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Case report: Large adrenal ganglioneuroma

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ABSTRACT

INTRODUCTION: Ganglioneuromas are localized tumors derived from neural crest tissues. Characteristically, they originate in the posterior mediastinum. Pure adrenal gangliomas are extremely rare.
PRESENTATION OF CASE: A left adrenal mass with the size of 68 mm × 50 mm × 86 mm on magnetic resonance imaging was documented in a 53-year-old female patient. Endocrine tests revealed a non-functioning adrenal mass. The actual size of the mass was macroscopically measured to be 16 cm × 8.5 cm × 6 cm after the surgery. Histopathological examination indicated ganglioneuroma.
DISCUSSION: Most adrenal ganglioneuromas can incorrectly be diagnosed as other adrenal tumors, since they are rare neurogenic benign tumors with no specific imaging properties. They have a slow growth pattern and usually asymptomatic. Our case represents a huge adrenal ganglioneuroma in a female patient with nondiagnostic flank pain. Radiological imaging showed a large adrenal mass with no differentiation from other adrenal tumors. Endocrine evaluation should be performed for such adrenal masses. Since our case had a relatively large size, open surgery was preferred. Pathology revealed the definitive diagnosis.
CONCLUSION: This case suggests that ganglioneuromas can wrongly be diagnosed as other adrenal tumors. It is significant that a proper differential diagnosis should be performed by using hormonal and imaging techniques. Nevertheless, pathological examination is usually required for definitive diagnosis.

1. Introduction

Adrenal incidentalomas are rare, small, and insidental masses.[1] In the case of an adrenal incidentaloma, benign/malignant, and functioning/non-functioning distinctions should be carried out. The most frequently reported one is the adrenal cortical adenoma with a prevalence of 36–94%.[2] Adrenal masses are classified according to their origin. Pheochromocytoma, ganglioneuroma and neuroblastoma are derived from the adrenal medulla. Adenoma, myelolipoma, and adrenocortical carcinoma are derived from the adrenal cortex. Furthermore, adrenal incidentalomas are categorized according to their hormonal activities. The vast majority (85%) of adrenal incidentalomas are nonfunctioning. When examined for hormone secretion, 20% of the cases exhibit subclinical dysfunction. Of these, 9% have subclinical Cushing's syndrome, and 1% has high levels of aldosterone. High cortisol and aldosterone levels are usually encountered in the cases of benign adenomas. Moreover, in the presence of sex steroids, a malign tumor should be considered.

Ganglioneuromas are tumors derived from neural crest tissues, which are mostly localized in the posterior mediastinum and retroperitoneal region. Pure adrenal ganglioneuromas are especially rare.[3] Ganglioneuromas comprise about 0–6% of all of adrenal incidentalomas.[4] Adrenal ganglioneuromas can stay asymptomatic until they reach a large size, and are usually incidentally diagnosed with imaging techniques. Sometimes radiological investigations can be performed as a result of nonspecific symptoms caused by pressure.[5] Adrenal ganglioneuromas can initially be misdiagnosed as adrenal carcinoma and pheochromocytoma. Therefore, a proper differential diagnosis prior to surgery is vital. In this case presentation, we incidentally discovered a large adrenal ganglioneuroma on magnetic resonance imaging (MRI) in a 53-year old female patient.

2. Case

A 53-year old female patient was admitted to our clinic with complaints of nonspecific, non-colic, intermittent bilateral flank pain, predominantly on the left side. She had pain for one year. The patient's history did not contain any systemic diseases or previous operations. Physical examination revealed no abnormality. A non-contrast abdominal CT (computed tomography) showed a 75 mm × 50 mm lobulated contour mass lesion in the left adrenal gland. The MRI revealed a 68 mm × 50 mm × 86 mm, mostly well-circumscribed, heterogeneous solid lesion with a slight contour

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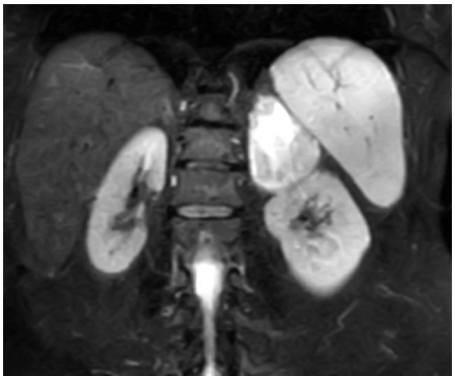

Fig. 1. MRI image of the adrenal mass of 68 mm × 50 mm × 86 mm.

irregularity on the left adrenal (Fig. 1). The mass showed progressive contrast increase in dynamic examinations. Consequently, lesion was evaluated to be "non-adenoma", and was reported as a metastatic lesion or adrenocortical carcinoma.

Serum cortisol, DHEA-SO4, urine cortisol levels were found to be 1.56 μg/dl, 88.48 μg/dl, 16.89 μg/dl respectively, and all in normal ranges. Dexamethasone 1 mg suppression test was performed. The lesion was non-functional according to this endocrine evaluation. Open left surrenalectomy (total surgical resection of the adrenal gland) was performed. Patient had no complaints after the operation and she was well at the follow-up visit after 1 year.

During macroscopic examination, the weight and size of the mass were measured to be 227 g, and 16 cm × 8.5 cm × 6 cm. Markers used were S100 and smooth muscle actin (SMA). Pathological examination revealed mature ganglioneuroma having fascicles of Schwann-like cells (Fig. 2a) with positive staining of S100 (Fig. 2b) and SMA. These Schwannian cells constituted the majority of stroma. The specimen composed of ganglion cells with no residual neuroblasts. The largest diameter of the tumor was 16 cm with negative surgical margins, and grossly no distinct hemorrhagic nodules were observed.

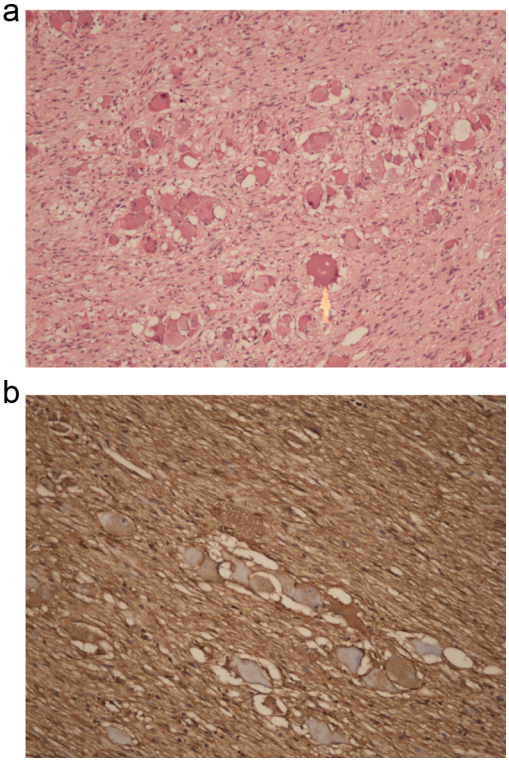

Fig. 2. (a) Pathological investigation shows that the stroma is furnished with fascicles of Schwann-like cells. Also ganglion cells form mature clusters. Hematoxylin and eosin, 40×. (b) Positive immunohistochemical staining with S100, 200×.

3. Discussion

A recent study states that pure adrenal gangliogliomas are very rare in Japan, and only 4 cases have been reported.[3] Adrenal gangliogliomas have a slow growth pattern and usually asymptomatic. Our case represents a huge adrenal ganglioneuroma in a female patient with nonsdiagnostic flank pain. Interestingly initial ultrasonography missed the adrenal mass. Therefore, such patients with persisted flank pain a careful evaluation should be considered. An appropriate ultrasonographic examination including adrenals should be performed and even CT can be used in differential diagnosis. The largest ganglioneuroma reported to date was 19 cm.[6] Our case had a relatively large tumor as 16 cm at its largest diameter.

Ganglioblastoma and neuroblastoma are also parts of this class. Ganglioneuroma can be distinguished from these two tumoral masses with the presence of mature sympathetic ganglion cells. Ganglioneuromas are hormonally nonfunctioning tumors, but sometimes may be associated with pheochromocytoma. In this case, they can secrete catecholamines and their metabolites. Rarely, some studies in the literature also suggest that, ganglioneuromas can secrete cortisol and androgen.[7] It was asserted that masses which are under 3 cm have very low probability of being functional, and the ones above 3 cm are most likely functional. Therefore, endocrine evaluation should be performed for such large adrenal masses. Additionally, when an adrenal mass is discovered, 75% of the time, the cause is metastasizes from other organs. These are primarily kidney, colon, breast, esophagus, pancreas, liver and stomach. Adrenal masses of metastasis are usually bilateral.

MRI and CT views of ganglioneuromas can match those of other adrenal tumors. In other words, when only focused on imaging techniques, it is clear that ganglioneuroma cannot be distinguished from adrenocortical carcinoma and pheochromocytoma. In all cases of adrenal incidentalomas, urine must be monitored for catecholamine and fractionated metanephrine for 24 h prior to the operation. The increases in levels of metanephrine and/or catecholamine indicate that this tumoral mass is pheochromocytoma with a 91% and 98% of sensitivity and specificity, respectively. In terms of differential diagnosis to rule out malignancy, fine-needle aspiration biopsy has a high rate of false negativity. In addition, some complications of biopsy are also present. Along with these, primary treatment modality in adrenocortical carcinoma is open or laparoscopic surgical excision. Since our case had relatively large size, open surgery was preferred.

Tumor sizes can be misidentified at about a rate of 20% and 16–47% for MRI and CT respectively; just as in our case.[8] Tumor size is very important to determine the prognosis for adrenal masses. Statistically, tumoral masses below 4 cm are 60% benign adenomas, and carry a 2% risk of adrenal cortical carcinoma. In the case that the tumor is larger than 6 cm, 25% chance of adrenocortical carcinoma is existent. Therefore, it is not appropriate to make a malign/benign decision solely based on sizes reported via imaging techniques. Mostly pathological investigation provided the definitive diagnosis of ganglioneuroma. A recent publication of 29 ganglioneuroma confirmed that histopathological diagnosis is essential and surgery is the main curative method.[9] However, another recent report of 27 patients shows that rarely local extension or malign transformation is possible for ganglioneuroma.[10] Therefore, surgery should be offered for these patients. Moreover, postoperative follow-up should not be ignored.

Due to the fact that ganglioneuromas can be erroneously diagnosed as other adrenal tumors, it is imperative that differential diagnosis should be performed by using appropriate hormonal and imaging techniques.

Conflict of interest

None.

Funding

None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Coşkun Kacagan: data collections, writing; Ekrem Basaran: data collections; Havva Erdem: data collections; Ali Tekin: study design, data collections; Ali Kayikci: data analysis, writing; Kamil Cam: study design, writing.

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