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CASE REPORT

Giant Bilateral Symptomatic Adrenal Myelolipomas Associated with Congenital Adrenal Hyperplasia

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Abstract Adrenal myelolipoma is an uncommon, benign, biochemically non-functioning and endocrinologically inactive tumor composed of variable amounts of mature adipose tissue and scattered islands of haemopoietic elements, including erythroid, myeloid and lymphoid series, as well as megakaryocytes. Diagnosis of myelolipomas is based on imaging, with ultrasonography, CT and MRI being effective in more than 90% of cases. Differential diagnosis includes other containing fat adrenal masses such as teratoma, lipoma and liposarcoma. The optimal treatment depends on the size and symptoms of the myelolipoma. For incidentally discovered, asymptomatic adrenal myelolipomas smaller than 4 cm surveillance seems to be enough while symptomatic, complicated, hormonally active and larger than 7 cm myelolipomas, should be surgically removed. We present a case of giant bilateral symptomatic adrenal myelolipomas associated with congenital adrenal hyperplasia. A 34 year old female, with congenital adrenal hyperplasia because of 21-hydroxylase deficiency, presented with diffuse abdominal pain and vomiting. Physical examination revealed hirsutism, pronounced virilization and palpable masses both on the right and left abdominal area. The abdominal CT demonstrated bilateral large masses in the anatomical position of the adrenal glands with densities indicating adipose tissue. The differential diagnosis was between myelolipoma and liposarcoma. For diagnostic and also therapeutical reasons, as the masses were large and symptomatic and causing pressure to the surrounding structures, the patient was submitted to laparotomy for bilateral excision. Histopathological examination established the diagnosis of adrenal myelolipoma.

Keywords Adrenal gland · Bilateral myelolipomma · Congenital adrenal hyperplasia · 21-hydroxylase deficiency · Giant myelolipoma · Symptomatic myelolipoma

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Introduction

Adrenal myelolipoma is an uncommon, benign, biochemically non-functioning and endocrinologically inactive, in most cases, tumor composed of variable amounts of mature adipose tissue and scattered islands of haemopoietic elements, including erythroid, myeloid and lymphoid series, as well as megakaryocytes, which represent the most important diagnostic feature [1–4] but is not extramedullary hematopoiesis and is not associated with haematologic disorders [3]. Myeololipoma may also rarely present in extra-adrenal sites, including the pelvis, mediastinum, retroperitoneum and paravertebral region, as an isolated soft tissue mass [2, 5]. While in the past myelolipomas were usually incidental findings during autopsy, today the noninvasive diagnostic imaging techniques have increased premortem incidental detection of clinically asymptomatic adrenal tumors [3, 4]. Despite the fact that their exact incidence is unknown, in autopsy series, their incidence

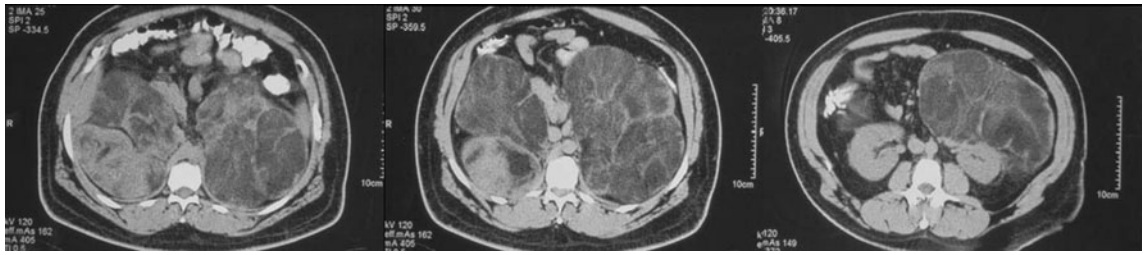

Fig. 1 The abdominal CT scan is showing bilateral large masses in the anatomical position of the adrenal glands with densities indicating adipose tissue

varies from 0.08 to 0.4% [2, 4, 7] and they account for approximately 3 to 5% of all primary adrenal tumors, being the most common fatty tumor of the adrenal gland [1–3, 6]. We report a case of giant bilateral symptomatic adrenal myelolipomas associated with congenital adrenal hyperplasia

Case Report

A 34 year old female presented to the emergency department of our hospital complaining about diffuse abdominal pain and vomiting. The patient had been diagnosed with congenital adrenal hyperplasia because of 21-hydroxylase deficiency during neonatal period. At the age of six she underwent a partial clitorectomy. At the time of presentation she wasn't receiving any steroid treatment on her will. The patient's height was 140 cm and she had amenorrhea. Physical examination revealed, besides hirsutism and pronounced virilization, the presence of palpable masses both on the right and left abdominal area. Thoracic and abdominal x-rays didn't show any pathologic findings while the laboratory examination revealed hematocrit 51.5%, white blood cell count 8720/mm^3 and platelets 280000/mm^3, glucose 114 mg/dL, urea 34 mg/dL, creatinine 1.36 mg/dL, Na 142 mEq/L and K 4.24 mEq/L. Hormonal examination showed an elevated level of 17-OH-progesterone 862 ng/dL and cortisol was 2,1 μg/dL in the morning and 0,8 μg/dL in the night while the 24 h urine cortisol was 27,3 μg/24 h. Mutation screening test was not performed. The US of the internal genitalia revealed a normal uterus, a left ovary that didn't contain any ovarian follicles and failed to depict the right ovary.

The abdominal CT demonstrated bilateral large masses in the anatomical position of the adrenal glands with densities indicating adipose tissue. The maximum diameter was 20 cm for the left mass and 15 cm for the right mass (Fig. 1). In the abdominal MRI the masses had high signal both in the T1 and T2 sequences (Fig. 2). The differential diagnosis was between myelolipoma and liposarcoma. For diagnostic and also therapeutical reasons, as the masses were large and symptomatic and causing pressure to the surrounding structures, the patient was submitted to laparotomy for bilateral excision. Preoperatively, the patient was given parenteral hydrocortisone infusion 100 mg three times a day. During surgery, the frozen section biopsy didn't reveal any signs of malignancy.

The left tumor weighed 1373 gr and measured 24×14×10 cm and the right tumor weighed 854 gr and measured 16×11×8 cm (Fig. 3). Macroscopically, both tumors were surrounded by a thin capsule, and consisted mainly of red areas, and focally yellowish areas and on gross section the tumor consisted of adipose tissue and red areas composed of fragile tissue. Histopathological examination revealed lobes of mature adipose tissue intermixed with abundant hematopoietic tissue, consisting of all three hematopoietic elements with mature and precursor cells. Also between the hematopoietic and lipoid cells and in the periphery of the tumours there were islets of cells from the zones of the adrenal cortex. These findings established the diagnosis of adrenal myelolipoma (Fig. 4).

Postoperatively, the patient received also parenteral hydrocortisone infusion 100 mg three times a day, which was gradually reduced to half every 3 days. The postoperative course was uneventful and the patient exited on the 10th day receiving 30 mg hydrocortisone per os per day

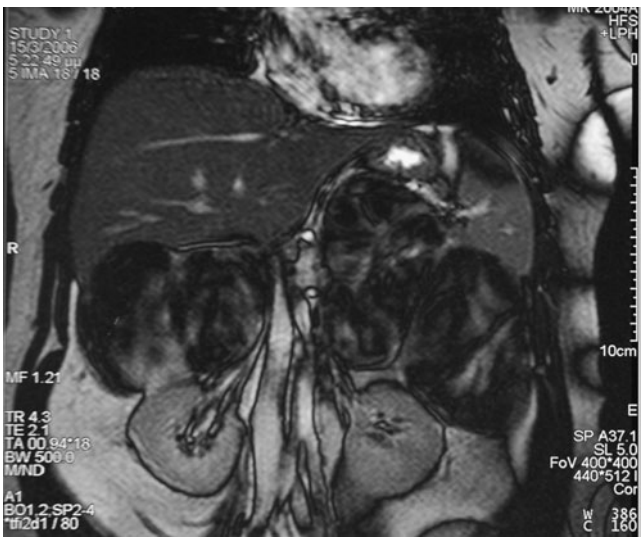

Fig. 2 MRI imaging demonstrating the masses above both kidneys

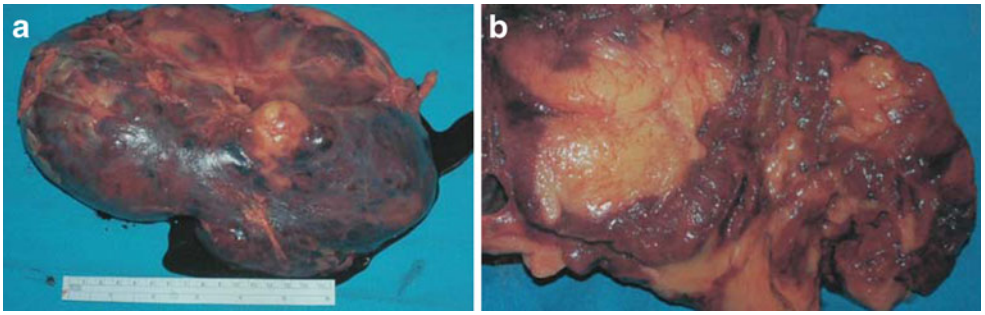

Fig. 3 Macroscopic view of the left myelolipoma (**a**) and gross section of the right myelolipoma demonstrating redudant adipose tissue (**b**)

(10 mg in the morning and 20 mg in the evening) and 0.2 mg fludrocortisone per os per day. Unfortunately the patient was lost on follow up.

Discussion

Adrenal myelolipoma usually presents late in adult life, and most cases are diagnosed during the fourth to seventh decade with the mean age being 62 years, while it has been found in patients from 17 to 93 years old [1, 4]. The male to female ratio appears to be 1:1 [1]. Adrenal myelolipomas are in the majority of cases unilateral and asymptomatic and often less than 4 cm in diameter [1, 2, 4]. However, they may attain very large sizes and also be bilateral, as in our case which was characterized by the presence of giant bilateral adrenal myelolipomas [1]. While, myelolipomas are usually incidental findings they may seldom become symptomatic, especially the larger one, causing flank pain, abdominal discomfort because of mass effect by causing pressure of surrounding structures or may also present with necrosis, rupture or haemorrhage and even haemodynamic shock [4, 6, 7].

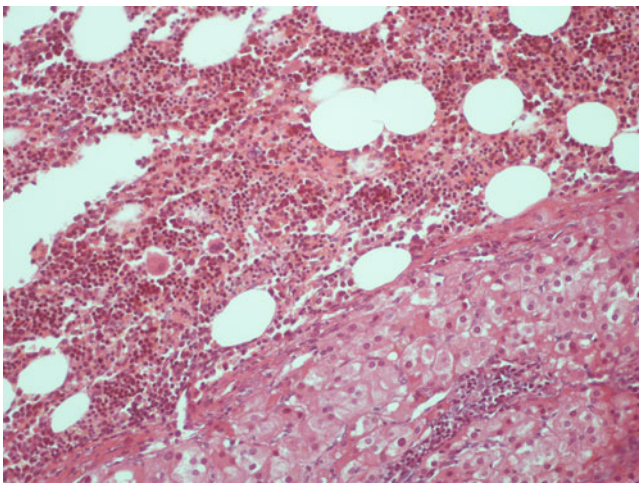

Fig. 4 A mixture of mature adipose tissue and bone marrow cells including erythroid, myeloid and megakaryocytes are present in the tumor. There is compression of the adjacent adrenal cortex (H&E X200)

The pathogenesis of the disease is uncertain with the prevalent hypothesis suggesting that they arise from the zona fasciculate of the adrenal cortex from metaplasia of undifferentiated stromal cells [1, 7]. More specifically, they are assumed to arise from metaplasia of either previously uncommitted adrenal cortical mesenchymal cells or of groups of choristomatous hematopoietic stem cells that transmigrate during intrauterine life to the developing adrenal gland [5]. Other theories, less favored, propose embolism of bone marrow cells and development from intra-adrenal embryonic rests of bone marrow [2, 5]. Also, adrenal myelolipoma has been associated with endocrine disorders, most commonly congenital adrenal hyperplasia and Cushing syndrome, and chronic stressful conditions such as obesity, diabetes mellitus, hypertension, chronic inflammatory processes and even malignancy [1, 2]. Less than 20 cases of adrenal myelolipomas in patients with congenital adrenal hyperplasia have been reported most of which were unilateral [8, 9], in contrast with our case which is characterized by presence of bilateral giant myelolipomas. It seems that prolonged stimulation of the adrenal cortex by high ACTH levels contributes to the development of myelolipomas [8, 9].

Diagnosis of myelolipomas is based on imaging, with ultrasonography, CT and MRI being effective in more than 90% of cases. On plain x-rays the classic myelolipoma is radiolucent and on angiography it is avascular [10, 11]. On ultrasonography, myelolipoma is hyperechoic if it consists mostly of fat and hypoechoic if it is composed primarily of myeloid cells. Usually the lesion has mixed hyperechoic and hypoechoic areas [3]. CT is the most sensitive imaging modality and the appearance of myelolipomas depends on their histologic composition. Myelolipomas often have a discrete capsule and appear as well-delineated heterogenous masses with regions of less than −30 Hounsfield units that correspond to low density mature fat. The presence of a true focal fat collection in an adrenal mass is virtually diagnostic of myelolipoma. In MRI fat tissue has high signal intensity in both T1 and T2 images while myeloid tissue has low signal intensity in T1 and moderate signal intensity in T2 images [3]. Calcification is a common feature with an incidence of 27% and may be an imaging feature of myelolipoma [6].

Differential diagnosis includes other containing fat adrenal masses such as teratoma, lipoma and liposarcoma which are less common and even rarely angiomyolipoma, mass forming extramedullary haematopoiesis and adenoma. In cases that the diagnosis hasn't been established fine needle aspiration can be helpful. The diagnosis of myelolipoma is made by the presence of mature adipocytes and hematopoietic elements. Macroscopically, myelolipomas are generally encapsulated and gross section reveals the presence of yellow adipose tissue and red to brown hematopoietic tissue [1]. Microscopically, myelolipoma consists of scattered islands of lipoid cells intermixed with haematopoietic cells, and also reticulum cells and myeloid precursors. The presence of megakaryocytes in a fat containing adrenal mass is pathognomonic of myelolipoma. Hemorrhage and calcification may also be present [1, 7, 12].

The optimal treatment depends on the size and symptoms of the myelolipoma. For incidentally discovered, asymptomatic adrenal myelolipomas smaller than 4 cm surveillance seems to be enough as there is a little risk for spontaneous rupture or bleeding [1, 10]. On the other hand, symptomatic myelolipomas, complicated myelolipomas, with rupture or hemorrhage, hormonally active myelolipomas, and larger than 7 cm, in which the risk of spontaneous rupture or bleeding is increased, should be surgically removed [1, 10]. Laparoscopic resection is a choice for smaller tumors, but for larger ones open surgical removal via a Chevron or even thoracoabdominal incision is indicated [1]. In cases of bilateral myelolipomas, it is suggested that the larger one should be removed and the smaller one should be monitored in order to avoid lifelong steroid substitution [1]. However, in the present case as there were bilateral giant symptomatic adrenal myelolipomas in a patient with congenital adrenal hyperplasia we performed bilateral surgical resection of the myelolipomas.

Adrenal myelolipoma is an uncommon, benign, biochemically non-functioning and endocrinologically inactive tumor composed of variable amounts of mature adipose tissue and scattered islands of haemopoietic elements, including erythroid, myeloid and lymphoid series, as well as megakaryocytes. Myelolipomas are usually incidental findings that they may seldom become symptomatic, especially the larger one, causing flank pain, abdominal discomfort and even haemodynamic shock in cases of rupture or haemorrhage. Diagnosis of myelolipomas is based on imaging, with ultrasonography, CT and MRI being effective in more than 90% of cases. Differential diagnosis includes other containing fat adrenal masses such as teratoma, lipoma and liposarcoma. The optimal treatment depends on the size and symptoms of the myelolipoma. For incidentally discovered, asymptomatic adrenal myelolipomas smaller than 4 cm surveillance seems to be enough while symptomatic, complicated, hormonally active and larger than 7 cm myelolipomas, should be surgically removed.

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