

DOPAMINE-SECRETING GIANT ADRENAL GANGLIONEUROMA: CLINICAL AND DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING FINDINGS

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We report a case of a dopamine-secreting giant primary adrenal ganglioneuroma (GN) in a 29-year-old male patient. Although the patient was clinically silent, the 24-hour urine levels of dopamine, normetanephrine, homovanillic acid and vanillyl mandelic acid were elevated. Abdominal ultrasonography and magnetic resonance imaging showed a large solid tumor with calcifications and a slightly lobular edge on the left adrenal gland. A tumor, 13 × 23 × 25 cm in size, was completely resected without morbidity. A 2-year follow-up with computed tomography showed that the postoperative course of the patient was uneventful.

Key-words: Ganglioneuroma – Magnetic resonance imaging – Diffusion-weighted imaging – Adrenal gland.

Ganglioneuroma (GN) is a rare well-differentiated benign slow-growing tumor, arising from the primordial neural crest tissue anywhere along the paravertebral sympathetic plexus. It is most commonly located in the posterior mediastinum, aortocaval sympathetic ganglia, and retroperitoneum. However, the adrenal gland is a rare location for a GN, and primary adrenal GNs in adults have been reported in small series so far. The increased use of various imaging modalities has led to an increase in the number of incidentally identified GNs. GN is composed of mature ganglion cells and Schwann cells in a fibrous stroma. Adrenal GN is usually asymptomatic and hormonally inactive, but some of them secrete catecholamines and their metabolites – cortisol or androgens (1-3).

Differential diagnosis in the case of adrenal incidentalomas is a crucial point before performing surgery. GN is considered benign; however, adrenal carcinomas and pheochromocytomas are the differential diagnoses that need detailed evaluation and special preoperative intervention.

We report diffusion-weighted magnetic resonance imaging (MRI) findings in a giant primary adrenal GN, which was found to secrete dopamine, and to the best of our knowledge, this case presents the largest pure GN in the literature.

Case

A 29-year-old male patient was suffering from chronic abdominal discomfort in the left upper quadrant for the past 2 years. When he was

admitted to the clinic, a palpable mass located in the left upper quadrant was found on physical examination. He had no headache, palpitation, flushing, hypertension, or Cushingoid phenotype. His blood pressure was 120/70 mm Hg and pulse was 72.

Laboratory tests, including peripheral blood examination, liver function tests, renal function tests, urinalysis, and electrolyte determination, conducted on admission showed no abnormal findings. Endocrine examination revealed increased levels of 24-hour urinary concentrations of dopamine, 18695 µg/dl (normal range, 0–500 µg/dl); normetanephrine, 461 µg/dl (normal range,

105–354 µg/dl); homovanillic acid (HMA), 280.84 mg (normal range, 2–7.4 mg); and vanillyl mandelic acid (VMA), 10.62 mg (normal range, 0–6.6 mg). On the other hand, levels of 5-hydroxy-indol-acetic acid (5-HIAA), adrenaline, noradrenaline, metanephrine, and 5-hydroxy-tryptamine (serotonin) were within normal ranges. Plasma levels of cortisol, adrenocorticotropin, dehydroepiandrosterone sulfate, and testosterone were within normal ranges. Cortisol response on 1 mg dexamethasone suppression test was < 1 µg/dl. Based on these findings, the patient's condition was diagnosed as a pheochromocytoma selectively secreting dopamine. Preoperatively, he was administered 2 mg doxazosin daily and was recommended adequate hydration.

Ultrasonography (US) was performed using Toshiba Aplio XG SSA-790A (Toshiba Medical Systems, Tokyo, Japan) with 3.5 MHz convex probes. US examination revealed a

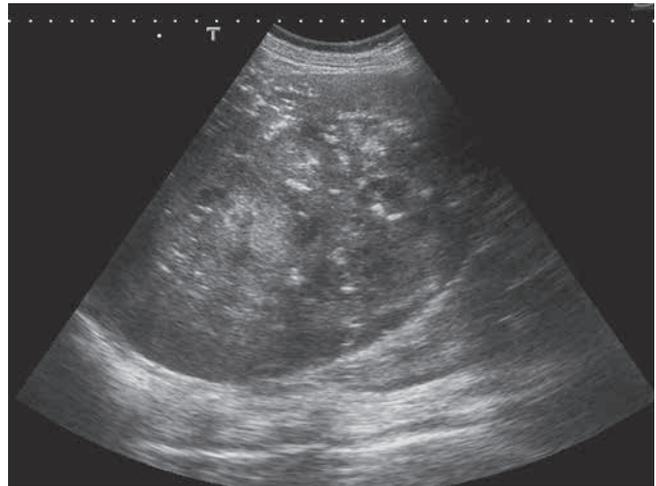


Fig. 1. — Abdominal ultrasonography showed a heterogeneous hypoechoic left adrenal solid mass with faint calcifications and a slightly lobular edge.

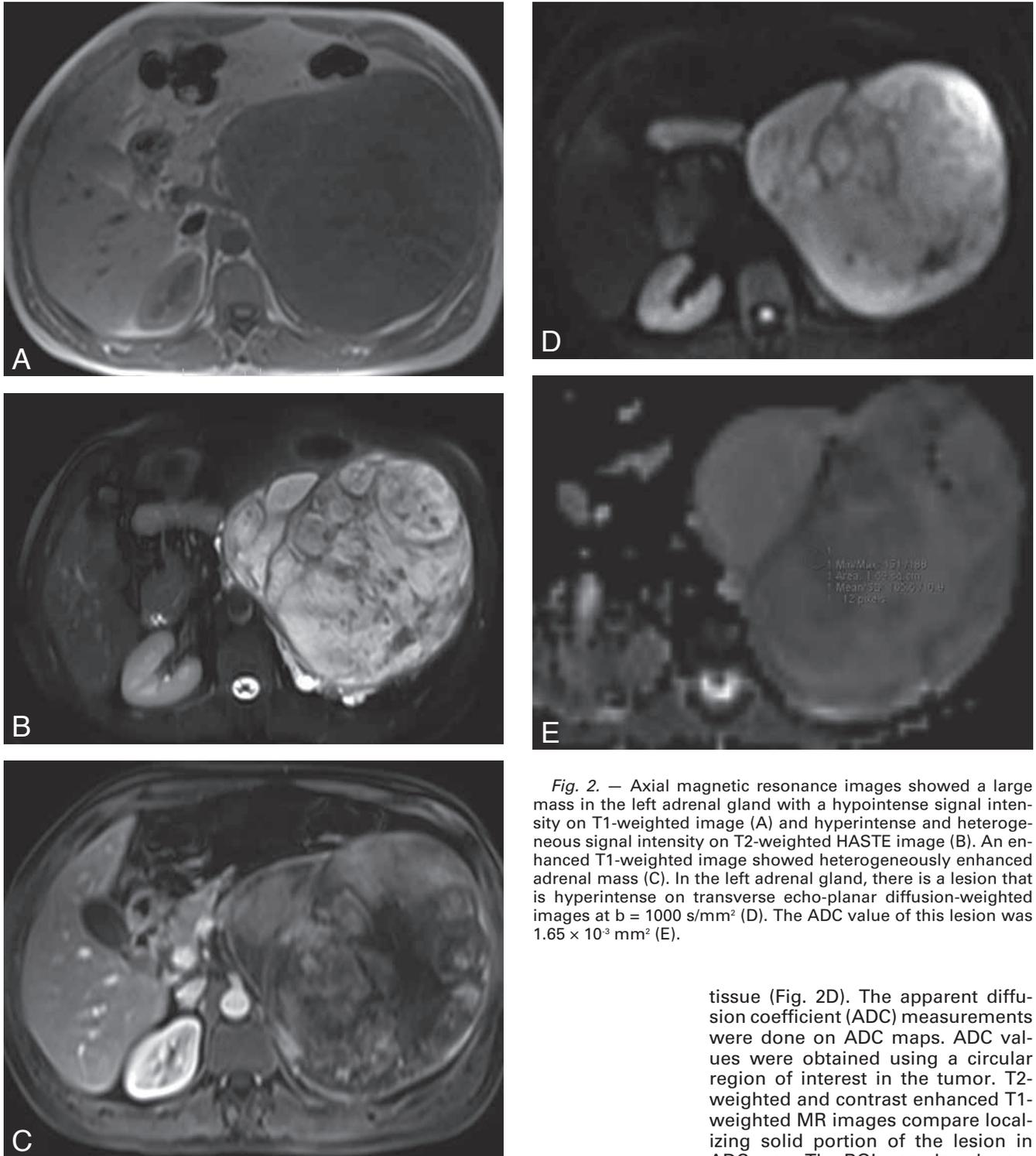


Fig. 2. — Axial magnetic resonance images showed a large mass in the left adrenal gland with a hypointense signal intensity on T1-weighted image (A) and hyperintense and heterogeneous signal intensity on T2-weighted HASTE image (B). An enhanced T1-weighted image showed heterogeneously enhanced adrenal mass (C). In the left adrenal gland, there is a lesion that is hyperintense on transverse echo-planar diffusion-weighted images at $b = 1000 \text{ s/mm}^2$ (D). The ADC value of this lesion was $1.65 \times 10^{-3} \text{ mm}^2$ (E).

heterogeneous hypoechogenic lobulated mass calcified in the left upper quadrant (Fig. 1).

Abdominal MRI was performed for further lesion characterization by using the 1.5-T Siemens Symphony system (Siemens Medical Solutions, Erlangen, Germany). The tumor in the adrenal gland showed low-signal intensity on T1-weighted MRI

(Fig. 2A), and a heterogeneous high-signal intensity and millimetric hypointensities consistent with calcifications on T2-weighted MRI (Fig. 2B). The mass demonstrated heterogeneous contrast enhancement after intravenous injection of gadolinium (Fig. 2C). On diffusion-weighted imaging (DWI), the lesion was hyperintense compared to the adjacent

tissue (Fig. 2D). The apparent diffusion coefficient (ADC) measurements were done on ADC maps. ADC values were obtained using a circular region of interest in the tumor. T2-weighted and contrast enhanced T1-weighted MR images compare localizing solid portion of the lesion in ADC map. The ROI was placed manually within the solid portion of the lesion. Multiple measurements were done for lesion, and the lowest one was accepted as the ADC value. This lesion showed lowest ADC value of $1.65 \times 10^{-3} \text{ mm}^2/\text{s}$ ($b = 1000 \text{ s/mm}^2$) (Fig. 2E). MRI showed signs of displacement of the left diaphragm, tail of the pancreas, and pressure signs throughout the splenic and renal vessels, all caused by the mass. There was no evidence of surround-

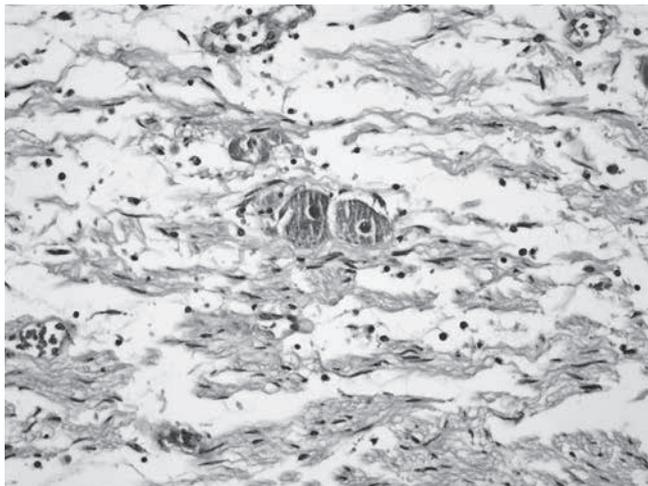


Fig. 3. — A microscopic view of the adrenal GN. The tumor was composed of mature ganglion cells and Schwann cells with abundant fibrous stroma (Hematoxylin and Eosin staining, original magnification $\times 400$).

ing tissue infiltration, regional lymph node enlargement, or intra-abdominal fluid.

Because the tumor was large, $13 \times 23 \times 25$ cm, an open transabdominal adrenalectomy with complete tumor excision was performed. The cut surface of the tumor was grayish-white with extensive mucoid degeneration and calcification. Histopathological examination revealed that the adrenal tissue was replaced by tumor composed of low cellular density consisted of mature ganglion cells and Schwann cells surrounded by more stroma. No evidence of malignancy or pheochromocytoma-related findings indicated that the tumor was a pure GN (Fig. 3). The immunohistochemical staining was performed using antibodies for S 100, synaptophysin for Schwann cells, and neuron specific enolase (NSE) positive staining for ganglion cells.

During the postoperative follow-up, the clinical and laboratory findings were normal. Two years after the operation, the clinical course of the patient was uneventful, and CT showed no residual tissue or tumor recurrence.

Discussion

GN is a slow-growing tumor in the group of neurogenic tumors that originates in the ganglion cells, like ganglioblastoma and neuroblastoma, but the main difference is that GN consists of mature and differentiated cells. GNs are rare, mostly asymptomatic, and hormonally non-functioning; however, occasionally they may cause nonspecific mass-

related symptoms and may be hormonally active, secreting catecholamine or its metabolites (1-3).

Unlike noradrenaline/adrenaline-secreting pheochromocytomas/paragangliomas, dopamine-secreting tumors lack a classical presentation, are extra-adrenal, and have a higher malignant potential (4). Measurement of urinary dopamine may be very useful in detecting this rare tumor with selective dopamine hypersecretion, because plasma metanephrine fractions are not direct metabolites of dopamine and may be normal in the setting of a dopamine-secreting tumor (5).

On CT, adrenal GNs appear as well-circumscribed, homogeneous masses that demonstrate mild enhancement. Calcifications appear in approximately 2.4–50% of the cases (1-3). Calcification was seen in our case. Accurate diagnosis of adrenal GN before surgery is usually difficult; Qing reported a 64.7% rate of misdiagnosis of adrenal GN with CT and MRI (3). On MRI, GN shows homogeneously low or intermediate signal intensity on T1-weighted images; and heterogeneous slightly high-signal intensity on T2-weighted images. The heterogeneity on T2-weighted images depends on the amount of myxoid stroma, collagen fibers, and cellular components in the tumor (6-8). Gahr et al. studied the differences between GN, ganglioneuroblastoma, and neuroblastoma by evaluating their ADC values on MRI. In their study, the mean ADC of the 4 GNs and 2 ganglioneuroblastomas was 1.60×10^{-3} mm²/s (SD 0.34×10^{-3} mm²/s; range, 1.13-1.99 \times

10^{-3} mm²/s), and it was suggested that the higher cellularity of malignant lesions restricted free diffusibility of water molecules; thus, increased cellularity and dense tissues have a relatively low ADC (9). In our case, the ADC value of lesion was 1.65×10^{-3} mm²/s, similar to the value in Gahr's study. Kim et al. (8) recently reported DWI findings of an intracranial GN that showed relatively low ADC values (mean ADC, 0.72×10^{-3} mm²/s). The difference between Kim's cases and our case may be due to the different tumor histopathologies. Although they concluded that differentiation was not yet clear, they found that all neuroblastomas had lower ADC values than did GNs and ganglioneuroblastomas.

The differential diagnosis among adrenal incidentalomas, adrenal carcinomas and pheochromocytomas need detailed evaluation is a crucial point before surgery. Preoperative pharmacologic preparation is indicated for all patients with catecholamine-secreting neoplasms. Resecting a pheochromocytoma is a high-risk surgical procedure and an experienced surgeon/anesthesiologist team is required. Cardiovascular and hemodynamic variables must be monitored closely. Controlling hypertension (including preventing a hypertensive crisis during surgery) and volume expansion is mandatory. As stated in the article, preoperatively, the patient was administered 2 mg doxazosin daily (alpha adrenergic blockade) and hydrated adequately. Unlike ganglioneuromas, adrenocortical carcinomas are rare and aggressive tumors. Complete surgical resection is the only potentially curative treatment for those tumors. Resection of pheochromocytomas has the risks of hypertensive crisis, malignant arrhythmia, and multiple organ failure (10). On the other hand, resection of adrenocortical carcinomas, with respect to choosing between open and laparoscopic procedures, is critical in the cases where invasion of perirenal tissue is suspected. On DWI, the ADC value of our case was consistent with a benign lesion, but because the tumor size was measured to be 25 cm and elevated hormone levels were coherent for pheochromocytoma endocrinologically, an open transabdominal adrenalectomy with complete tumor excision was performed.

Macroscopically, GNs are large encapsulated firm masses with homogeneous, grayish-white cut surface. On immunohistochemical staining,

they are characterized with S-100, NSE, and synaptophysin positivity (1, 3). The histology of adrenal GN has been reported to be overlap with that of cortical adenoma/pheochromocytoma, and myelolipoma (1). The present case showed histological findings specific for GN, and despite elevated hormone levels, the patient symptoms were clinically silent.

Prognosis of mature GN is excellent when resected completely. In our case, two years after complete resection, the patient was evaluated endocrinologically and with CT and no sign of recurrence was observed.

In conclusion, GNs are rare benign tumors and have a favorable prognosis when completely resected. However, their mixed histopathological pattern, variability in hormonal activity, and possible suspicious imaging characteristics of adrenal masses occasionally make accurate preoperative diagnosis difficult. Suspicious malignant imaging findings were size and calcifications

in this case. However, DWI was able to contribute the diagnosis of lesion as benign with obtaining high ADC value.

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