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Case Report

Adrenal Ganglioneuroma Presenting as an Incidentaloma in an Adolescent Patient

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ABSTRACT

Objective: In an adult endocrine clinic, the majority of patients referred for evaluation of an incidentally discovered adrenal mass are aged more than 30 years, for which many national and international societies have developed management guidelines. However, adrenal incidentalomas in children and young adults are uncommon. We report the case of an 18-year-old woman with an incidentally discovered right-sided adrenal mass.

Methods: We present the adrenal tests, computed tomography, and magnetic resonance imaging results and treatment of a young woman with an adrenal mass that proved to be a ganglioneuroma.

Results: A computed tomography scan showed a 2.2 × 2.6 cm right-sided adrenal mass with noncontrast Hounsfield units >10 and <50% washout. Magnetic resonance imaging was not typical of a lipid-rich adenoma. Blood and urine tests demonstrated normal secretion of cortisol, aldosterone, adrenal androgens, and catecholamines. Based on the patient's age and imaging studies, she underwent a right adrenalectomy, removing a 2.2 × 2.0 × 2.7-cm ganglioneuroma.

Conclusion: The differential diagnosis of an adrenal mass in children and adolescents is quite different compared with adult patients. There are no standardized guidelines for the management of adrenal masses in these younger age groups, although some authors recommend removing all adrenal masses, regardless of size or imaging characteristics, in all children aged more than 3 months. This case emphasizes how the management of adrenal masses in pediatric patients and young adults differs from guidelines published by endocrine and urologic societies.

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Introduction

In an adult endocrine clinic, the majority of patients referred for evaluation of an incidentally discovered adrenal mass are aged more than 30 years, for which many national and international societies have developed management guidelines.^{1–8} The majority of adrenal masses in adults are nonfunctioning, relatively small in size, and can be followed up without surgery. Adrenal incidentalomas in children and young adults are uncommon, and there are no standardized guidelines; however, there are recommendations

to remove all adrenal nodules, regardless of size or imaging characteristics, found in children aged more than 3 months.^{9–11} We report the case of an 18-year-old woman who presented with a right-sided adrenal mass that proved to be a ganglioneuroma to emphasize that although a patient may be diagnosed with an adrenal nodule at any age, the etiology differs and management should vary depending on the age at presentation.

Case Report

An 18-year-old woman with no significant past medical problems presented with a 2-month history of abdominal pain associated with nausea and vomiting. An abdominal computed tomography (CT) scan followed by a dedicated adrenal CT scan showed a right-sided adrenal mass measuring 2.2 × 2.6 cm. Non-contrast Hounsfield units (HU) were 36; enhanced HU, 106; and 10-minute washout HU, 70. The calculated washout was 34%, inconsistent with a lipid-rich adrenal adenoma (Fig. 1). Magnetic

Abbreviations: CT, computed tomography; HU, Hounsfield units; MRI, magnetic resonance imaging.

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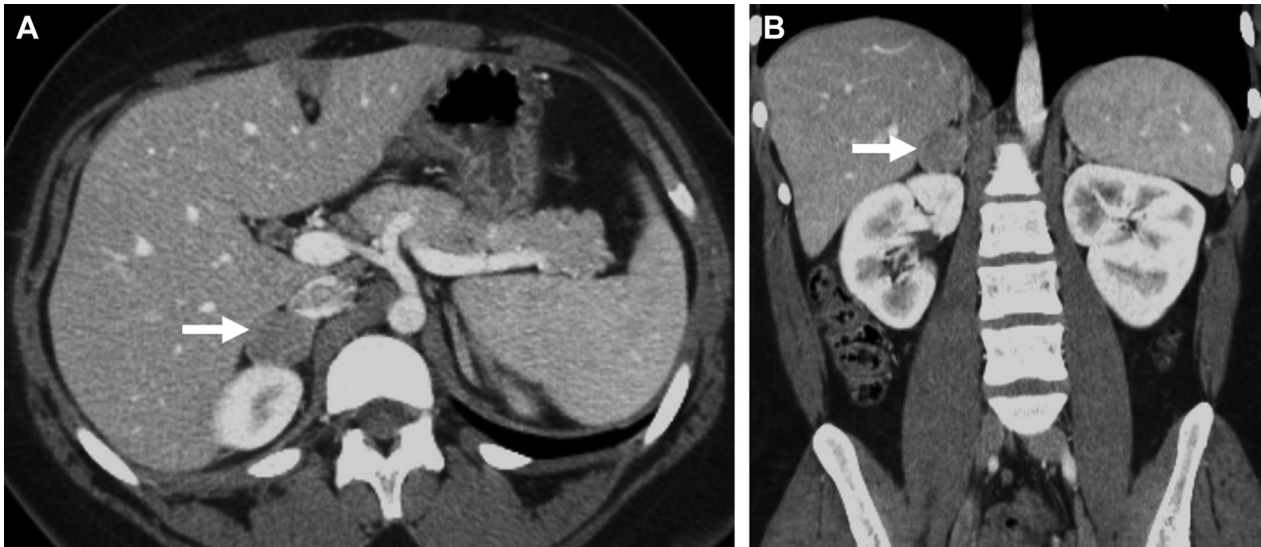


Fig. 1. Axial (A) and coronal (B) computed tomography images of the upper abdomen after the injection of intravenous water-soluble contrast material. There is a nodule in the right adrenal gland (arrows). The left adrenal gland is normal. Noncontrast HU of the right-sided adrenal nodule, 36; enhanced HU, 106; and 10-min washout HU, 70; with a calculated washout of 34%. No calcification or fat was detected. HU = Hounsfield units.

resonance imaging (MRI) of the abdomen demonstrated a 2.5-cm right-sided adrenal nodule. The lesion did not demonstrate significant loss of signal between in-phase and out-of-phase imaging; therefore, it did not have the characteristics typical of a lipid-rich adenoma (Fig. 2). Table 1 lists the laboratory tests indicating that the adrenal mass did not result in increased secretion of cortisol, aldosterone, dehydroepiandrosterone, or catecholamines. Her 24-hour urine norepinephrine, epinephrine, and metanephrines were all normal; however, her 24-hour urine dopamine was elevated at 824 µg/24 hours (reference range: 52–480 µg/24 hours). On subsequent testing, plasma dopamine, norepinephrine, and epinephrine were all within the reference ranges (Table 1). The patient underwent robotic-assisted right adrenalectomy, removing a 5.7 × 3.5 × 1.7-cm gland weighing 16.3 grams. The gross pathology examination identified a 2.2 × 2.0 × 2.7 cm well-demarcated tumor in the adrenal gland. Microscopic examination demonstrated typical histological features of a ganglioneuroma, with numerous large ganglion cells, Schwann cells, and some short nerve bundles (Figure 3). Focal hemorrhage was noted at the periphery of the tumor, and no tumor necrosis or mitotic figures were present. The entire tumor appeared to be encapsulated in the adrenal parenchyma, with a low proliferative index (negative Ki-67 stain in tumor cells), and no immaturity, such as neuroblastoma or ganglioneuroblastoma components, was identified. After surgery, her symptoms of nausea and abdominal pain persisted. One month later, she underwent esophagogastroduodenoscopy that documented mild gastritis and a small duodenal ulcer with positive immunostaining for *Helicobacter pylori*. Following treatment with antibiotics and a proton pump inhibitor, her gastrointestinal symptoms resolved.

Discussion

We report the case of a young woman with a right-sided adrenal mass that proved to be a 2.2 × 2.0 × 2.7-cm ganglioneuroma. She complained of gastrointestinal symptoms, and a CT scan identified a right-sided adrenal incidentaloma. A dedicated adrenal CT scan and MRI were extremely concerning. The adrenal mass on the CT scan had noncontrast HU >10 and <50% washout, and the MRI was not typical of a lipid-rich adenoma. Based on these findings, the



Fig. 2. T2-weighted coronal MRI of the abdomen showed a 2.5-cm right-sided adrenal nodule (arrow). The lesion did not demonstrate significant loss of signal between in-phase and out-of-phase imaging and was inconsistent with a lipid-rich adenoma. MRI = magnetic resonance imaging.

diagnostic considerations included neuroblastoma, adrenocortical malignancy, pheochromocytoma, or ganglioneuroma. Following surgery, she was diagnosed with a duodenal ulcer, and her symptoms resolved after treating for *H. pylori*.

Most adrenal masses in adults are discovered incidentally when an imaging study is conducted for an unrelated problem. The prevalence of these incidentalomas increases as the population ages and is estimated to be as high as 10% in those aged over 70 years.^{1,2,4,6} There are many potential etiologies, including adrenal carcinomas, pheochromocytomas, hormone-secreting adrenal adenomas, myelolipomas, and adrenal hemorrhage (Table 2). However, most of these incidentalomas are benign, nonfunctioning adenomas that can be followed up without surgery unless they are larger than 4 cm.^{1,3,4,7,8,12} The management of children and younger

Table 1
Laboratory Test Results

| Test | Results | Reference range |
|-------------------------|-------------|------------------|
| ACTH | 31 pg/mL | 6–48 pg/mL |
| Cortisol (AM) | 8.7 µg/dL | 5.3–22.4 µg/dL |
| Cortisol DST | <0.5 µg/dL | <1.8 µg/dL |
| Aldosterone | 10.1 ng/dL | 4–31 ng/dL |
| Renin | 2.2 ng/mL/h | 0.5–4.0 ng/mL/h |
| DHEA-S | 129 µg/dL | 4.5–16.9 µg/dL |
| Plasma metanephrines | 0.10 nmol/L | 0.00–0.49 nmol/L |
| Plasma normetanephrines | 0.41 nmol/L | 0.00–0.89 nmol/L |
| Plasma dopamine | <10 pg/mL | <20 pg/mL |
| Plasma epinephrine | <20 pg/mL | <95 pg/mL |
| Plasma norepinephrine | 239 pg/mL | 21–1109 pg/mL |
| Urine epinephrine | <6 µg/24 h | 2–14 µg/24 h |
| Urine norepinephrine | 40 µg/24 h | 15–100 µg/24 h |
| Urine dopamine | 824 µg/24 h | 52–480 µg/24 h |
| Urine metanephrines | 341 µg/24 h | 300–900 µg/24 h |

Abbreviations: ACTH = adrenocorticotropic hormone; AM = morning; DST = dexamethasone suppression test; DHEA-S = dehydroepiandrosterone sulfate.

adults versus older adults found to harbor an adrenal incidentaloma requires a unique approach for each age group because the differential diagnosis varies widely.

In the pediatric age group, adrenal adenomas are uncommon, and adrenal masses are more likely to be tumors arising from the neural crest, many of which prove to be malignant.^{2,10,13} Emre et al reported a series of 50 children who had adrenal masses that were surgically resected. In this series, 58% were neuroblastomas, 20% ganglioneuromas, 10% adrenal cortex tumors, 4% cysts, and 2% due to adrenal hemorrhage.¹¹ Other reported causes of adrenal masses in children include pheochromocytomas, adrenal teratomas, and myelolipomas as well as adrenal hyperplasia. In an earlier series of incidentally discovered adrenal masses in children, 30% were malignant, 23% were ganglioneuromas, and 15% were cortical adenomas.⁹

Adrenal ganglioneuromas are rare, accounting for only 4% to 5% of adrenal tumors and less than 2% of adrenal incidentalomas.^{4,14–17} Ganglioneuromas are members of a family of tumors that also include ganglioneuroblastomas and neuroblastomas that arise from neural crest cells that form the sympathetic ganglia and adrenal medulla.^{10,14–19} They can arise de novo or from the maturation of a ganglioneuroblastoma or neuroblastoma into a ganglioneuroma.^{18,20}

Ganglioneuromas are benign neoplasms, but they can grow aggressively and cause compression on local structures. In younger adults, ganglioneuromas are usually found in the retroperitoneum and posterior mediastinum, while adrenal ganglioneuromas are most frequently diagnosed in the fourth and fifth decades of life.^{15,18,19,21} Most adrenal ganglioneuromas are asymptomatic, but depending on the location and size, some patients experience abdominal or back pain due to local mass effect.^{14,17–19}

Ganglioneuromas can mimic neuroblastomas on imaging characteristics, so the diagnosis is made by histologic examination. On CT scan imaging, ganglioneuromas are well-defined, encapsulated, hypodense lesions with mild enhancement on postcontrast images. Calcification is seen in 50% of ganglioneuromas.^{10,13,18,19} In selected cases, MRI can be useful to evaluate invasion into surrounding vascular structures and shows low signal intensity in T1-weighted images and heterogeneous intermediate or high signal intensity in T2-weighted images.^{10,13,19}

A histological examination is the gold standard for establishing the diagnosis of adrenal ganglioneuromas.^{9,14,15} They typically consist of mature, large neuronal ganglion cells in a stroma composed of Schwann cells.^{14,15,18} The detection of neuroblasts indicates that the tumor is a neuroblastoma or

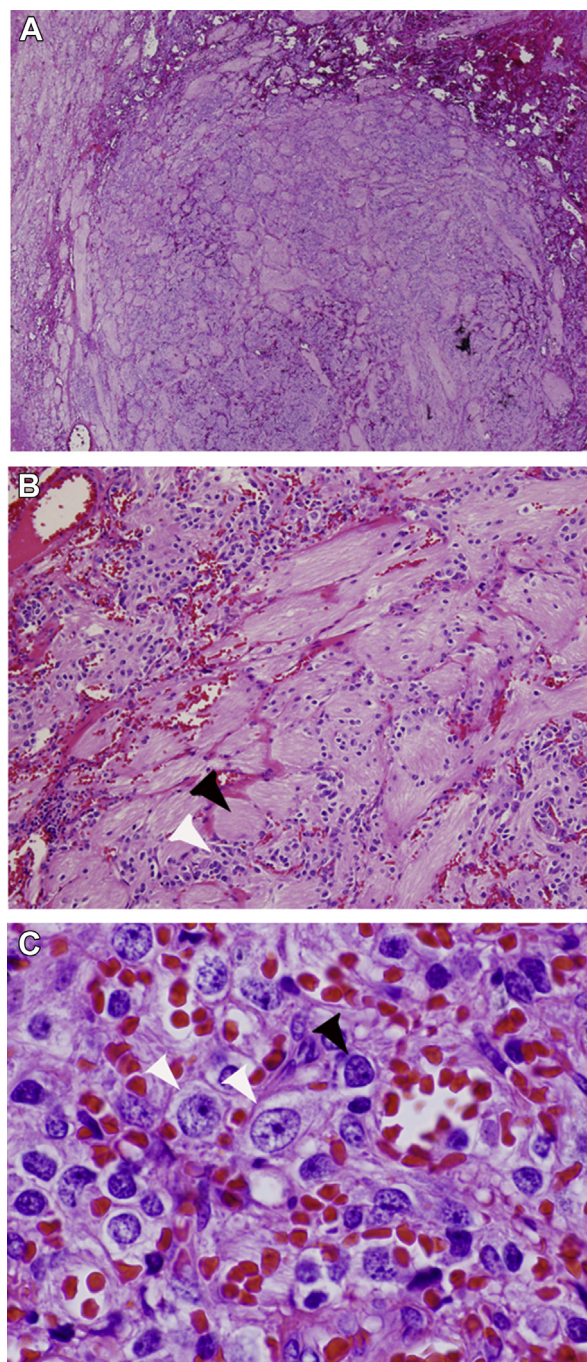


Fig. 3. A, Low-power view of the tumor. The tumor is composed of groups of short nerve bundles mixed with ganglion cells, Schwann cells, and perineural cells. The normal adrenal tissue is displaced to the periphery (upper left), and adjacent hemorrhage is noted. B, Adjacent to the nerve bundles (black arrowhead), mature ganglion cells mixed with Schwann cells and perineural cells (white arrowhead) can be observed. C, High-power view of a group of ganglion cells (white arrowheads) mixed with perineural cells (black arrowhead) in a rich capillary background. The ganglion cells contain large round nucleoli, open chromatin, prominent nucleoli, and abundant clear to eosinophilic cytoplasm. All tumor cells are mature, lacking features of nuclear pleomorphism, tumor cell necrosis, or mitosis.

ganglioneuroblastoma rather than a benign ganglioneuroma. While ganglioneuromas demonstrate positive immunohistochemical staining for S-100, vimentin, synaptophysin, and neuron-specific enolase, malignant neurogenic tumors also stain positive for these peptides.^{14,15}

Table 2
Etiology of Adrenal Masses

| |
|--|
| Adrenocortical adenoma |
| Nonfunctioning |
| Cortisol-secreting |
| Aldosterone-secreting |
| Pheochromocytoma |
| Adrenocortical carcinoma |
| Metastasis |
| Adrenal hyperplasia |
| Myelolipoma |
| Cyst |
| Ganglioneuroma |
| Inflammatory lesions |
| Sarcoidosis, tuberculosis, systemic fungal disease |
| Hemorrhage |

The challenge of this case was weighing the risk versus the benefit of surgical intervention in this transitional age group. There are numerous published guidelines on the management of adrenal incidentalomas.^{1–8} Four do not address the question of the age of patients in their recommendations.^{1,3,7,8} The European guidelines state, “we recommend urgent assessment of an adrenal mass in children, adolescents, pregnant women and adults <40 years of age because of a higher likelihood of malignancy,” and the Korean guidelines include “immediate testing of adrenal incidentaloma in children, adolescents, adults under the age of 40, and pregnant women is recommended because of the high risk of malignancy.”^{2,4} Despite these statements, neither modifies the recommendation for surgery based on the age of the patient. Guidelines from the Polish Society of Endocrinology endorse “hormonally inactive adenomas should be approached individually, taking into consideration lesion size, growth dynamics, the patient’s age, and concomitant diseases,” while the Italian Society of Clinical Endocrinologists’ guidelines include “we recommend excluding primary adrenal malignancies in all pediatric patients with adrenal incidentalomas.”^{5,6} However, as with the European and Korean guidelines, neither provides specific recommendations about how age impacts the recommendation for surgery.

The patient we report emphasizes that published guidelines for the management of incidentally discovered adrenal masses are not applicable to children and young adults. While there are no standardized guidelines for the management of adrenal incidentalomas in younger populations, there are recommendations to remove all adrenal nodules, regardless of size or imaging characteristics, found in children aged more than 3 months.^{9–11} Cases such as this one could lead to potential opportunities for experts who develop and publish future guidelines to modify them so that they include more specific recommendations about the management of adrenal masses in younger populations.

Disclosure

The authors have no multiplicity of interest to disclose.

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