 mm (transverse) in size. It appeared hypointense on T1-weighted sequences and hyperintense and inhomogeneous on T2-weighted sequences. It didn't show any signal drop in the out-of-phase sequence and no areas of restriction in DWI sequences and ADC map. After intravenous administration of the contrast medium, the lesion showed late and inhomogeneous contrast enhancement (Figure 2).

The features of the left adrenal lesion in the different MRI sequences confirmed the main diagnostic suspicious of a lipid-poor adrenal adenoma. Therefore,

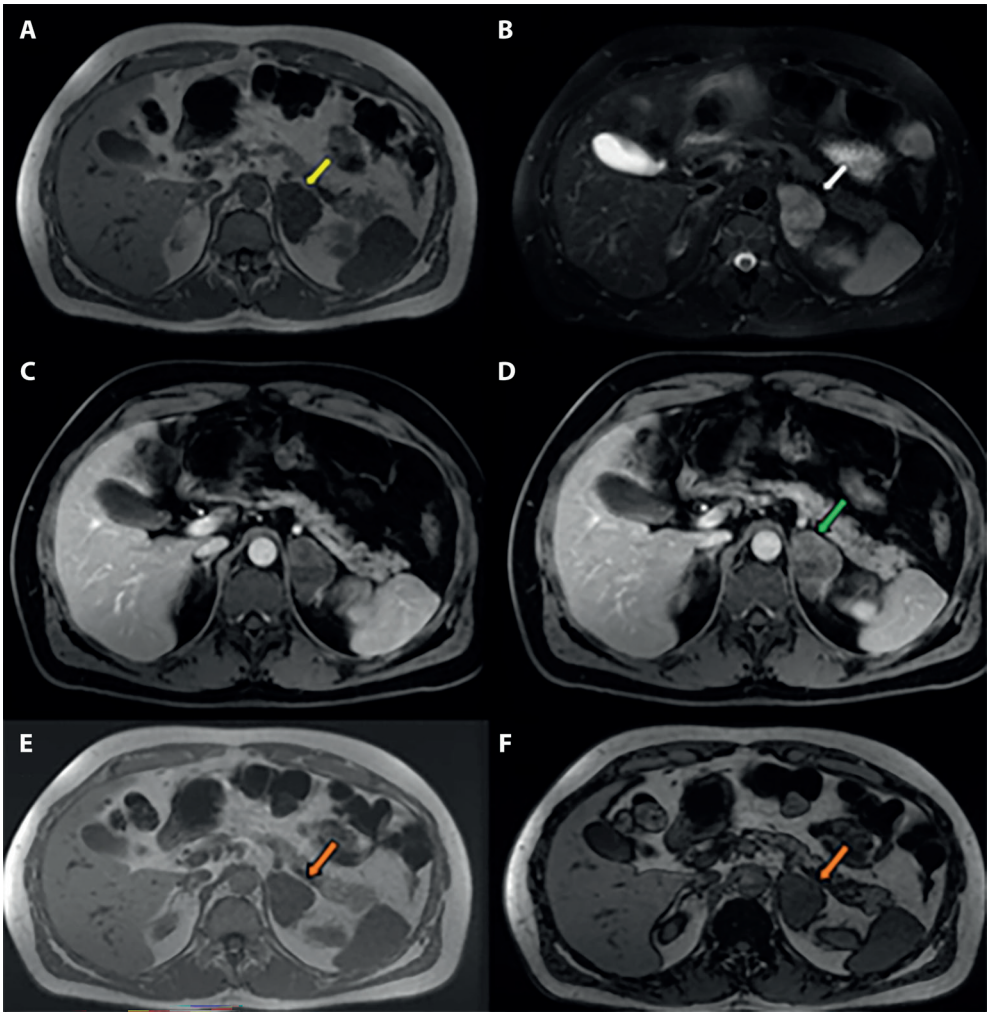

Figure 2. The left adrenal lesion showed a hypointense signal (yellow arrow) on the T1-W axial sequence (A) and an inhomogeneous hyperintense signal (white arrow) on the T2-W axial fat-suppressed sequence (B). After the contrast medium administration, on the axial T1-W sequences (C and D) the left adrenal lesion showed a late contrast enhancement (green arrows). The left adrenal lesion showed no signal drop (orange arrow) in the out-of-phase sequence (F) compared to the in-phase sequence (E).

the absence of a drop signal in the out-of-phase and the T2-W fat-suppressed sequences excluded a lipid-rich adenoma.

In addition to instrumental examinations, the patient underwent endocrinological tests to assess the adrenal function. All the test results were within the normal range, underlining that the adrenal lesion was not producing hormones (Table 1).

Subsequently, the patient underwent an endocrinological examination that revealed no endocrinopathy disorders and adrenal dysfunction; sexual characteristics were regular; blood pressure of 120/80 mmHg; and weight of 85 kg.

Based on the tests performed, the endocrinologist ruled out possible hypersecretions of adrenal hormones and he did not consider alpha-blocker therapy or glucocorticoid replacement therapy necessary after the surgical exeresis.

The surgical treatment performed was a video-laparoscopic left adrenalectomy.

The histopathological examination reported:

- the gross examination showed an adrenal gland (64g) with a well-circumscribed tumor (7 x 6 x 3,5 cm), with a homogeneous white color and small bundles aspect cut surface. The tumor appeared encapsulated in adrenal parenchyma.
- The microscopic examination showed a tumor composed of Schwann cells forming fascicles with scattered small clusters and nests of mature ganglion cells. Mature ganglion cells were characterized by abundant eosinophilic cytoplasm and round, eccentrically localized nuclei. No tumor necrosis or mitotic figures were present. The Schwann cells and ganglion cells were positive for S100 stains and for synaptophysin stains (Figure 3).

All these findings were typical features of ganglioneuroma, a mature subtype (according to the

Table 1. Results of endocrinological tests before surgery.

	Results	**Normal values**
Urinary metanephrines	105,0 µg/24h	52-341 µg/24h
Urinary normetanephrines	355 µg/24h	88-444 µg/24h
Urinary 3-methoxytyramine	35 µg/24h	55-247 µg/24h
Cortisol	17,9 µg/dl	4,8-19,5 µg/dl
Urinary cortisol	342 µg/24h	58-403 µg/24h
Urinary epinephrine	8 µg/24h	2-22 µg/24h
Urinary norepinephrine	43,7 µg/24h	20-81 µg/24h
Urinary dopamine	99,1 µg/24h	40-400 µg/24h
Epinephrine	22 pg/ml	3,7-82 pg/ml
Norepinephrine	634 pg/ml	80-499 pg/ml
Dopamine	45 pg/ml	2-58 pg/ml
17-OH-progesterone	0,2 ng/ml	men: 0,5-2,1 ng/ml
DHEA-S (dehydroepiandrosterone-S)	227,4 mcg/dl	54 y.o.: 35,4-256 mcg/dl
Total testosterone	13,06 nmol/l	men: 6-27 nmol/l
Aldosterone	69 pg/ml	25,2-392 pg/ml
ACTH	29,5 pg/ml	0-60 pg/ml
Androstenedione	0,38 ng/ml	adults: 0,5-3,5 ng/ml
SHBG (sex hormone binding globulin)	33,06 nmol/l	men: 20,6-76,7 nmol/l
Renin	5,42 mUI/ml	4,4-46,1 mUI/ml

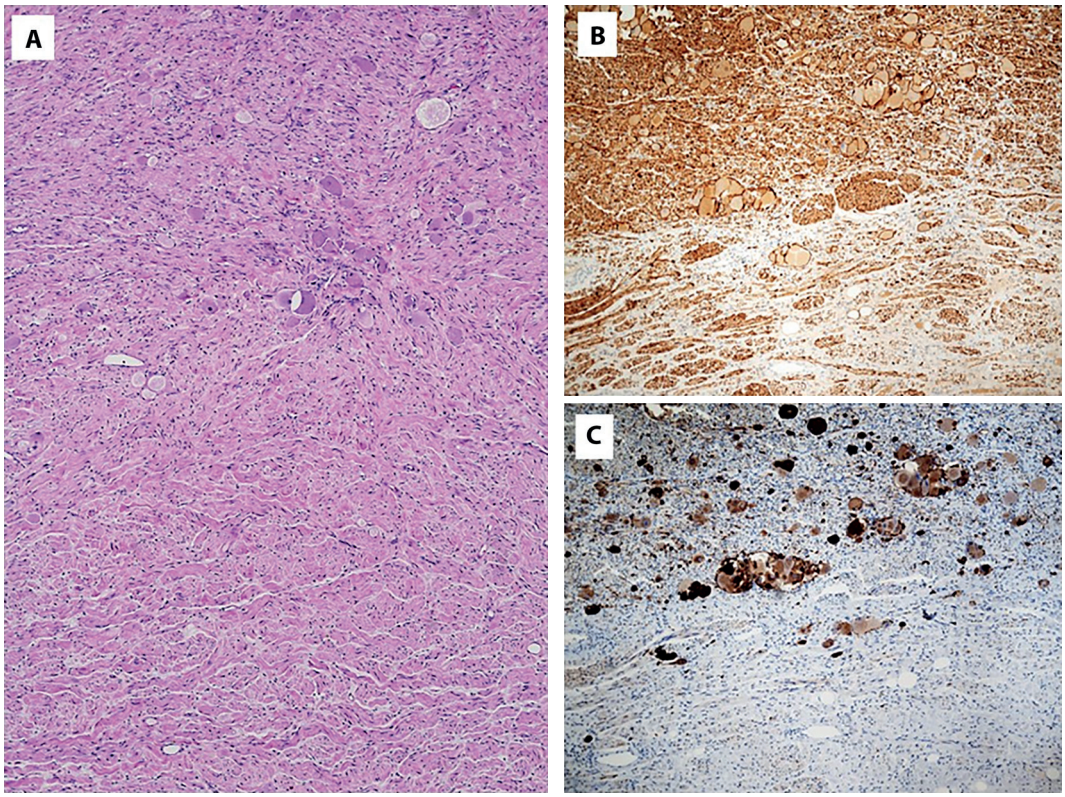

Figure 3. Tumor composed of Schwann cells forming fascicle with scattered small clusters and nests of mature ganglion cells (hematoxylin and eosin 100x magnification) (A). Schwann cells and ganglion cells are positive for S100 stains (100x magnification) (B) and synaptophysin (100x magnification) (C).

International Neuroblastoma Pathology Classification - INPC), and this was the final diagnosis.

About a month after the surgical treatment, the patient went to a new endocrinological check-up which showed no altered adrenal function, apart from a slight drop in blood pressure (104/74 mmHg), therefore only hormonal checks were requested. The latter were within the normal limits.

Discussion

The International Neuroblastoma Pathology Classification (INPC) divides neuroblastic tumors into four subcategories based on their morphology, clinical features, and behavior: neuroblastoma, nodular ganglioneuroblastoma, intermixed ganglioneuroblastoma, and ganglioneuroma (5).

Radiologically, an abdominal neurogenic tumor typically appears as a well-defined, smooth, or lobulated mass. Unless distant metastatic foci are found, it is difficult to distinguish between benign and malignant neurogenic tumors. However, CT and MRI imaging can be useful to determine the tumor's local extent and to exclude other malignancies (6).

Considering the location, 56% of ganglioneuromas develop in the mediastinum or retroperitoneum, 30% in the adrenal gland, and 14% from unusual locations such as the pharynx, bladder, uterus, or gastrointestinal tract (2).

AGN is a benign, differentiated, and very rare tumor with slow growth. The peak incidence of AGN is in the 4th–5th decade of life (5). It is usually asymptomatic, but in some cases, patients might complain of abdominal pain/discomfort, back pain, weight loss, and hot flashes. When it grows to a large size, it

determines a palpable abdominal mass. An AGN may rarely elicit symptoms of virilization and hypertension due to its non-secreting hormonal nature (1).

Most ganglioneuromas are discovered incidentally in imaging studies (7).

Ultrasonography shows a well-defined, homogeneous, hypoechogenic mass, separated from the kidney that in some cases is displaced (8, 9).

On unenhanced CT, attenuation values equal to or less than 10 HU are selective for lipid-rich lesions and thus have high specificity for adenomas. Other radiographic criteria are the appearance (i.e., integrity and invasiveness) the heterogeneity, the lesion borders, and the size. A malignant tumor is indicated also by necrosis, calcifications, bleeding foci, and heterogeneity (10).

The CT findings of AGN are quite like those of other benign adrenal tumors. Given the low invasiveness of tumors, invasion of surrounding tissues or organs is generally not observed. CT imaging typically indicates a homogenous or slightly heterogeneous mass that surrounds major blood vessels without compression or blockage. The tumor is well-defined, hypodense, and it usually does not present a high contrast enhancement. Calcifications, which are generally fine and punctate, are found in 42-60% of GNs. The early enhancement of linear septae has been described, as the delayed heterogeneous contrast uptake in some circumstances (11, 12).

MRI typical features are a hypointense T1-W signal and a hyperintense heterogeneous T2-W signal, as described in this case (13, 14).

However, none of these characteristics can distinguish AGNs from malignant adrenal tumors.

It is extremely important to perform the Chemical Shift Imaging (CSI) to be able to differentiate an AGN from an adenoma. When compared to 'in-phase' sequences, adenomas have at least 30% of their signal dropout on 'out-of-phase' sequences, due to the presence of small amounts of intracellular fat (10).

Biopsy with histological examination is the current diagnostic gold standard and should be thorough to exclude ganglioneuroblastoma or neuroblastoma foci, which have a poorer prognosis.

Definitive treatment of ganglioneuromas is either laparoscopic or open surgical resection of the tumor. The prognosis in these patients is excellent after resection and no tumor recurrence or metastasis occurs (4).

Ethics Approval and Consent to Partecipate: Written consent was obtained from the patient to publish the case report.

Informed consent: Written informed consent for publication was obtained from the patient.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement, etc.) that might pose a conflict of interest in connection with the submitted article.

References

1. Zilberman DE, Drori T, Shlomai G, et al. Adrenal ganglioneuroma resected for suspicious malignancy: multicenter review of 25 cases and review of the literature. Ann Surg Treat Res. 2021 Aug;101(2):79-84. doi: 10.4174/astr.2021.101.2.79.
2. Burroughs MA Jr, Urits I, Viswanath O, Kaye AD, Hasoon J. Adrenal Ganglioneuroma: A Rare Tumor of the Autonomic Nervous System. Cureus. 2020 Dec 31;12(12):e12398. doi: 10.7759/cureus.12398.
3. Aynaou H, Salhi H, El Ouahabi H. Adrenal Ganglioneuroma: A Case Report. Cureus. 2022 Aug 3;14(8):e27634. doi: 10.7759/cureus.27634.
4. Deflorenne E, Peuchmaur M, Vezzosi D, et al. Adrenal ganglioneuromas: a retrospective multicentric study of 104 cases from the COMETE network. Eur J Endocrinol. 2021 Aug 27;185(4):463-474. doi: 10.1530/EJE-20-1049.
5. Lam AK. Update on Adrenal Tumours in 2017 World Health Organization (WHO) of Endocrine Tumours. Endocr Pathol. 2017 Sep;28(3):213-227. doi: 10.1007/s12022-017-9484-5.
6. Rha SE, Byun JY, Jung SE, et al. Neurogenic tumors in the abdomen: tumor types and imaging characteristics. Radiographics. 2003 Jan-Feb;23(1):29-43. doi: 10.1148/rg.231025050.
7. Qing Y, Bin X, Jian W, et al. Adrenal ganglioneuromas: a 10-year experience in a Chinese population. Surgery. 2010 Jun;147(6):854-860. doi: 10.1016/j.surg.2009.11.010.

8. Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma: radiologic-pathologic correlation. Radiographics. 2002 Jul-Aug;22(4):911-934. doi: 10.1148/radiographics.22.4.g02jl15911.
9. Aderotimi TS, Kraft JK. Ultrasound of the adrenal gland in children. Ultrasound. 2021 Feb;29(1):48-56. doi: 10.1177/1742271x20951915.
10. Viëtor CL, Creemers SG, van Kemenade FJ, van Ginhoven TM, Hofland LJ, Feelders RA. How to Differentiate Benign from Malignant Adrenocortical Tumors? Cancers (Basel). 2021 Aug 30;13(17):4383. doi: 10.3390/cancers13174383.
11. Otal P, Mezghani S, Hassissene S, et al. Imaging of retroperitoneal ganglioneuroma. Eur Radiol. 2001;11(6):940-5. doi: 10.1007/s003300000698.
12. Majbar AM, Elmouhadi S, Elaloui M, et al. Imaging features of adrenal ganglioneuroma: a case report. BMC Res Notes. 2014 Nov;7:791. doi: 10.1186/1756-0500-7-791.
13. Alqahtani SM, Alshehri M, Adi H, Moharram L, Moustafa Y, Alalawi Y. Left Adrenal Ganglioneuroma Treated by Laparoscopic Adrenalectomy in a 41-Year-Old Woman: A Case Report. Am J Case Rep. 2022 May;23:e936138. doi: 10.12659/ajcr.936138.
14. Wang F, Liu J, Zhang R, et al. CT and MRI of adrenal gland pathologies. Quant Imaging Med Surg. 2018 Sep;8(8):853-875. doi: 10.21037/qims.2018.09.13.

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