Int J Clin Exp Pathol 2015;8(8):9693-9697
www.ijcep.com /ISSN:1936-2625/IJCEP0011409

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 heterogenous 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.

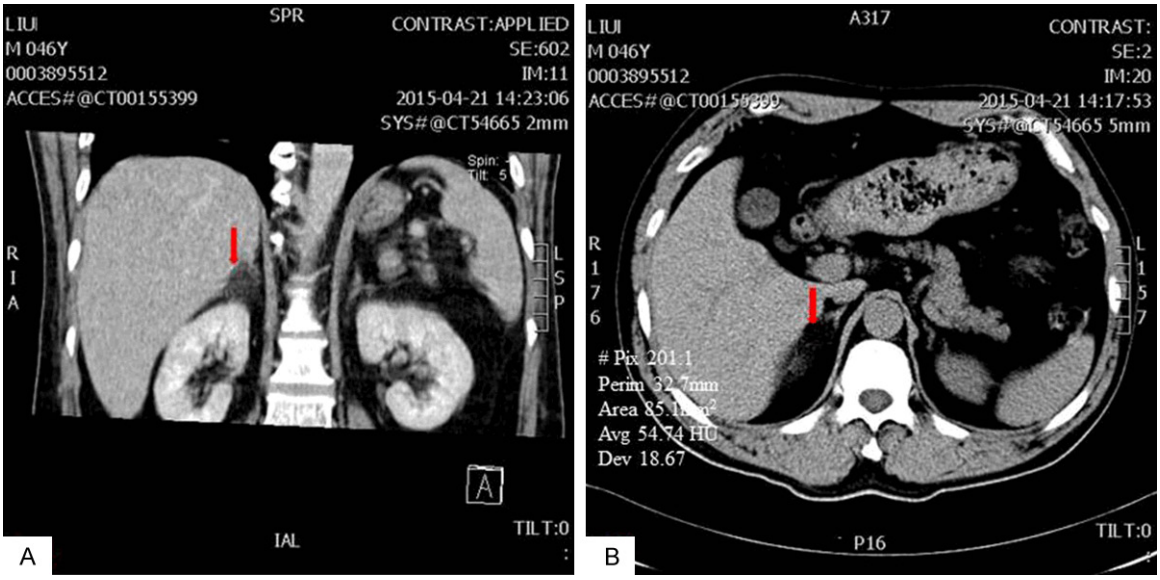

Figure 1. Contrast enhanced computed tomography in vertical section (A) and transverse section (B), showing a 1.7 cm in diameter well-defined heterogenous enhancing predominantly fat attenuating lesion involving the lateral branch of right adrenal gland (red arrow).

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

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

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

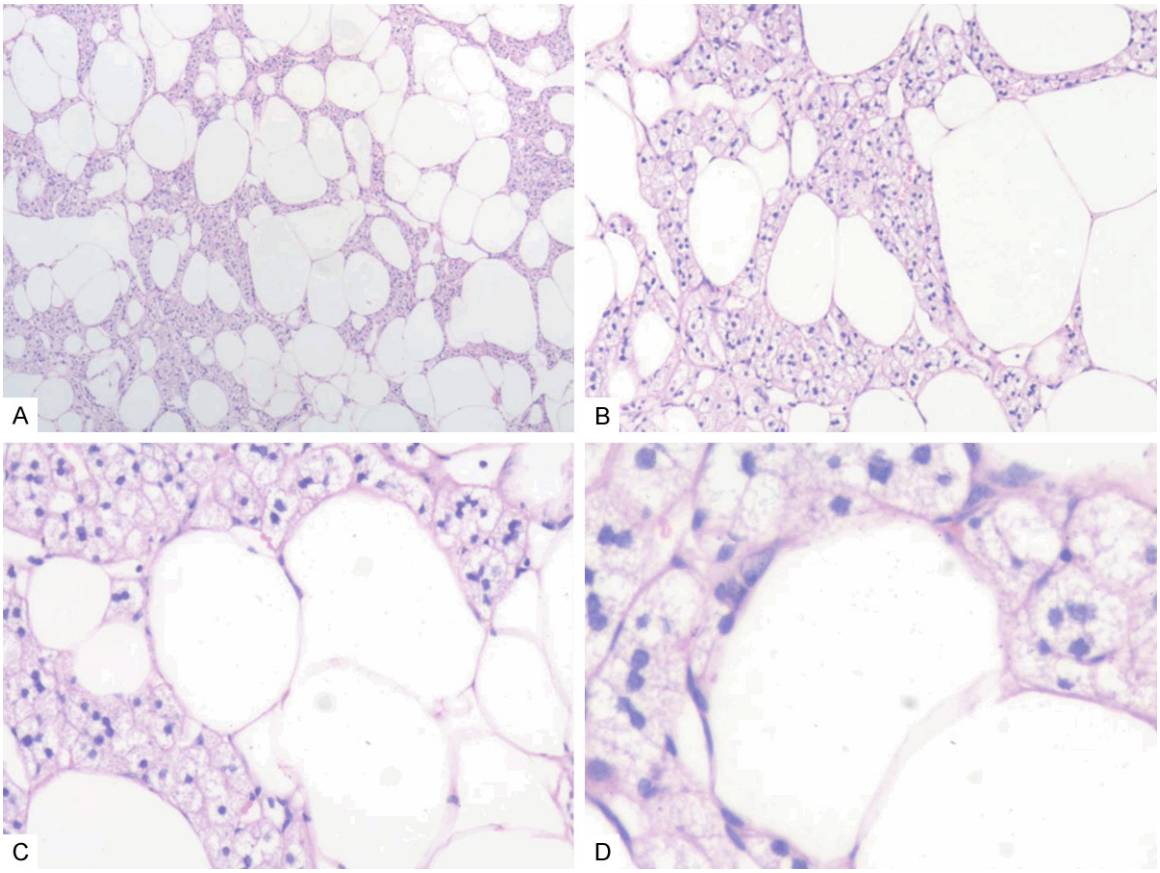

Figure 2. Hematoxylin & eosin (H&E) staining from sample of the tumor of adrenal gland by surgical resection. A, B: The low microscopic view showed the lesion comprised sheets and nests of adrenocortical cells and mature fat cells. The mature fat tissue occupies about 60% to 70% of the tumor (A: H&E 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).

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].

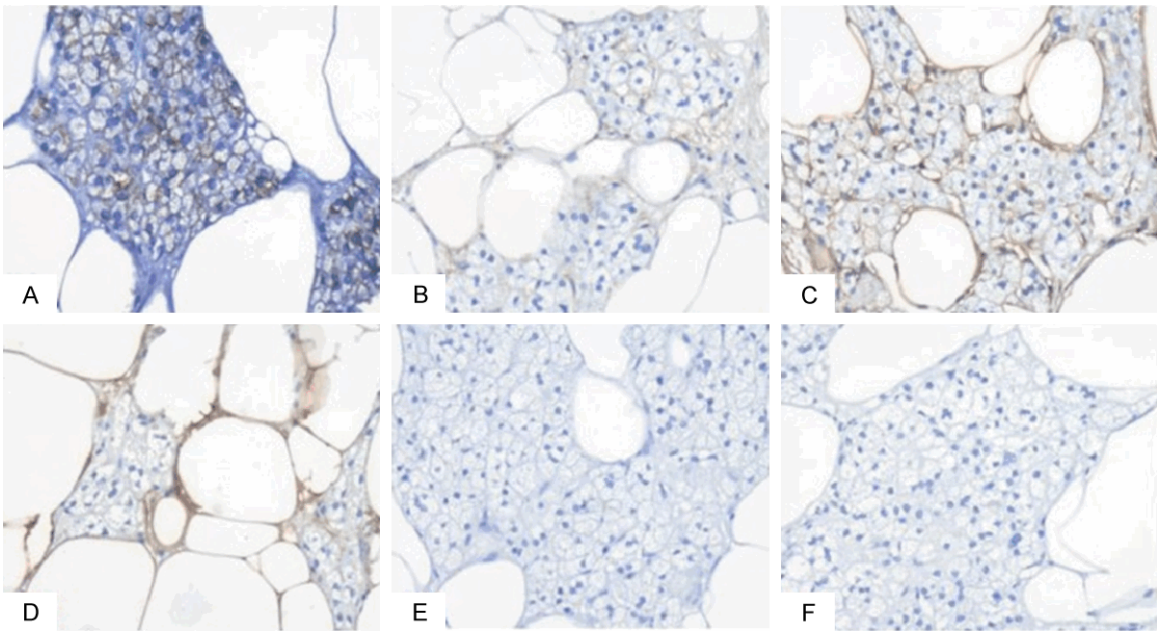

Figure 3. Immunohistochemical phenotypes of the adrenal tumor cells were detected by different antibodies. A: The adrenocortical cells were strongly positive for CD56 in the cell membrane (IHC, DA staining, ×200); B: The adrenocortical cells were strongly positive for EMA in the cell membrane (IHC, DA staining, ×200); C: Vimentin was positive expression in adipose tissue (IHC, DA staining, ×200); D: Fat cells were strongly positive for S-100 in the cell cytoplasm and nucleus (IHC, DA staining, ×200); E: The adrenocortical cells were negative immunohistochemical phenotype for Chromogranin (IHC, DA staining, ×200); F: The adrenocortical cells were also negative immunohistochemical phenotype for Syn (IHC, DA staining, ×200).

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

Reference	Age (yr)	Gender	Location	Size (cm)	Weight (g)	functional endocrine
Papotti M et al. [1]	46	Female	Adrenal cortex	10	270	Present
Papotti M et al. [1]	74	Female	Adrenal cortex	6.5	50	Present
Uriev L et al. [2]	51	Female	Adrenal cortex	4	18	Present
Mylarappa P et al. [2]	12	Female	Adrenal cortex	10	unknown	Present
Present case	46	Male	Adrenal cortex	2	8	Absent

The vital differential diagnose of adrenal lipoadenoma is adrenal myelolipoma because they represent very uncommon but distinct pathological 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 myelolipoma is relatively much higher compared to lipoadenoma [10]. It is acknowledged that pathological morphology is the essential differentiate point. The myelolipoma is microscopically composed of hematopoietic elements of different lines that are conserved maturational gradients, combined with mature adipose tissue in varying proportions [11, 12], and, sometimes areas of calcification and ossification can be observed in sections [13]. The only discrepancy 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 lipoadenoma, which is characteristically comprised of a mixture of oncocytes and adipocytes with or without sebaceous differentiation and derives

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

[1] Papotti M, Sapino A, Mazza E, Sandrucci S, Volante M, Bussolati G. Lipomatous changes in adrenocortical adenomas: report of two cases. Endocr Pathol 1996; 7: 223-228.

[2] Uriev L, Maslovsky I, Ben-Dor D, Barak F. Adrenal lipoadenoma. Pathol Discov 2014; 2: 2.

[3] Mylarappa P, Pathade A, Javali T, Ramesh D. Virilizing lipoadenoma of the adrenalgland in a pre-pubertal girl: A rare case. Indian J Urol 2014; 30: 219-221.

[4] Michalkiewicz E, Sandrini R, Figueiredo B, Miranda EC, Caran E, Oliveira-Filho AG, Marques R, Pianovski MA, Lacerda L, Cristofani LM, Jenkins J, Rodriguez-Galindo C, Ribeiro RC. Clinical and outcome characteristics of children with adrenocortical tumors: A report from the international pediatric adrenocortical tumor registry. J Clin Oncol 2004; 22: 838-845.

[5] Stiller CA. International variations in the incidence of childhood carcinomas. Cancer Epidemiol Biomarkers Prev 1994; 3: 305-310.

[6] Tenenbaum F, Lataud M, Groussin L. [Update in adrenal imaging]. Presse Med 2014; 43: 410-419.

[7] Doddi S, Singhal T, Leake T, Sinha P. Management of an incidentally found large adrenal myelolipoma: a case report. Cases J 2009; 2: 8414.

[8] Lau SK, Weiss LM. The Weiss system for evaluating adrenocortical neoplasms: 25 years later. Hum Pathol 2009; 40: 757-768.

[9] Lam KY, Lo CY. Adrenal lipomatous tumours: a 30 year clinicopathological experience at a single institution. J Clin Pathol 2001; 54: 707-712.

[10] Kerkhofs TM, Roumen RM, Demeyere TB, van der Linden AN, Haak HR. Adrenal Tumors with Unexpected Outcome: A Review of the Literature. Int J Endocrinol 2015; 2015: 710514.

[11] López Martín L, García Cardoso JV, Gómez Muñoz J, González Enguita C. Adrenal myelolipoma: Contribution of a case and bibliographic review. Arch Esp Urol 2010; 63: 880-883.

[12] Jung SI, Kim SO, Kang TW, Kwon DD, Park K, Ryu SB. Bilateral adrenal myelolipoma associated with hyperaldosteronism: report of a case and review of the literature. Urology 2007; 70: 1223.e11-1223.e13.

[13] Pascual García X, Bujons Tus A, Rodríguez Faba O, Gómez Ruíz JJ, Palou Redorta J, Villavicencio Mavrich H. Myelolipoma extraadrenal perirenal: aportación de un caso y revisión de la literatura. Actas Urol Esp 2007; 31: 932-934.

[14] Parmar HV. Oncocytic lipoadenoma of submandibular gland: a case report. J Clin Diagn Res 2015; 9: ED05-06.

[15] Chi CL, Kuo TT, Lee LY. Oncocytic lipoadenoma: a rare case of parotid gland tumor and review of the literature. J Pathol Transl Med 2015; 49: 144-147.

[16] Lau SK, Thompson LD. Oncocytic lipoadenoma of the salivary gland: a clinicopathologic analysis of 7 cases and review of the literature. Head Neck Pathol 2015; 9: 39-46.

[17] Yoon V, Treat K, Maalouf NM. Ectopic atypical parathyroid lipoadenoma: a rare cause of severe primary hyperparathyroidism. J Bone Miner Metab 2013; 31: 595-600.

[18] Ogrin C. A rare case of double parathyroid lipoadenoma with hyperparathyroidism. Am J Med Sci 2013; 346: 432-4.

[19] Melo GM, Bezerra Nde A, Nicolellis LP, Fontainha BC, Souza e Souza RA. Thyroid lipoadenoma: a case report of a rare condition. Braz J Otorhinolaryngol 2014; 80: 542-543.