Case Report
Lipoadenoma of the adrenal gland: report of a rare entity and review of literature

Jiadi Luo, Lingjiao Chen, Qiuyuan Wen, Lina Xu, Shuzhou Chu, Weiyuan Wang, Mohannad Ma Alnemah, Songqing Fan

Department of Pathology, The Second Xiangya Hospital, Central South University, Changsha, Hunan, China

Received June 14, 2015; Accepted July 23, 2015; Epub August 1, 2015; Published August 15, 2015

Abstract: Adrenal lipoadenoma is an extremely rare tumor. Only four cases have been reported so far. The authors reported a case of adrenal lipoadenoma in a 46-year-old man with the history of abdominal pain. The present case, manifesting as a nonfunctional adrenal tumor, is characteristically comprised of a mixture of mature adipocytes and adrenocortical cells. We also reviewed this tumor in different organs which have been published in the literature.

Keywords: Lipoadenoma, adrenal gland, mature adipocytes, myelolipoma

Introduction

Lipoadenoma, confirmed as a rare entity by document retrieval, is a benign encapsulated tumor composed of mature adipocytes and other components, occurring mainly in salivary glands or much less frequently in other organs, especially in adrenal gland. As far as we are aware, there are only four cases of lipoadenoma in adrenal gland, which have been reported in the English literature [1-3]. We herein present a case of lipoadenoma of the adrenal gland in a 46-year-old man without endocrine function.

Case presentation

A 46-year-old man presented with the history of right abdominal pain for more than 10 days. No obvious incentive, the patient depicted spontaneous right abdominal pain without other discomfort. Abdominal computed tomography scan (CT) discovered a mass with heterogeneous density (average-54.74 HU) and a fatty component in the lateral branch of right adrenal gland (Figure 1A). The mass measured about 1.7 cm in diameter and had a well-defined boundary (Figure 1B). Clinical examination and routine laboratory screening did not show any evidence of adrenal disorder. Blood tests were carried out for functional assessment of the right adrenal tumor and all of the adrenocortical hormones including their metabolite levels were normal (Table 1).

A surgical resection of this adrenal gland mass was performed, revealing a solitary mass measuring 2.0×1.5×1.3 cm with a thin capsule, weighing about 8 grams (g). The cut surface was tan with yellow areas. Microscopically, the mass was encapsulated and comprised sheets and nests of adrenocortical cells and fat cells with mature adipose tissue occupying about 60% to 70% of the tumor (Figure 2A-D). Cells bland, uniform with no pleomorphism, mitosis, necrosis, or capsular invasion and no hematopoietic tissue were observed in any of the sections. Ki-67 proliferation rate of the tumor cells is only 1%.

The different immunohistochemical markers, such as CD56, epithelial membrane antigen (EMA), vimentin (Vim), chromogranin (CgA), synaptophysin (Syn), neuron-specific enolase (NSE), pan-cytokeratin (pan-CK), leukocyte common antigen (LCA), mesothelial cell (MC) and calretinin (CR) were available for immunohistochemical diagnosis of the adrenal gland tumor. Immunohistochemical staining showed CD56, EMA, Vim, S-100 was positive (Figure 3A-D), while negative for CgA (Figure 3E) and Syn (Figure 3F), NSE, pan-CK, LCA, MC and CR.
Based on the clinical manifestation, microscopic findings and immunohistochemical results, we made the diagnosis of lipoadenoma in the adrenal gland without functional endocrine.

Discussion

Adrenal lipoadenoma is an extremely rare tumor, which was first reported by Papotti M et al. in 1996 [1]. Only four cases of adrenal lipoadenoma have been reported so far [1-3] (Table 2). Although the overwhelming female: male ratio of 4:1 in these cases, we cannot claim there is gender predilection for the sample size is too small to draw a conclusion. The patients' ages range from 12 to 74 years (median of 45.8 years) with 80% being adults. Case investigation revealed that adrenocortical tumors were rare in childhood and adolescence [4]. Besides, the world-wide annual incidence ranges from 0.3 to 0.38/million children below the age of 15 years with 65% of them occurring in children younger than 5 years of age [5]. While it was investigated that subclinical adrenocortical adenomas were the most frequent cause of adrenal incidentalomas that are present in 5% of adult abdominal imaging [6]. Therefore it is safe to assume that adrenal lipoadenoma occurs mainly in adults despite of the microscale sample volume. However, the situation of functional endocrine is not the same with sole one's absence of abnormal hormone

Table 1. Adrenocortical hormones and their metabolite levels tested in our lab

<table>
<thead>
<tr>
<th>Object</th>
<th>Sample</th>
<th>Testing value</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metanephrine</td>
<td>Blood</td>
<td>113.74 pmol/L</td>
<td>0-456 pmol/L</td>
</tr>
<tr>
<td>17-hydroxyprogesterone (17OHP)</td>
<td>Blood</td>
<td>1.74 ng/ml</td>
<td>0.31-2.17 ng/ml</td>
</tr>
<tr>
<td>Urinary free cortisol for 24 h</td>
<td>Urine</td>
<td>323.4 nmol/24 h</td>
<td>78.6-589.6 nmol/24 h</td>
</tr>
<tr>
<td>VMA for 24 h</td>
<td>Urine</td>
<td>40.80 µmol/24 h</td>
<td>0-68.60 µmol/24 h</td>
</tr>
<tr>
<td>Cortisol secretion rhythm 12.pm</td>
<td>Blood</td>
<td>106.8 nmol/L</td>
<td>85.3-618.0 nmol/L</td>
</tr>
<tr>
<td>Cortisol secretion rhythm 4.pm</td>
<td>Blood</td>
<td>152.9 nmol/L</td>
<td>85.3-618.0 nmol/L</td>
</tr>
<tr>
<td>Cortisol secretion rhythm 8.am</td>
<td>Blood</td>
<td>372.6 nmol/L</td>
<td>85.3-618.0 nmol/L</td>
</tr>
<tr>
<td>Adrenocorticotropic hormone (ACTH) 12.pm</td>
<td>Blood</td>
<td>16.2 ng/L</td>
<td>0-46 ng/L</td>
</tr>
<tr>
<td>Adrenocorticotropic hormone (ACTH) 4.pm</td>
<td>Blood</td>
<td>14.9 ng/L</td>
<td>0-46 ng/L</td>
</tr>
<tr>
<td>Adrenocorticotropic hormone (ACTH) 8.am</td>
<td>Blood</td>
<td>19.0 ng/L</td>
<td>0-46 ng/L</td>
</tr>
</tbody>
</table>

Figure 1. Contrast enhanced computed tomography in vertical section (A) and transverse section (B), showing a 1.7 cm in diameter well-defined heterogenous enhancing predominantly fat attenuating lesion involving the lateral branch of right adrenal gland (red arrow).
One case report of adrenal lipoadenoma

secretion of adrenal gland. There exist no statistical condition to analyze the correlation between tumor functional endocrine and other characteristics such as size, weight, age. The matter, having been confirmed, is that all the tumors within abnormal hormone levels are more than 2 cm in size (Table 2), which of all the cases are from 2 to 10 cm (median of 6.5 cm).

The clinical manifestation of adrenal lipoadenoma, including abdominal pain, Cushing syndrome, even non-perceivable clinical changes, is really not typical. In other words, asymptomatic lipoadenoma is intensely arduous to discover unless further health examination. So its rarity attributes to the stealthiness to some extent, like so-called adrenal incidentaloma. Imaging tests are indispensable and rewarding to catch such a tumor, especially cross-sectional imaging ascertaining the density and origin of the lesion [7]. The lipoadenoma masses of adrenal gland are encapsulated entirely or partly and composed by adrenocortical cells and diverse proportional mature adipose tissue. And the adipose tissue is dispersed throughout the adrenal cortical tumor, lacking the characteristics of lipoma. Pleomorphism, mitosis, necrosis, capsular invasion and hematopoietic tissue haven’t been detected in these cases. All reported cases demonstrated benign clinical courses after excision. So assessing the malignant potential of it is rather difficult. Weiss criteria are employed to distinguish between benign and malignant adrenocortical tumors. It is considered malignant when the tumor size is > 10 cm, weight > 400 g and mitosis > 15/20 HPF [8].

Figure 2. Hematoxylin & eosin (H&E) staining from sample of the tumor of adrenal gland by surgical resection. A, B: The low microscopic view showed the lesion comprised sheets and nests of adrenocortical cells and mature fat cells. The mature fat tissue occupies about 60% to 70% of the tumor (A: H&E staining, ×40; B: H&E staining, ×100). B-D: The high microscopic view showed cells bland, uniform with no pleomorphism, mitosis, necrosis, or capsular invasion and no hematopoietic tissue were observed in any of the sections (B: H&E staining, ×200; D: H&E staining, ×400).
The vital differential diagnose of adrenal lipo
denoma is adrenal myelolipoma because they
represent very uncommon but distinct patho-
logical entity which display indistinguishable
imageology features in the scan of computed
tomography or ultrasonography and analogous
clinical symptoms [9]. The adrenal myelolipoma
is also a rare tumor whose actual frequency is
pretty few, presenting fairly limited proportion
in adrenal tumors, but the incidence of myeloli-
poma is relatively much higher compared to
lipoadenoma [10]. It is acknowledged that
pathological morphology is the essential differ-
entiate point. The myelolipoma is microscopi-
cally composed of hematopoietic elements of
different lines that are conserved maturational
gradients, combined with mature adipose tis-
sue in varying proportions [11, 12], and, some-
times areas of calcification and ossification can
be observed in sections [13]. The only discrep-
ancy is that there are no hematopoietic tissue
and no calcification in the lipoadenoma.

Besides adrenal gland, previous research has
reported that lipoadenoma was also present in
other minority solid organs, such as salivary
gland [14-16], parathyroid [17, 18] and thyroid
[19]. Among these rare cases, salivary gland
and parathyroid lipoadenoma have a relatively
higher frequency. Parotid gland lipoadenoma is
the most common one in salivary gland lipoad-
enoma, which is characteristically comprised of
a mixture of oncocytes and adipocytes with or
without sebaceous differentiation and derives

Table 2. Clinical summary of the reported cases of adrenal lipoadenoma

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Weight (g)</th>
<th>functional endocrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papotti M et al. [1]</td>
<td>46</td>
<td>Female</td>
<td>Adrenal cortex</td>
<td>10</td>
<td>270</td>
<td>Present</td>
</tr>
<tr>
<td>Papotti M et al. [1]</td>
<td>74</td>
<td>Female</td>
<td>Adrenal cortex</td>
<td>6.5</td>
<td>50</td>
<td>Present</td>
</tr>
<tr>
<td>Uriev L et al. [2]</td>
<td>51</td>
<td>Female</td>
<td>Adrenal cortex</td>
<td>4</td>
<td>18</td>
<td>Present</td>
</tr>
<tr>
<td>Mylarappa P et al. [2]</td>
<td>12</td>
<td>Female</td>
<td>Adrenal cortex</td>
<td>10</td>
<td>unknown</td>
<td>Present</td>
</tr>
<tr>
<td>Present case</td>
<td>46</td>
<td>Male</td>
<td>Adrenal cortex</td>
<td>2</td>
<td>8</td>
<td>Absent</td>
</tr>
</tbody>
</table>
One case report of adrenal lipoadenoma

from the striated duct [15]. Parathyroid lipoadenoma, constituted by parathyroid cells and fat tissue, may be functional with secretion of parathyroid hormone or nonfunctional. What is interesting is that it appears ectopic atypical parathyroid lipoadenoma in the mediastinum [17]. Thyroid lipoadenoma is the minimum in all lipoadenoma with just one case report in English literature [19].

In summary, lipoadenoma of the adrenal gland is an extremely rare tumor, with a significant component of mature adipose tissue dispersed in the benign adrenocortical elements. Being functional or nonfunctional, adrenal lipoadenoma express obvious or unconspicuous clinical manifestation. Without any evidence of bone marrow elements, histopathological examination and immunohistochemical studies contribute to an accurate diagnosis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Songqing Fan, Department of Pathology, The Second Xiangya Hospital, Central South University, Changsha, Hunan, China. E-mail: songqingfan2000@yahoo.com

References