

Adenomatoid tumor of the adrenal gland in young woman: from clinical and radiological to pathological study

Brankica Krstevska,¹
Sasha Jovanovska Mishevska,¹
Rubens Jovanovic²

¹Clinic of Endocrinology, Diabetes and Metabolic Disorders, Medical Faculty, Skopje; ²Institute of Pathology, Medical Faculty, Skopje, Macedonia

Abstract

Adenomatoid tumors are neoplasms of mesothelial origin, usually occurring in the male and female genital tracts. Extragenital localization sites such as adrenal glands are rare but have been reported. When found in the adrenals, they represent great clinical, radiological and pathological diagnostic challenge, with wide range of differential diagnoses to be considered. We present a case of a 30 years old female, with incidental ultrasound finding of unilateral tumor in the right adrenal gland. Multi slices CT scan was of value in localizing this tumor, but not in the precise diagnosis. The tumor ranged from 5.6 cm to 6.4 cm in greatest diameter. Clinical and hormonal examinations excluded Sy. Cushing, M. Conn and pheochromocytoma. The patient underwent laparoscopic right adrenalectomy. A large tumor (d: 8×7×3 cm) was removed showing no infiltration of the adrenal cortex or medulla, or extra-adrenal extension into the periadrenal adipose tissue. Histological examination showed numerous cystic spaces lined by flattened cubical epithelial cells. The small cystic spaces were separated by edematous fibrovascular stroma with rare epithelial cells with vacuolated cytoplasm. Immunohistochemical staining was positive with vimentin (+), S100 (+), MCA mesothelial Ag (+), CD 68 (+) and negative with acitin (-), CK7 (-), CD3 (-). Adenomatoid tumor is a rare benign neoplasm that should be added in the differential diagnosis of any adrenal tumor occurring in adrenal gland. The histological and immunohistochemical profiles of this adrenal adenomatoid tumor are very supportive in reaching the diagnosis of this benign tumor of a mesothelial cell origin, helping to avoid invasive treatment.

Introduction

Adenomatoid tumors are usually benign

neoplasms of mesothelial origin usually occurring in the genital tracts of both sexes, such as paratesticular sites in males and uterus, fallopian tubes, and ovary in females.¹ Also, these tumors can occur in extra-genital organs and anatomic sites, including liver, intestinal mesentery, omentum, pancreas, heart, pleura, mediastinum, lymph nodes and adrenal glands.² Their occurrence in the adrenal glands is rare and unexpected, so a variety of differential diagnostic challenges both clinically and morphologically could be elicited.

The first adenomatoid tumor of the genital tract was described in 1945 by Golden,³ but with the improvement of the imagining techniques such as ultrasound, computed tomography (CT) and magnetic resonance imaging (MR) scans in the late 1980s, more adrenal adenomatoid tumors were described.⁴ These radiological techniques are very useful in detecting adrenal incidentalomas,⁵ but not in the precise diagnosis of adenomatoid tumors. Until 2015, in the English language medical literature, only 38 cases of adrenal adenomatoid tumors have been reported, summarized by Ming Zhao *et al.*⁶ The incidence/per year of adrenal adenomatoid tumors is unknown. In this paper, we report another case of an adenomatoid tumor of the adrenal gland in young woman, radiologically misdiagnosed as myelolipoma, and to the best of our knowledge, this case is the first published from our country.

Case Report

We present a case of a 30 years old female referred to our clinic due to incidental ultrasound finding of right sided adrenal mass. She was admitted to the Clinic of endocrinology for workup of the right adrenal mass. At admission, the patient was alert and comfortable, with blood pressure 110/70 mmHg, and heart rate 90 beats/min. Her weight was 52 kg and height 168 cm. Other physical examinations were unremarkable. The patient denied any symptoms of palpitations, diaphoresis, flushing or uncontrolled high blood pressure. There were no clinical symptoms and signs for Sy. Cushing, M. Conn or pheochromocytoma. On examination she had no palpable mass in the right hypochondrium, only abdominal tenderness; there was no abdominal pain or macroscopic hematuria. The laboratory test showed normal serum sodium (147 mmol/L) and potassium (4.37 mmol/L) levels. Her 24-hour urine catecholamines, serum aldosterone and plasma rennin activity were all normal. The serum cortisol level at 08:00 am was 890 nmol/L (normal 55-690 nmol/L) and 39 nmol/L after 1 mg dexamethasone test, showing normal response to suppression.

Correspondence: Brankica Krstevska, Clinic of endocrinology, diabetes and metabolic disorders, Vodnjanska 17, 1000 Skopje, Macedonia
Tel.: +389 70 359072
E-mail: branakrstevska@yahoo.com

Key words: Adenomatoid tumor; Adrenal tumors; CT scan; Immunohistochemistry.

Contributions: the authors contributed equally.

Conflict of interest: the authors declare no potential conflict of interest.

Received for publication: 13 March 2016.
Revision received: 13 September 2016.
Accepted for publication: 13 September 2016.

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

©Copyright B. Krstevska *et al.*, 2016
Licensee PAGEPress, Italy
Rare Tumors 2016; 8:6506
doi:10.4081/rt.2016.6506

An abdominal ultrasonography was performed, which showed anechoic multiple small spots (cysts) within a hypoechoic lesion measuring 5.6×6.4 cm in diameter in the right adrenal gland. To confirm this finding, abdominal multi-slice CT scan was done; it demonstrated an expansive hypo-dense, heterogenous mass with visible septas and fat content, oval in shape, relatively well-demarcated. The mass measured 6.4 cm in the largest diameter (Figure 1). This finding was suggestive of myelolipoma. Imaging studies of the contralateral adrenal and all other organs were unremarkable. Based on the above finding, the diagnosis was nonfunctional adrenal adenoma - incidentaloma. The decision for surgery, as treatment of choice, was made upon the size of the tumor (>6 cm).⁷ The patient underwent a laparoscopic right adrenalectomy with no post operative complications. She is still alive today, four years after surgery and gave birth to a healthy baby. There is no recurrence of the tumor or metastatic disease, on the early follow-ups.

Pathologic findings

On gross examination the tumor was 8×7×3 cm in size, with grey and smooth surface and adhered atrophic adrenal gland on one side (Figure 2). On cross-section, there were numerous cystic spaces with smooth inner surface and variable size, filled with yellowish transparent gelatinous and hemorrhagic content (Figure 2). Microscopic analysis showed many cystic spaces lined with flattened epithelial cells (Figure 3). The cysts were separated

with oedematous fibrovascular stroma containing mesothelial and inflammatory cells (Figure 4). The tumor was confined within intact connective tissue capsule. In order to prove the origin, the following immunohistochemical staining was performed: vimentin, S100, MCA mesothelial Ag, CD69, actin, CK7 and CD34. Immunohistochemical staining was positive for vimentin(+), S100(+), MCA mesothelial Ag(+), CD69(+) and negative for actin (-), CK7(-); CD34(-). The cells lining the cysts as well as some of the cellular substrate in the stroma were positive for mesothelial cell markers, favoring the diagnosis of adenoma-

toid tumor (Figure 5). The morphological and immunohistochemical analyses were consistent with adenomatoid tumor.

Discussion

Adenomatoid tumors most commonly occur in the genital tract. They have rarely been reported to occur in the adrenal glands. Adrenal adenomatoid tumors are derived from mesothelial rests in the adrenal gland. During embryogenesis there is close relationship

between the adrenal glands and the Mullerian tract, so mesothelial rests could be present in this unexpected site such as the adrenal gland.² Adenomatoid tumors have definitive male predilection, with only case found in women published up to date.⁸ The age of occurrence ranges from 24 to 64 years, with a peak incidence in the fourth decades. These tumors are mostly nonfunctional, asymptomatic and discovered incidentally, during radiological examinations, surgery or on autopsy. Some of them showed hormonal hyperactivity: one with high levels of urine homovanilic acid, one with high levels of aldosterone (adrenal micronodular cortical hyperplasia - primary hyperaldosteronism)⁹ and high level of basal plasma cortisol due to stress (hospitalisation) and normal cortisol suppression after overnight 1 mg dexamethasone, in our case. Occasionally, patients may present symptoms linked to the adrenal mass, such as palpable mass, abdominal tenderness (notable in our case), abdominal pain in 3 cases and gross hematuria in one case.⁴ Another point which should be considered in patients with adrenal mass is the metabolic status including hypertension and diabetes mellitus. Adenomatoid tumors are not associated with diabetes, but seven cases were found to be associated with hypertension.⁹⁻¹⁴ Specific diseases are not found with adrenal adenomatoid tumors, but two cases with concomitant myelolipoma are reported in the literature¹⁴, one patient with human immunodeficiency virus¹⁵ and one with coccidiomycosis. Radiologically, adenomatoid tumors of the adrenal gland lack specific imaging features and are usually solid, but rarely may be extensively cystic.^{6,16} Various radiologic techniques were used including ultrasound, computed tomography scans, magnetic resonance imaging scans and positron emission scans, and not one of them was able to precise the diagnosis. So, adenomatoid tumors can be confused with other more common adrenal benign non-functional adenomas and adrenocortical carci-

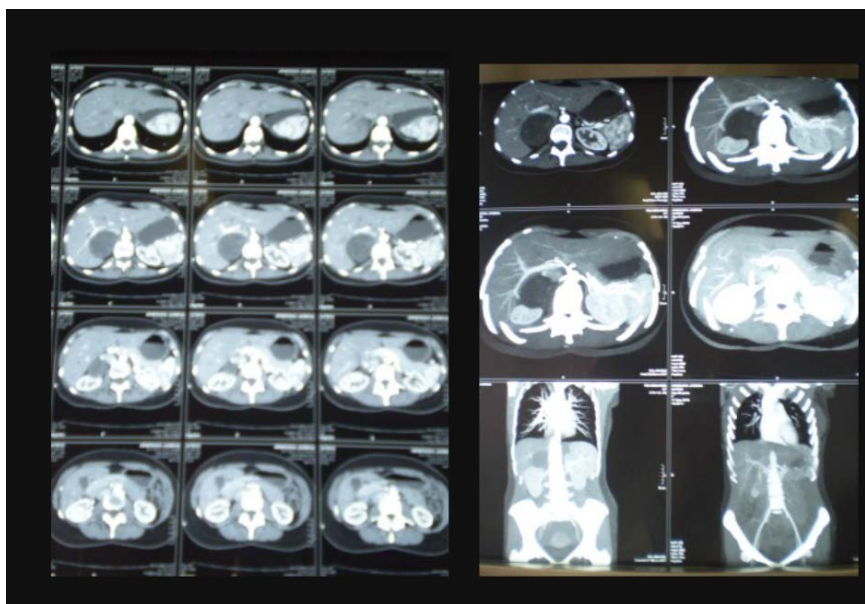


Figure 1. Abdominal computed tomography scan shows right side adrenal mass with 6.4 cm in diameter.



Figure 2. Macroscopic finding: large tumor with pale grey and smooth surface and adhered atrophic adrenal gland on one side. On cross-section, numerous cystic spaces with smooth inner surface and variable size, filled with yellowish transparent gelatinous and hemorrhagic content.

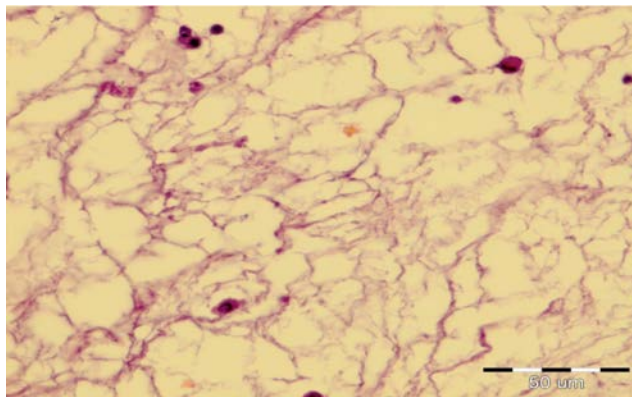


Figure 3. Microscopic appearance of the tumor: Hematoxylin and Eosin staining 40x.

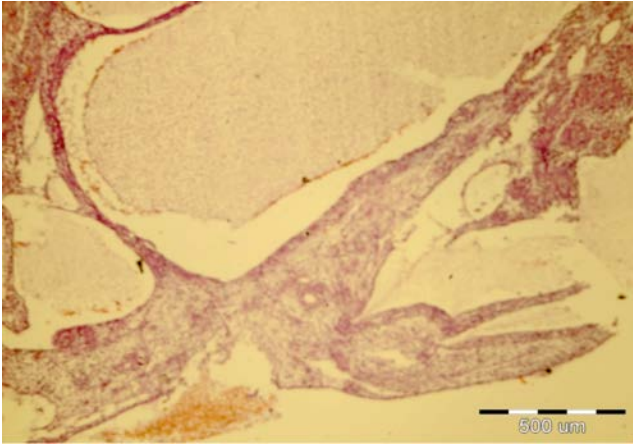


Figure 4. Higher magnification microphotograph of the cystic spaces and intervening stroma: Hematoxylin and Eosin staining 200x.

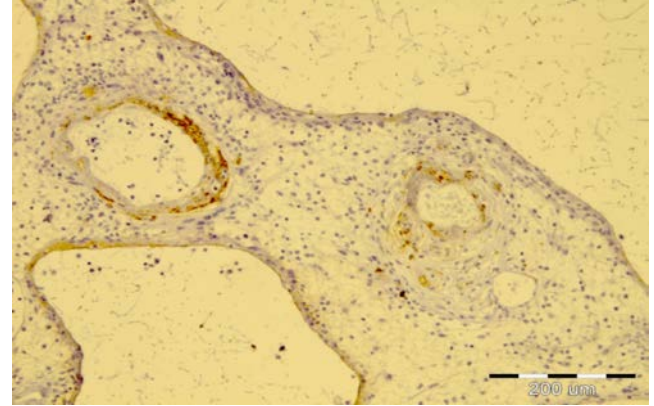


Figure 5. Immunohistochemical staining for MCA 100x.

nomas, as well as other entities such as myelolipoma, lymphangioma, hemangioma, angiosarcoma and cysts.^{6,14,17}

Adenomatoid tumors are benign neoplasms of mesothelial origin with the same characteristics of the adenomatoid neoplasms from the urogenital system.¹ Tumor cells can form solid nests, but more often they form fenestrated channels or anastomosed tubules with variable size and form, located in the fibrous stroma in variable order. Tumor cells have significant vacuolisation, with eccentrically located nucleus (signet- ring cell). Immunohistochemically the tumor is positive on calretinin, epithelial membrane antigen, creatinin, creatinin 7, mesothelial cell antigen, vimentin, and negative on endothelial markers (CD 31, CD 34 and factor VIII- related antigen, CD 56). Pathohistological and immunohistochemical examination are the only way to confirm the diagnosis for adenomatoid tumor.^{2,4,8,15}

Surgical removal is first line therapy, using laparoscopic adrenalectomy as gold standard, or in some cases open approach. Local resection limited to adrenal gland is sufficient, with no post-operative complications and long-life survival from 4 months to 177 months. The surgical treatment is final treatment and no cases with local reappearance or metastatic disease have been reported so far.

Conclusions

Adrenal adenomatoid tumor is a rare benign neoplasm that should be added in the differential diagnosis of any adrenal tumor occurring in adrenal gland. The histological and immunohistochemical profiles are very supportive in reaching the diagnosis of this

benign tumor of a mesothelial cell origin, helping to avoid invasive treatment.

References

1. Wachter DL, Wunsch PH, Hartmann A, Agaimy A. Adenomatoid tumors of the female and male genital tract. A comparative clinicopathologic and immunohistochemical analysis of 47 cases emphasizing their site-specific morphologic diversity. *Virchows Arch* 2011;458:593-602.
2. Travis WD, Lack EE, Azumi N, et al. Adenomatoid tumor of the adrenal gland with ultrastructural and immunohistochemical demonstration of a mesothelial origin. *Arch Pathol Lab Med* 1990;114:722-724.
3. Golden A, Ash JE. Adenomatoid tumors of the genital tract. *Am J Pathol* 1945;21:63-79.
4. Evans CP, Vaccaro JA, Storrs BG, Christ PJ. Suprarenal occurrence of an adenomatoid tumor. *J Urol* 1988;139:348-9.
5. Rodrigo Gasque C, Marti-Bonmati L, Dosda R, Gonzalez Martinez A. MR imaging of a case of adenomatoid tumor of the adrenal gland. *Eur Radiol* 1999;9:552-4.
6. Zhao M, Li C, Zheng J, et al. Cystic lymphangioma-like adenomatoid tumor of the adrenal gland: report of a rare case and review of the literature. *Int J Clin Exp Pathol* 2013;6:943-50.
7. Krstevska B, Dimitrovski C, Pemovska G. Evaluation the methods in decision-making for surgery of adrenal incidentalomas. *Maced Med J* 2003.
8. Raaf HN, Grant LD, Santoscoy C, et al. Adenomatoid tumor of the adrenal gland: a report of four new cases and a review of the literature. *Mod Pathol Off J United States Can Acad Pathol Inc* 1996;9:1046-51.
9. Chung-Park M, Yang JT, McHenry CR, Khiyami A. Adenomatoid tumor of the adrenal gland with micronodular adrenal cortical hyperplasia. *Hum Pathol* 2003;34:818-21.
10. Simpson PR. Adenomatoid tumor of the adrenal gland. *Arch Pathol Lab Med* 1990;114:725-7.
11. Denicol NT, Lemos FR, Koff WJ. Adenomatoid tumor of supra-renal gland. *Int Braz J Urol* 2004;30:313-5.
12. Hamamatsu A, Arai T, Iwamoto M, et al. Adenomatoid tumor of the adrenal gland: case report with immunohistochemical study. *Pathol Int* 2005;55:665-9.
13. Fan SQ, Jiang Y, Li D, Wei QY. Adenomatoid tumour of the left adrenal gland with concurrent left nephrolithiasis and left kidney cyst. *Pathology* 2005;37:398-400.
14. Timonera ER, Paiva ME, Lopes JM, et al. Composite adenomatoid tumor and myelolipoma of adrenal gland: report of 2 cases. *Arch Pathol Lab Med* 2008;132:265-7.
15. Angeles-Angeles A, Reyes E, Munoz-Fernandez L, Angritt P. Adenomatoid tumor of the right adrenal gland in a patient with AIDS. *Endocr Pathol* 1997;8:59-64.
16. Liu Y, Zhang H, Wang G, et al. A giant cystic adenomatoid tumor of the adrenal gland: a case report. *Chin Med J (Engl)* 2010;123:372-4.
17. Taskin OC, Gucer H, Mete O. An unusual adrenal cortical nodule: composite adrenal cortical adenoma and adenomatoid tumor. *Endocr Pathol* 2015;26:370-3.