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Case report

Catecholamine-secreting adrenal lipomatous ganglioneuroma: A case study ☆☆☆★★★

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ABSTRACT

Ganglioneuroma, which arise from neural crest cells, typically occurs in adolescents and young adults. Most ganglioneuromas are clinically asymptomatic and hormonally silent, therefore may be diagnosed incidentally during imaging studies. Ganglioneuroma containing fat (lipomatous ganglioneuroma) is a rare variant of ganglioneuroma that is histologically characterized by a mature adipocytic component admixed with a conventional ganglioneuroma. Herein, we report the case of adrenal lipomatous ganglioneuroma with elevated urinary catecholamine level.

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Introduction

Ganglioneuroma typically occurs in adolescents and young adults, and may be diagnosed incidentally during imaging

studies. Ganglioneuroma containing fatty elements, referred to as lipomatous ganglioneuroma, is a rare variant of ganglioneuroma that is histologically characterized by a mature adipocyte component admixed with a conventional ganglioneuroma. Cases of lipomatous ganglioneuromas on the

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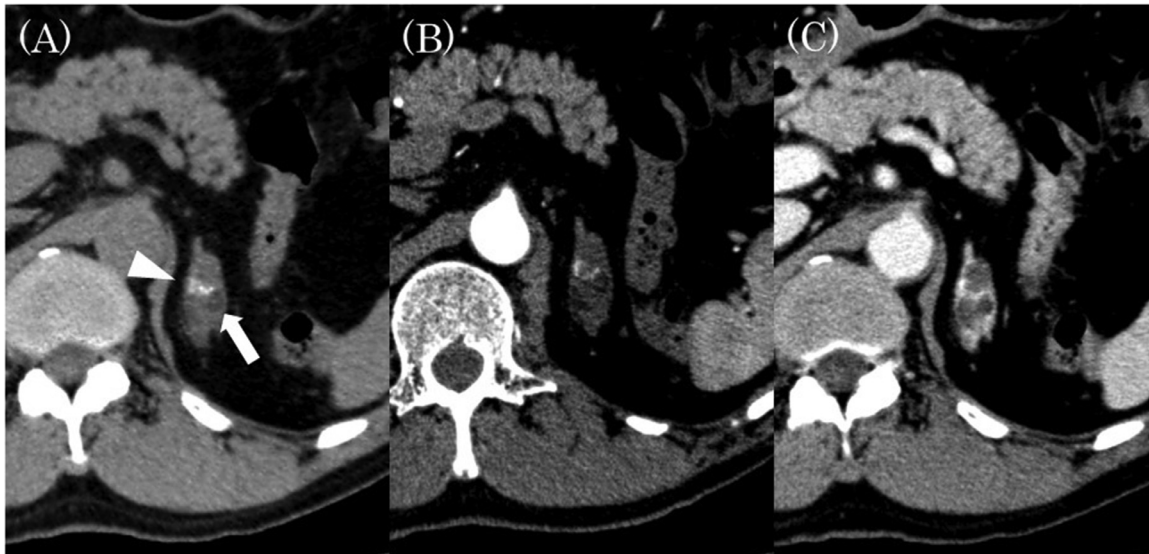


Fig. 1 – Computed tomographic findings. (A) Plain CT showed a well-defined 35 × 15 × 35 mm, lobulated, left adrenal mass composed of fat (CT number –21 HU; white arrow), minor calcification (white arrowhead), and soft tissue elements. **(B)** Enhanced CT in the arterial phase showed a slight enhancement in the mass. **(C)** Enhanced CT in the delayed phase showed a gradual and heterogeneous enhancement in the mass, consistent with the presence of cystic elements.

posterior mediastinum and in the retroperitoneal area have previously been reported [1–9], but there have been no reports of adrenal lipomatous ganglioneuroma. In the present report we describe the case of adrenal lipomatous ganglioneuroma with a fatty component, which was identified using computed tomography (CT) and magnetic resonance imaging (MRI), and was associated with high urinary catecholamine concentrations.

Case report

A 66-year-old man was referred to our hospital for follow-up of a colonic polyp. During his assessment, an incidental left adrenal mass was detected using CT. The patient had reported no symptoms and showed no clinical signs, with the exception of hypertension, which had been present for 5 years. His urinary adrenaline, dopamine, and vanillylmandelic acid concentrations were both high (428.8 µg/day, normal range: 3.4–26.9 µg/day; and 2000 µg/day, normal range: 365.0–961.5 µg/day; and 5.0 mg/day, normal range: 1.5–4.9 mg/day, respectively).

Plain CT demonstrated a well-defined, 35 × 15 × 36 mm, lobulated, left adrenal mass composed of fat (CT number –21 HU), minor calcification, cystic elements, and soft tissue elements (Fig. 1A). Contrast-enhanced CT demonstrated that the soft tissue component of the mass gradually enhanced from the early to the delayed phase (Fig. 1B, C).

The mass had a heterogeneous appearance on MRI, similar to that demonstrated using CT. On both T2- and diffusion-weighted images, the mass had a heterogeneous high signal intensity (Fig. 2A, B). The subtraction image of chemical-shift imaging indicated that the mass contained a fatty element

(Fig. 3) and ¹²³I-metaiodobenzylguanidine (MIBG) scintigraphy showed a slightly abnormally high uptake by both adrenal glands.

The preoperative differential diagnosis was adrenal adenoma, because of the fatty element, or pheochromocytoma, because of the high urinary catecholamine concentrations and history of hypertension.

Surgical resection was then performed. Surgical exploration revealed a thinly encapsulated lobulated left adrenal mass of 35 × 15 × 35 mm that varied in color from bright yellow to white, and was located in the adrenal medulla.

Microscopic examination of the mass revealed an interlacing pattern of adipose tissue, Schwann cells, and mature ganglion cells (Fig. 4A). Immunohistochemistry showed that the Schwann cells were positive for S-100 protein (B; 100× magnification, Fig. 4B), whereas the ganglion cells were positive for chromogranin A (C; 100× magnification, Fig. 4C). The pathologic diagnosis was ganglioneuroma with fatty replacement, which is referred to as lipomatous ganglioneuroma. The patient's urinary adrenaline and dopamine concentrations subsequently decreased to 9.7 µg/day (normal range; 3.4–26.9 µg/day) and 770.0 µg/day (normal range; 365.0–961.5 µg/day), respectively. After surgery the patient's blood pressure was normalized.

Discussion

Ganglioneuroma is a rare, differentiated, benign, and slow-growing tumor that commonly originates from primordial neural crest cells and is composed of mature Schwann cells, ganglion cells, and nerve fibers. Ganglioneuromata are most

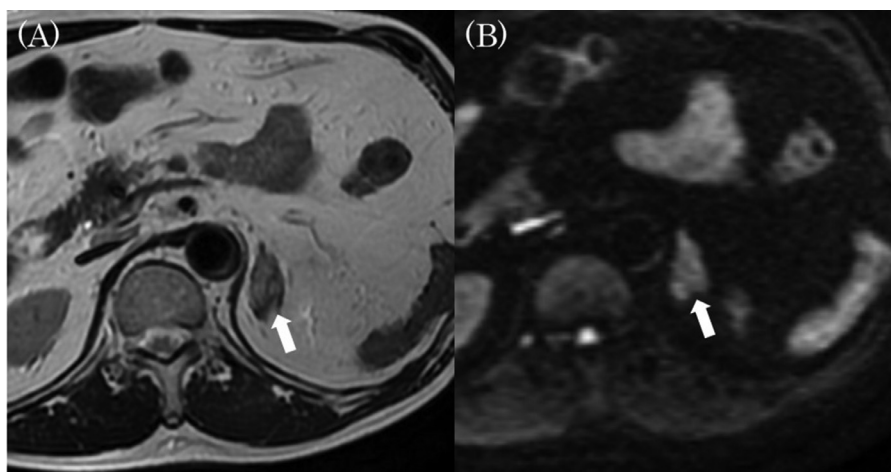


Fig. 2 – Magnetic resonance imaging findings. (A) The T2-weighted image and (B) diffusion-weighted image showed heterogeneous high signal intensity in the mass.



Fig. 3 – Subtraction image obtained using chemical-shift MRI of the mass. This showed an area of high signal intensity in the left adrenal mass (white arrow), consistent with the presence of a fatty element.

commonly located in the posterior mediastinum, followed by the retroperitoneum.

Lipomatous ganglioneuroma, previously called “ganglioneuroma with fatty replacement,” is an extremely rare variant of ganglioneuroma that was first reported in 1999 by Hara et al [1]. It is characterized by a mature adipocytic component admixed with a conventional ganglioneuroma. We comprehensively searched electronic databases of the PubMed for articles containing “lipomatous” or “fatty” or “adipocyte,” and “ganglioneuroma” in the title. To date, there have been some case reports of lipomatous ganglioneuroma [1-9]. The posterior mediastinum and retroperitoneum have been the common locations reported for an lipomatous ganglioneuroma to date, but here we report the lipomatous

ganglioneuroma to be identified in an adrenal gland of the rare location.

The characteristic microscopic feature of lipomatous ganglioneuroma is a combination of ganglioneuroma-like and lipomatous elements. The ganglioneuroma-like element is composed of relatively mature ganglion cells, Schwann cells, and nerve fibers. The ganglion cells can be identified by their abundant eosinophilic cytoplasm, large nuclei, and prominent nucleoli, and the lipomatous areas consist of mature adipocytes without atypia. Typically, immunohistochemistry demonstrates that Schwann cells diffusely and strongly express S-100 protein and glial fibrillary acidic protein, whereas the ganglion cells are positive for chromogranin and synaptophysin.

There are 2 interesting aspects of the present case. The first is the histogenesis of the fat element of the tumor, because this is controversial in lipomatous ganglioneuromas [2,3]. One hypothesis is that the presence of adipose tissue in the tumor is the result of the replacement of degenerating tumor by adipocytes, but a second holds that adipocytes in the tumor are derived from tumor cells.

The second aspect of interest is that we identified high concentrations of catecholamines. Although ganglioneuromas are thought to have a low or no metabolic activity, several previous studies have reported high concentrations of catecholamines or MIBG uptake in intra- and extra-adrenal ganglioneuromas [10-13]. Specifically, Georger et al reported that 39% of ganglioneuromas (18 of 46 cases) were associated with higher concentrations of catecholamines and 57% (17 of 30 cases) were associated with detectable MIBG uptake [10].

The secretion of catecholamines and MIBG uptake may be dependent on the degree of maturity of the tumor. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma represent tumors of neural crest origin that have a continuous spectrum of neuronal maturation, and the cell maturity within a single tumor may not be homogeneous. Most ganglioneuromas contain slightly atypical ganglion cells and have therefore been subclassified as immature ganglioneuromas, whereas fully mature ganglioneuromas are rare. Thus, high concentra-

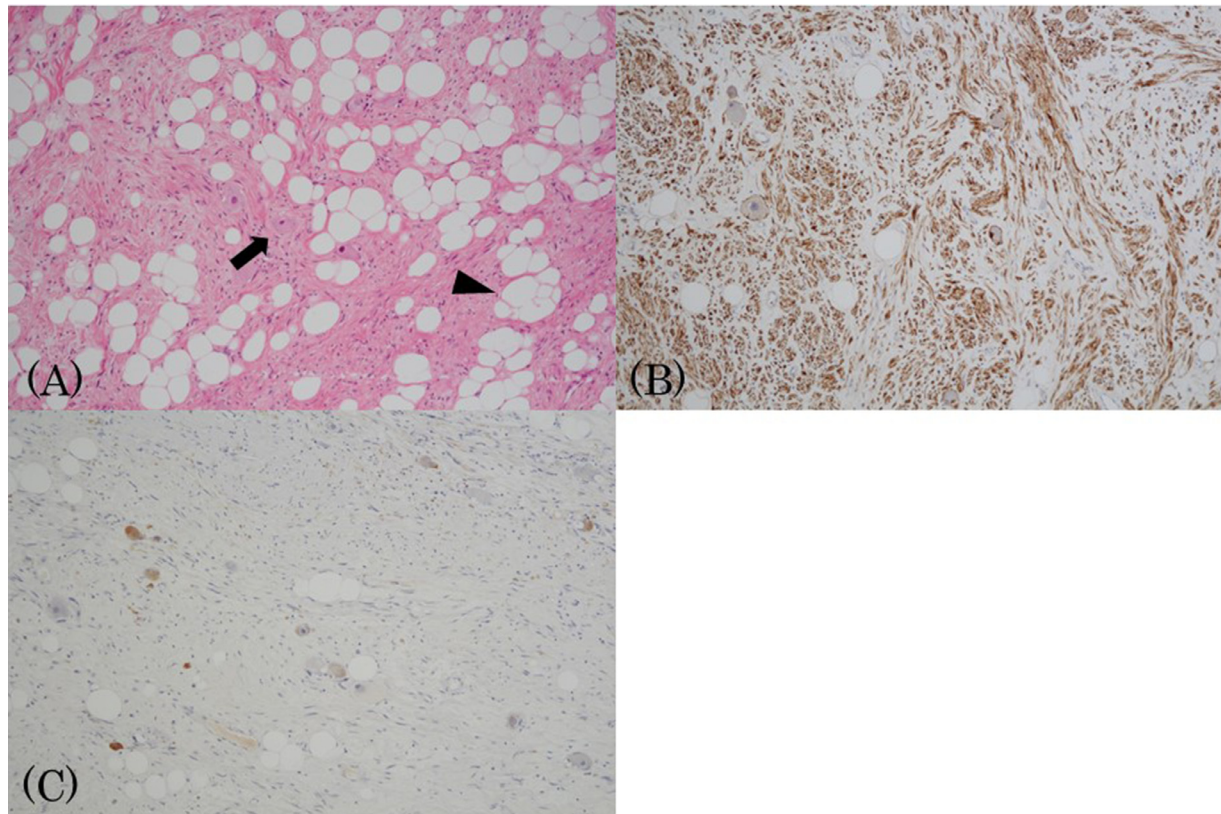


Fig. 4 – Histology of the mass. Hematoxylin and eosin staining (A; 100× magnification) from one of the consecutive tissue sections of the mass revealed an interlacing pattern of adipose tissue (black arrowhead), Schwann cells, and mature ganglion cells (black arrow). The ganglion cells can be identified by their abundant eosinophilic cytoplasm, large nuclei, and prominent nucleoli. Immunohistochemistry showed that the Schwann cells were positive for S-100 protein (B; 100× magnification), whereas the ganglion cells were positive for chromogranin (C; 100× magnification).

tions of catecholamines and MIBG uptake do not exclude the diagnosis of ganglioneuroma and vice versa.

In conclusion, we report the case of adrenal lipomatous ganglioneuroma, a rare variant of ganglioneuroma that contains fatty elements and secretes catecholamines. It contained a combination of fatty cells, Schwann cells, and ganglion cells, which is a pathognomonic feature of lipomatous ganglioneuroma.

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