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Case Report

Cystic adrenal ganglioneuroma: a case report and review of the literature

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Abstract: Ganglioneuroma with cystic degeneration occurs rarely and preoperative diagnosis is difficult. In this paper, we report a case of cystic adrenal ganglioneuroma in a 47 year-old female patient. Like with a typical adrenal cyst, the patient was asymptomatic with negative hormonal changes. Abdominal computerized tomography (CT) revealed a homogeneous cystic mass in left suprarenal area. Laparoscopic excision of cysts was performed, and final histopathological diagnosis was adrenal ganglioneuroma with cystic degeneration. With a review of the literature, we conclude that surgical removal of the cystic adrenal ganglioneuroma is an effective therapeutic method, and accurate pathological identification is essential for optimal patient management.

Keywords: Adrenal gland, ganglioneuroma, cyst, adrenal incidentaloma

Introduction

Ganglioneuromas (GNs) are rare, benign, slow-growing, and well-differentiated tumors which originate from the neural crest cells. These tumors are usually asymptomatic and often discovered by a CT scan, MRI scan, or an ultrasound [1, 2]. Currently, histopathology is the only tool to diagnose ganglioneuromas, which are made of Schwann mesenchymal cells and gangliocytes [3, 4]. GNs occur along the distribution of sympathetic nervous system, commonly located in the retroperitoneum (32% to 52%), mediastinum (39% to 43%), cervical region (8% to 9%), and these tumors rarely occur in adrenal gland [1-3, 5]. During the progression of adrenal GN, once severe hemorrhage occurs and the blood is subsequently reabsorbed, cystic adrenal ganglioneuroma could occur [6].

Preoperative diagnosis of cystic adrenal GN is difficult. Just like ganglioneuroma, patients with cystic GN often present with negative results by physical examination, routine laboratory and hormonal tests [4]. In addition, imaging is not effective for differential diagnosis. Assessment and management of a cystic adrenal GN is similar to other adrenal incidentalomas (AI) [7, 8]. The present study describes a cyst-like cystic adrenal ganglioneuroma, which was incidentally identified in a 47 year-old female. The diagnosis was finally confirmed by histopathological examination. We also include a review of the relevant literature in order to provide clinicians with information concerning this uncommon malignancy. Written informed consent was obtained from the patient.

Case presentation

A 47 year-old woman was admitted to the hospital because of an incidentally homogenous, anechoic cystic mass in left suprarenal area by a routine ultrasonic examination, measuring 65 × 54 mm (**Figure 1**). The patient had no symptoms of fever, dizziness, headaches, abdominal pain, nausea, hypertension, or urinary urgency, and with no loss of appetite or weight change. Routine laboratory studies reported no significant abnormality. Endocrine tests, including plasma cortisol, renin, angiotensin, aldosterone, adrenocorticotropin hormone (ACTH), 24-hr urinary vanillylmandelic acid (VMA), and urinary homovanillic acid (HVA),

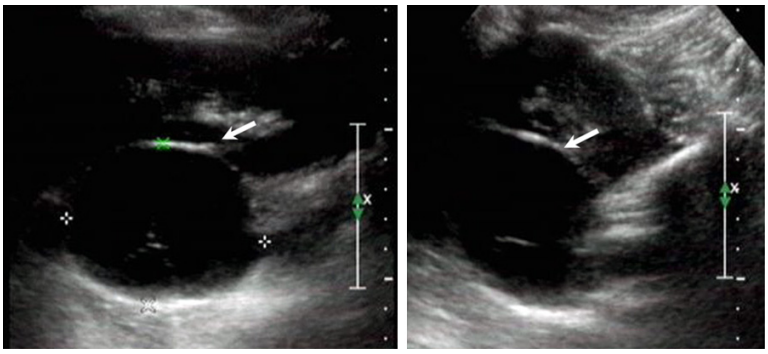

Figure 1. Abdominal US of cystic adrenal ganglioneuroma. The images show a homogenous, anechoic, smooth-walled cystic mass (65 × 54 mm) with slight internal septation in right suprarenal area.

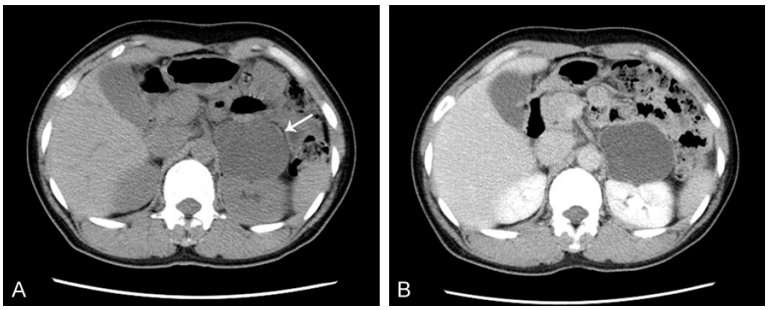

Figure 2. CT images of cystic adrenal ganglioneuroma. The images reveal a homogeneous and low-density left adrenal cystic mass (arrow, 63 × 56 × 60 mm) with no contrast enhancement, no septation, no solid component or calcification. (A. CT scan; B. contrast-enhanced CT scan).

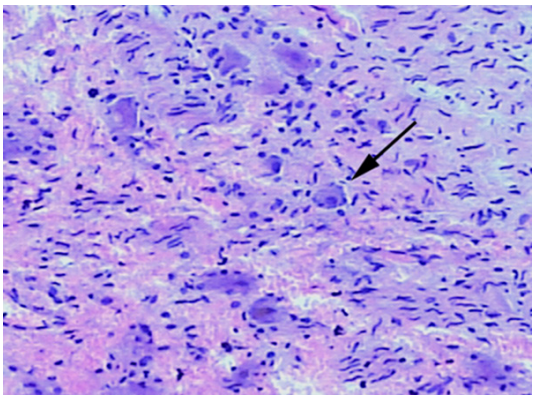

Figure 3. Microscopic examination of cyst wall. The cyst wall is rich in nerve fibers and spindle-shaped Schwann cells, and ganglionic cells (arrow) are present among the nervous fibrous tissue (HE, × 100).

were all within normal ranges. Computed tomography (CT) displayed a well-demarcated, hypodense and homogeneous mass without contrast enhancement in left cystic adrenal, measuring 63 × 56 × 60 mm (**Figure 2**). With these findings, our preliminary diagnosis was a non-functioning adrenal cyst.

With adequate preparation, laparoscopic removal of the mass was performed. During the process, a cystic lesion of the left adrenal was identified, and 60 × 50 mm mass was completely excised. On microscopic examination, the cyst wall was composed of nerve fibers, Schwann cells, and mature ganglion cells (**Figure 3**). The immunohistochemical analysis showed that the cyst wall was positively stained for synaptophysin (SYN) and neuro-specific enolase (NSE) (**Figure 4**). The final histopathologic report revealed adrenal ganglioneuroma with cystic degeneration. The patient recovered quickly without complication after the operation. There was no evidence of recurrence by ultra sound during the 6-month follow-up.

Discussion

GN is a benign, slow-growing neoplasm originating from neural crest tissue, and is made up of mature ganglion cells, Schwann mesenchymal cells, gangliocytes, and nerve fibers. The tumors were commonly found in the retroperitoneum (32% to 52%), mediastinum (39% to 43%), or cervical region (8% to 9%), with only a small proportion originated from adrenal [2, 5]. When severe hemorrhage with subsequent blood resorption within a tumor, or ischemic necrosis followed by liquefaction, the cystic tumor would form. However, these types of cystic degeneration often happen in faster growing tumors while slow-growing ganglioneuromas usually present with solid masses. Focal central hemorrhage and partially cystic degeneration are rarely reported in any above-mentioned locations [9, 10].

GNs mainly occur in adolescents and young adults, equally distributed between males and females, with most patients with adrenal GN being clinically asymptomatic. Even if the

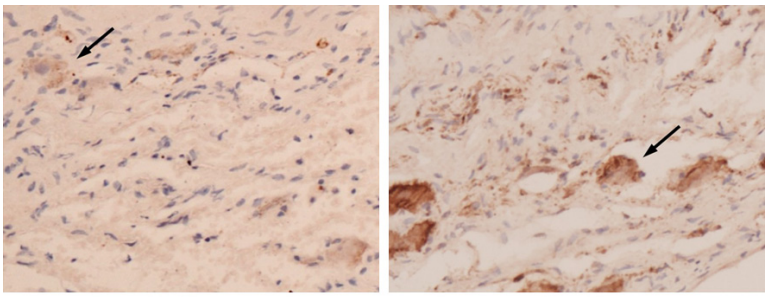

Figure 4. Immunohistochemical analysis of cyst wall. The cyst wall was assessed by immunohistochemistry analysis, and ganglionic cells (arrow) were positively stained for SYN and NSE (× 100).

tumors reach a large size, most of these neoplasms are still hormonally silent. In contrast, some GNs are endocrinologically active as evidenced by secretion from vasoactive intestinal peptide, catecholamine or androgen [11-13].

Identifying cystic adrenal ganglioneuroma with image is challenging. The cystic components of GNs are low in attenuation without contrast enhancement on CT imaging, and the solid components showing a slight to moderate contrast enhancement of less than 40 Hounsfield units. On MRI, cystic degeneration has a hyper-intense signal on T2-weighted images, and the solid components show a late and gradual enhancement on dynamic MRI [10, 14]. However, due to the extremely rarity of cystic GN and lack of a massive solid component in the lesion, preoperative diagnosis of cystic adrenal ganglioneuroma is challenging, especially when extensive cystic degeneration occurs as in the present case.

As to differential diagnosis, cystic adrenal neuroblastoma should be excluded because of their malignant tendency. Secretion of catecholamines is uncommon in ganglioneuromas, while increased level of VMA and HMA are encountered in 80%-95% of neuroblastomas, although these tumors rarely lead to symptoms of catecholamine excess. Additionally, neuroblastomas occur at earlier age. More than 95% of neuroblastomas are diagnosed by age ten, while ganglioneuromas tend to occur in adolescents and young adults [2, 15].

In addition to cystic adrenal neuroblastoma, pheochromocytoma should be ruled out because of the potential uncontrollable hypertension during surgery. Heochromocytoma is a catecholamine-secreting tumor originating from chromaffin cells in the adrenal medulla [16]. Hypertension is the cardinal symptom, and may accompany with headache, palpitation, and sweating [1, 4, 6, 14]. However, cystic pheochromocytoma may show particular characteristics, such as a higher probability of being asymptomatic and a negative biochemical assessment [1]. Image modalities are valuable at distinguishing cystic pheochromocytoma from cystic adrenal ganglioneuromas [1, 5]. After the administration of contrast media, the adrenal cystic mass in pheochromacytoma preserves an enhanced thick wall [1, 7]. Furthermore, ^{131}I-metaiodobenzyl guanidine (MIBG) scanning can aid in the differential diagnosis [6].

Cystic adrenal ganglioneuromas are commonly asymptomatic and hormonally inactive. Operation indications are in accordance with the standards of adrenal incidentaloma. In our department, patients with either symptoms or abnormal hormone level, regardless of their adrenal lesion size, are treated surgically. Patients with an incidental mass larger than 40 mm in diameter, regardless of the presence of symptoms, are also advised to have surgery. But, for the small adrenal incidental with diameter less than 4 cm, we employ a “wait and see” strategy. In the present case, we conducted surgical removal of the lesion because its size reached 65 mm. Laparoscopic surgery has become a reasonable choice for benign adrenal tumors, including cystic adrenal GNs and the characteristic of previous similar cases are shown in **Table 1**. Prognosis of cystic adrenal ganglioneuromas after surgical resection is excellent, although metastasis has been reported in several cases [11, 15].

Conclusion

Ganglioneuroma with cystic degeneration occurs rarely. According to our knowledge, preoperative diagnosis is difficult, and the disease is usually confirmed by histopathological findings. Surgical removal of the neoplasm is an effective therapeutic method. Due to increased and improved utilization of imaging tech-

Table 1. Characteristics of previous cystic adrenal ganglioneuroma

Authors	Cases	Symptom	Detection	Treatment	Size (cm)
Komai Y, et al. [10]	1	Abdominal distension and left upper quadrant pain	Imaging examination	En bloc resection	22 × 20 × 8
Andreoni C, et al. [6]	6	3 are asymptomatic	CT/MRI	En bloc resection	Mean size 6.6 cm
Fusheng Zheng, et al. [7]	1	Asymptomatic	Ultrasound/CT/MRI	En bloc resection	–
Zhenmeng Zhao, et al. [8]	1	Asymptomatic	Ultrasound/CT/MRI	En bloc resection	–
Chunming Yang, et al. [16]	1	Asymptomatic	Ultrasound/CT/MRI	En bloc resection	–
Lifa Hu, et al. [17]	1	Paroxysmal hypertension and vertigo	Ultrasound/CT	En bloc resection	7 × 7.5 × 8

niques, detection of such tumors will continue to rise. Therefore, cystic ganglioneuroma should be considered as a differential diagnosis in patients with cystic adrenal lesions.

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Disclosure of conflict of interest

None.

Abbreviations

GNs, Ganglioneuromas; AI, Adrenal incidentalomas; ACTH, Adrenocorticotropin hormone; VMA, Urinary vanillylmandelic acid; HVA, Urinary homovanillic acid; CT, Computed tomography; SYN, Synaptophysin; NSE, Neuro-specific enolase; MIBG, ^{131}I-meta-iodobenzyl guanidine.

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