Int J Clin Exp Pathol 2017;10(8):8908-8915
www.ijcep.com /ISSN:1936-2625/IJCEP0058603

Case Report

Myxoid adrenocortical adenoma with a pseudoglandular pattern: a case report and literature review

Zhi Zeng[1*], Li-Juan Gu[2*], Zi-Ying Zhou[1], Lin Liu[1], Hong-Lin Yan[1], Ya-Bing Huang[1], Ze-Sheng Wang[1], Jun Chen[3], Jing-Ping Yuan[1]

Departments of [1]Pathology, [2]Central Laboratory, [3]Radiology, Renmin Hospital of Wuhan University, Wuhan, Hubei Province, P. R. China. [*]Equal contributors.

Received June 1, 2017; Accepted July 27, 2017; Epub August 1, 2017; Published August 15, 2017

Abstract: Adrenocortical adenoma is a benign neoplasm derived from cells of the adrenal cortex. The myxoid variant of this tumor is extremely rare. To our knowledge, only 23 cases of myxoid adrenocortical adenoma have been reported so far and 19 of them mentioned the pseudoglandular pattern. We reported a new case of 56-year-old Chinese female patient whose left adrenal gland was shown a neoplastic lesion by computed tomography (CT) and magnetic resonance (MR) imaging. Histopathological study showed that the mass was a myxoid adrenocortical adenoma with a pseudoglandular pattern. Then, we performed immunohistochemistry with 28 biomarkers to make differential diagnosis and found that tumor cells were diffusely positive for vimentin, melan-A, CD56, NSE and USP10, and focally positive for cytokeratin pan, cytokeratin 8/18 and VEGF. The labeling index of Ki-67 and Cyclin D1 were about 1% and 50%, respectively. No immunoreactivity was found for EMA, cytokeratin 7, HMB45, S-100, alpha-inhibin, calretinin, synaptophysin, chromogranin A, P53, EGFR, MMP2, DNA topo II alpha, CA125, E-cadherin, P63, P16 and Her-2. The patient has been followed up for 37 months after tumor resection and no evidence was found to suggest any local recurrence or any metastatic disease. Myxoid adrenocortical adenoma with a pseudoglandular pattern is extremely rare. The accurate diagnosis should be based on combined consideration of clinical characteristics, CT, MR imaging and pathological features, and should be distinguished from other retroperitoneal myxoid tumors.

Keywords: Adrenocortical adenoma, myxoid variant, pseudoglandular pattern

Introduction

Myxoid variant is a rather rare change in adrenocortical adenomas and carcinomas. Up to present, 56 cases (23 cases of myxoid adrenocortical adenomas, 2 cases of borderline myxoid adrenocortical neoplasms and 31 cases of myxoid adrenocortical carcinomas) have been reported [1]. Among them, 23 cases of these tumors were pseudoglandular pattern [1-13]. We here present another case of myxoid adrenal cortical neoplasm with a pseudoglandular pattern. Histologically, it was alike those reported benign-looking tumor cells arranged in pseudoglandular pattern with myxoid stroma. We made a definite diagnosis combining the common pathological results with CT, MRI, angiographic results and immunohistochemistry.

Case presentation

Clinical history

A 56-year-old female presented a repeating limb weakness in the past six months with a historical hypertension for 8 years, which was controlled by taking Nifedipine and Hydrochlorothiazide. Laboratory tests showed abnormality of FT3 (12.42 pg/ml), FT4 (4.04 ng/dl), TSH (0.007 μIU/ml), potassium (3.1 mmol/L), which presented the syndrome of hyperthyroidism with limb weakness and hypertension. Endocrine evaluation showed the levels of cortisol, aldosterone, angiotensin I, norepinephrine, epinephrine, adrenocorticotropic hormone and total catecholamine were within the normal limits, except higher rennin (29.60 pg/mL) and lower angiotensin II (6.40 pg/mL).

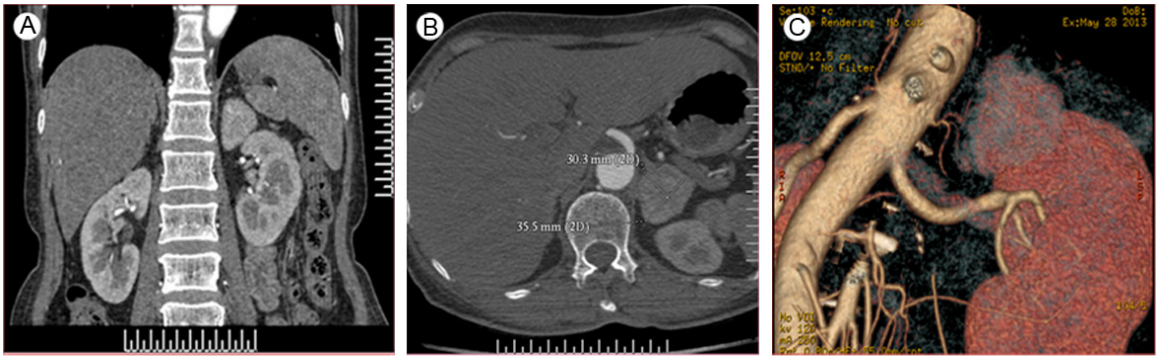

Figure 1. CT and MR imaging findings of a pseudoglandular myxoid adrenocortical adenoma. A. CT scan showed a rounded low-density mass in the left adrenal gland (coronal plane). B. CT scan presented a mass shadow whose maximum cross-sectional area was about 35.5×30.3 mm in the transverse plane. C. DSA indicated the tumor was located on the upper pole of left kidney and got its blood supply from abdominal aorta.

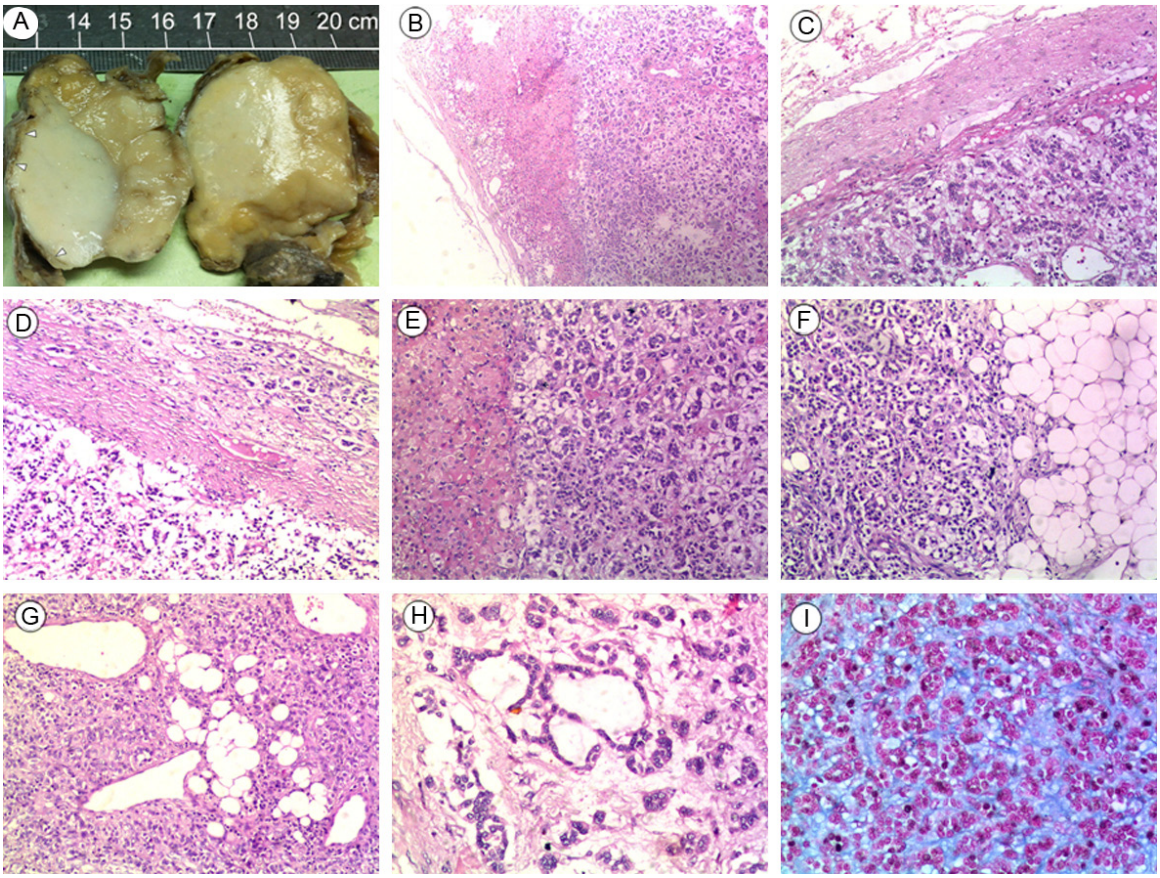

Figure 2. Pathologic findings of a pseudoglandular myxoid adrenocortical adenoma. A. Macroscopic appearance of the resected adrenal tumor. The mass was roundish with clear boundaries, measured 3.5×3.3×3.0 cm with partial capsule, surrounded by less well-formed fat, and had a grayish-white color. The outermost adrenal cortex (arrowheads) was compressed and bordered by a fibrous capsule. B. Tumor cells were loosely anastomosing and had a clear demarcation from the compressed adrenal gland (HE, ×40). C. The tumor was encapsulated (HE, ×100). D. Focal capsular penetration (HE, ×100). E. The tumor had a clear demarcation from the compressed adrenal gland (HE, ×100). F. The tumor had a clear demarcation from the adipose tissue (HE, ×100). G. Focal lipomatous metaplasia within the tumor (HE, ×100). H. Tumor cells were showing distinct pseudoglandular pattern with myxoid material inside (HE, ×200). I. The tumor contained large amounts of extracellular acidic mucous material (Alcian blue staining, ×200).

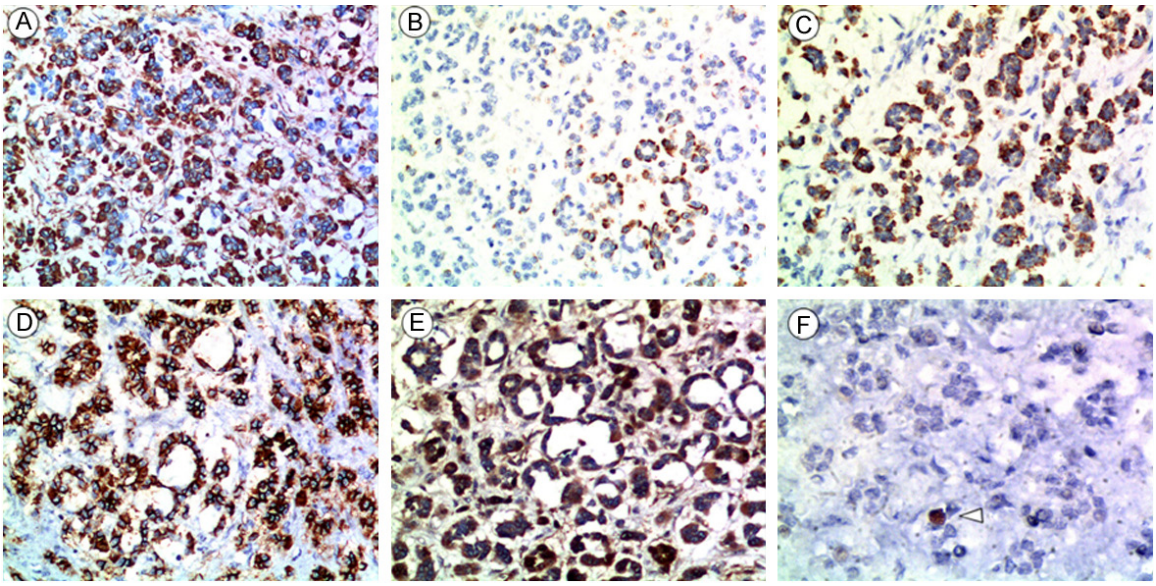

Figure 3. Immunohistochemical staining of a pseudoglandular myxoid adrenocortical adenoma. A. Strong and diffuse immunoreactivity for Vimentin (×200). B. Focal CK 8/18 positivity (×200). C. Strong and diffuse immunoreactivity for melan-A (×200). D. Strong and diffuse immunoreactivity for CD56 (×200). E. Diffuse immunoreactivity for USP10 (×200). F. Ki-67 labeling index showed a fraction of 1% of positive tumor cells (arrowhead represented a positive tumor cell, ×400).

Unenhanced CT showed an abnormality on the left adrenal gland (**Figure 1A**). MRI also revealed a mass shadow whose maximum cross-sectional area was about 33.3×39.3 mm in the coronal plane and 35.5×30.3 mm in the transverse plane, which was consistent with the CT result (**Figure 1B**). All these results led to a neoplastic lesion that was most likely to be an adrenal pheochromocytoma, but did not rule out the possibility of an adenoma. Digital subtraction angiography (DSA) displayed the tumor was located on the upper pole of the left kidney and blood-supplied by branches of the abdominal aorta (**Figure 1C**).

Materials and methods

The tumor cells were fixed in 10% formaldehyde and embedded in paraffin for pathological study. Sections (4 μm) were cut from each paraffin block for histopathological examination and special stains (periodic acid-Schiff and Alcian blue).

Immunohistochemistry analysis was performed as previously described [14]. A large panel of primary antibodies were used (source and solutions): Vimentin (RMA-0547, SP20), HMB45 (MAB-0098, HMB45), S-100 (MAB-0585, 4C4.9), Melan-A (MAB-0275, A103), Cytokeratin 8/18 (CK8/18, MAB-0650, 5D3), Cytokeratin 7 (CK7, MAB-0166, OV-TL 12/30 + 72.2), Synaptophysin (RMA-0537, SP11), Chromogranin A (RMA-0548, SP12), CD56 (MAB-0256, 56C04), Calretinin (RMA-0524, SP13), VEGF (MAB-0243, VG1), CD34 (MAB-0034, QBEnd/10), EGFR (RMA-0554, SP9), Cyclin D1 (RMA-0541, SP4), Actin (Smooth Muscle) (SMA, Kit-0006-2, 1A4), E-cadherin (MAB-0589, A42C7), P53 (MAB-0142, DO-7), P63 (MAB-0365, 4A4), P16 (INK4A) (MAB-0673, MX007), Bcl-2 (MAB-0014, 8C8), CD45 (LCA, MAB-0037, PD7/26 + 2B11), C-erbB-2 (Her-2, RMA-0555, SP3), Ready-to-use; Maixin Bio, Fujian, China; Cytokeratin pan (ZM-0069, AE1/AE3), Epithelial Membrane Antigen (EMA, ZM-0095, E29), Neuron Specific Enolase (NSE, ZM-0203, E27), CD31 (ZM-0044, JC70A), CA125 (ZM-0019, TA347), Ki-67 (ZM-0166, K2), Ready-to-use; ZSGB-Bio, Beijing, China; alpha-inhibin (GM36-0902, R1), Ready-to-use; Gene Tech (Shanghai) Company Limited, Shanghai, China. Ubiquitin-specific protease 10 (USP10, ab109219), 1:250; Abcam, Cambridge, MA, USA.

Sections were lightly counterstained with hematoxylin. Appropriate positive and negative controls were performed concurrently for all the applied antisera.

Table 1. Review of the English literature of the last 16 years

No.	Information Literatures	Age	Sex	Clinical record			Pathology	
				Diameter/ size(cm)	Side	Symptom	Myxoid area	Pseudoglandular pattern
1	Brown et al., 2000	21	F	7.5		Slightly elevated cortisol	95%	4/6 +
2		35	F	3.5			40%	
3		31	F	6.0		Normal lab values	70%	
4		73	M	4.0			50%	
5		16	F	7.0		Conn's syndrome	80%	
6		62	F	6.0		Normal lab values	40%	
7	Honda et al., 2001	56	M	3.2×2.0×3.0	R	Slightly elevated cortisol and aldosterone	2/3	+
8	Dundr et al., 2003	45	M	5.0	R	Arterial hypertension	90%	+
9	Bollito et al., 2004	58	M	5.0×4.0	R	Hypertension	>75%	+
10	Fine et al., 2005	64	M	8.8×7.0×4.0	L	Normal lab values	Multiple	+
11	du et al., 2005	41	M	3.3×2.8×2.7	R	Hypertension	Showed	+
12	Zhang et al., 2006	45	M	3.3×2.8×2.7	R	Mild hypertension	Nearly all	+
13	Wang et al., 2007	66	M	6.0×4.5×4.0	R	Normal lab values	90%	+
14	Lu et al., 2008	32	F	5.0×4.5×2.0	L	Hypertension	Most	+
15	Zhang et al., 2011	43	F	5.5		Elevated aldosterone	90%	+
16		37	M	3.0		Hypertension	30%	-
17		45	M	6.5		Hypertension	30%	+
18		53	M	3.5		Hypertension	70%	+
19		45	F	3.0		Elevated aldosterone	90%	+
20		51	M	4.0		Hypertension	70%	+
21	De Padua et al., 2014	67	F	8.0×7.0×5.5	L	Hypertension	20%	+
22	Kim et al., 2014	74	F	6.0×4.7×1.6	R	Hypertension	>90%	-
23	Wang et al., 2014	34	F	3.0×3.0×2.5	L	Normal lab values	Showed	+
Present case		56	F	3.5×3.3×3.0	L	Conn's syndrome	Showed	+

F, female; *M,* male; *L,* left; *R,* right.

Pathological findings

Grossly, the mass was roundish with clear boundaries, measured 3.5×3.3×3.0 cm with partial capsule, surrounded by less well-formed fat, and had a grayish-white color. A small amount of atrophic brown-colored adrenal tissue could be seen on one side of the mass and had a clear demarcation with the margin of tumor (**Figure 2A**).

At light microscopy, most of the tumor was demarcated by a fibrous capsule (**Figure 2B**, **2C**). Focal capsular penetration was observed (**Figure 2D**). Atrophic adrenal gland tissue was found at the periphery of the tumor (**Figure 2B**) and had a clear demarcation from the solid (**Figure 2E**). Adipose tissue was around the tumor cells (**Figure 2F**), while focal lipomatous metaplasia was found within the tumor (**Figure 2G**). Some of the tumor cells arranged in compact cords and tubules, while other cells were anastomosing irregularly, or formed the so called pseudoglandular characteristics, floating loosely in the myxoid background. The medium-sized polygonal cells with clear boundaries had abundant of eosinophilic cytoplasm. The deep-dyed caryons were roundish or oval, karyotheca and nucleolus were clear (**Figure 2H**). The lesion showed limited dysplasia or cell pleomorphism, rare mitoses and no evidence of necrosis or vascular invasion. Diffuse histochemical staining for Alcian blue highlighted the abundant eosinophilic myxoid material in the glandular cavity and interstitial (**Figure 2I**).

Immunohistochemistry

The immunohistochemical data displayed that tumor cells were diffusely positive for vimentin, melan-A, CD56, NSE and USP10, focally positive for cytokeratin pan, cytokeratin 8/18 and VEGF. The labeling index of Ki-67 and Cyclin D1 was about 1% and 50%, respectively (**Figure 3**). Other markers, including EMA, CK7, HMB45, S-100, alpha-inhibin, calretinin, synaptophysin, chromogranin A, P53, EGFR, MMP2, DNA topo II alpha, CA125, E-cadherin, P63, P16 (INK4A), CD31, CD34, SMA and Her-2, were all negative.

Table 2. Antibodies used and results in this case

Antibodies	Result	Antibodies	Result
Vimentin	(Diffuse) +	CgA	-
Melan-A	(Diffuse) +	HMB45	-
CD56	(Diffuse) +	S-100	-
NSE	(Diffuse) +	EMA	-
USP10	(Diffuse) +	CK 7	-
pan-CK	(Focal) +	Syn	-
CK 8/18	(Focal) +	α-inhibin	-
VEGF	(Focal) +	Calretinin	-
Cyclin D1	(50%) +	CA125	-
Ki-67	(1%) +	EGFR	-
LCA	(Lymphocytes) +	E-cadherin	-
CD34	(Vascular) +	P53	-
CD31	(Vascular) +	P63	-
SMA	(Basement membrane) +	P16 (INK4A)	-
		Her-2	-

CK, cytokeratin.

Based on the above findings, this tumor was diagnosed as myxoid adrenocortical adenoma with a pseudoglandular pattern.

Here, 23 cases of myxoid adrenocortical adenoma were summarized (**Table 1**). We also analysed all the immunohistochemical results that have been evaluated in this case (**Table 2**). In addition to basic immunohistochemistry test, indicators for differential diagnosis among myxoid adrenocortical adenoma, pheochromocytoma, adenocarcinoma metastatic, melanoma, PEComa and chordoma were detected (**Table 3**). Six markers for differential diagnosis between adrenocortical adenoma and carcinoma were examined (**Table 4**). Moreover, we presented the negative data of the immunohistochemical markers which could be referenced for other researchers.

Clinical follow-up

The patient has been followed up for 37 months after laparoscopic adrenalectomy. The levels of potassium recurred to the normal ranges and BP was within normal limits by treated with medicine for hyperthyroidism. And there was no evidence to suggest any palindromia.

Discussion

Myxoid adrenocortical adenoma, reported by Brown et al. for the first time in 2000 [4], is a rare adenoma originated from adrenal cortex. We referred to 23 cases and summarized them (see **Table 1** for details and references). The age of these patients ranged from 16 to 74 years old (mean 47.5) with a male-to-female ratio of 1:1. Tumor diameter ranged from 3 to 8.8 cm. A characteristic feature of these tumors is that cords and nests of tumor cells were floating loosely in a myxoid background, some of which exhibited lumens imparting a pseudoglandular appearance [1, 4-6, 8, 9, 11-13]. All cases noted myxoid change and the range of myxoid area was 40%-95%. Pseudoglandular pattern was showed in 19 cases and revealed a strong connection between pseudoglandular pattern and myxoid change [1, 3-9, 11, 12]. Since the pseudoglandular pattern has been seldom observed in conventional adrenal tumor, the possible reason may due to the myxoid change which induces the formation of pseudoglandular structure. The tumor cells in most cases were polygonal with clear cell boundaries and finely granular eosinophilic cytoplasm [1, 4-6, 8, 9, 11-13]. Necrosis and vascular invasion were absent in adenomas [1, 4-6, 8, 9, 11-13]. In current reporting case, we could hardly observe significant gelatinous areas in gross as other reports mentioned. However, under the microscope, pseudoglandular areas were found and characterized with small tubulars containing mucintype material. The tumor cells were medium-sized and polygonal with clear boundaries and eosinophilic cytoplasm. Roundish or oval caryons were deep-dyed with clear karyotheca and nucleolus. The lesion showed limited dysplasia or cell pleomorphism, rare mitoses and no evidence of vascular invasion or necrosis. All the above evidences supported our diagnosis.

A serial of markers were detected in our case for differential diagnosis with pheochromocytoma, adenocarcinoma metastatic, melanoma, PEComa and chordoma. Vimentin was diffusely positive while EMA was negative, and cytokeratin pan was focally positive. These markers excluded the possibility of epithelial origined tumor and suggested that the glandular structures were pseudoglandular pattern but not adenocarcinoma. Melan-A was diffusely positive while S-100 and HMB45 were negative, and this suggested that the tumor might be originated from the adrenal cortex, rather than

Table 3. Differential diagnosis of myxoid adrenocortical adenoma with a pseudoglandular pattern

	Myxoid adrenocortical adenoma	Pheochromocytoma	Adenocarcinoma metastatic	Melanoma/PEComa	Chordoma
Vimentin	+	+	-	+	+
Cytokeratins	(Focal) +/-	-	+	-	+
EMA	-	-	+	-	+
Melan A	+	-	-	+	-
CgA	-	+	-	-	-
HMB45	-	-	-	+	-
S-100	-	-	-	+	+

Table 4. Immunohistochemical markers in adrenal cortical adenoma, carcinoma and this case

Immunohistochemical markers	LI or Positive rate (%)			This case
	Adenoma	Carcinoma	Reference	
Ki-67 (LI)	LI<4.0%	LI≥4.0%	Aubert S et al.	LI = 1%
p53 (LI>20%)	6.6%	73.0%	Gupta D et al.	Negative
MMP2	2.0%	74.0%	Volante M et al.	Negative
DNA topo II alpha	0.0%	64.7%	Iino K et al.	Negative
EGFR	27.3%	63.6%	Zhang J et al.	Negative
VEGF	30.0%	71.4%	Wang CP et al.	Focal positive

LI, labeling index.

malignant melanoma or a metastatic one. Our previous study showed that the expression of USP10 was found in 100% of adrenocortical adenomas, 88.89% of adrenocortical carcinomas, and 10% of pheochromocytomas; the difference between adrenocortical adenoma/carcinoma and pheochromocytoma was statistically significant. Thus, a positive USP10 immunoreaction can be useful in distinguishing adrenal cortical tumors from pheochromocytoma [15]. In this article, Melan-A and USP10 were positive and chromogranin A was negative, which excluded pheochromocytoma and supported the diagnosis that the tumor was originated from the adrenal cortex rather than adrenal medulla [15]. EMA was negative and cytokeratin pan was focally positive, which ruled out the possibility of chordoma. Alcian blue staining highlighted the extracellular acidic mucosubstances in all reported myxoid adrenal tumors and so did in this case. The observed staining of the myxoid material existing outside rather than inside the cells indicated that its origin was probably related to degenerative changes, instead of mucosubstances produced by tumor cells [11].

Several multiparametric systems have been published in differential diagnosis between benign and malignant adrenocortical tumors. The Weiss scoring system and its modified version appear to be most utilized due to its simplicity and reliability [16]. According to the modified Weiss system, our case fitted the criteria of a conventional adenoma for having only partial capsular infiltration. Moreover, Aubert et al. reported that Ki-67 was a reliable marker in the differential diagnosis of adrenocortical tumors [16]. A 4% Ki-67 labeling index threshold for malignancy achieved 95.7% sensitivity and 91.7% specificity. In our case, Ki-67 labeling index showed a fraction of 1% of positive tumor cells. Recently, several additional markers have been described to identify adrenocortical tumors, such as P53 [17], MMP2 [18], DNA topo II alpha [19], EGFR [20] and VEGF [21]. P53 plays a role in apoptosis, genomic stability, and inhibition of angiogenesis. Gupta et al. evaluated a set of molecular markers including p53, and correlated their expression with histological diagnosis and clinical outcome [17]. The authors found higher p53 labeling index was present in 73% of malignant adrenal cortical tumors but was found in only 6.6% of benign adrenal cortical tumors, the difference was statistically significant. Metalloproteinases were demonstrated to be implicated in malignant progression and metastatization of solid tumors, including endocrine ones. Volante et al. reported the expression of MMP2 was detected in neoplastic cells in 74% of adrenocortical carcinomas and 2% of adrenocortical adenomas, which gave the most significant results [18]. As a cell cycle-related intranuclear protein, DNA topo II alpha did help to differentiate carcinoma from adenoma in resected adrenocortical neoplasms [19]. EGFR

had strong regulatory effects on cell differentiation, proliferation, survival, and migration. And, VEGF was an important signaling protein involved in both vasculogenesis and angiogenesis [21, 22]. It was reported that the expression of EGFR and VEGF was higher in adrenocortical carcinoma than in adrenocortical adenomas [20, 21]. Integrated above information, these markers could be allegedly stained in most of carcinomas but a few of adenomas. In present case, no immunoreactivity was found for these markers, supporting the diagnosis of adrenocortical adenoma. Furthermore, the clinical outcome of this case being uneventful in the following 37 months also confirmed the diagnosis.

Conclusions

In conclusion, the immunohistochemical profiles including vimentin, cytokeratin pan, melan-A, USP10, chromogranin A, etc. differentiated adrenocortical adenoma from other retroperitoneal myxoid tumors. The negative expressions of Ki-67, MMP2, EGFR, etc. supported the tumor as benign. The histological features of pseudoglandular myxoid pattern differentiated this tumor from a conventional adrenocortical tumor. Moreover, CT and MRI results were of great help in showing the size and the location of the tumor.

Acknowledgements

This work was supported by grants from National Natural Science Foundation of China (Grant No. 81602535 to Zhi Zeng and No. 81301019 to Li-Juan Gu), Hangzhou science and technology development project (Grant No. 20140633B33). We thank the patient, who requested anonymity, for agreeing to our report and for providing a detailed medical history. We also thank Mr Furkan Dogan for polishing the language to improve the readability.

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

Disclosure of conflict of interest

None.

Address correspondence to: Jing-Ping Yuan, Department of Pathology, Renmin Hospital of Wuhan University, 99 Ziyang Road, Wuchang District, Wuhan 430060, Hubei Province, P. R. China. Tel: +86-27-88041911-85523; E-mail: yuanjingping-2003@aliyun.com

References

[1] Kim TU, Kim S, Lee JW, Lee NK, Ha HK and Park WY. Myxoid adrenocortical adenoma: magnetic resonance imaging and pathology correlation. Korean J Radiol 2014; 15: 245-249.

[2] Tang CK, Harriman BB and Toker C. Myxoid adrenal cortical carcinoma: a light and electron microscopic study. Arch Pathol Lab Med 1979; 103: 635-638.

[3] Forsthoefel KF. Myxoid adrenal cortical carcinoma. A case report with differential diagnostic considerations. Arch Pathol Lab Med 1994; 118: 1151-1153.

[4] Brown FM, Gaffey TA, Wold LE and Lloyd RV. Myxoid neoplasms of the adrenal cortex: a rare histologic variant. Am J Surg Pathol 2000; 24: 396-401.

[5] Honda K, Kashima K, Daa T, Gamachi A, Nakayama I and Yokoyama S. Myxoid adrenal cortical adenoma. Pathol Int 2001; 51: 887-891.

[6] Dundr P and Novak K. Pseudoglandular myxoid adenoma of the adrenal gland. Pathol Res Pract 2003; 199: 493-496.

[7] Peterson RA 2nd, Kiupel M and Capen CC. Adrenal cortical carcinomas with myxoid differentiation in the domestic ferret (Mustela putorius furo). Vet Pathol 2003; 40: 136-142.

[8] Bollito ER, Papotti M, Porpiglia F, Terzolo M, Cracco CM, Cappia S, Gubetta L and Mikuz G. Myxoid adrenocortical adenoma with a pseudoglandular pattern. Virchows Arch 2004; 445: 414-418.

[9] Fine SW, Pindzola JA, Uhlman EJ and Epstein JI. Pathologic quiz case: a 64-year-old man with an adrenal mass. Myxoid adrenal cortical neoplasm. Arch Pathol Lab Med 2005; 129: 541-542.

[10] Suresh B, Kishore TA, Albert AS and Joy A. Myxoid adrenal cortical carcinoma--a rare variant of adrenocortical carcinoma. Indian J Med Sci 2005; 59: 505-507.

[11] De Padua M and Rajagopal V. Myxoid adrenal adenoma with focal pseudoglandular pattern. Indian J Med Sci 2008; 62: 199-203.

[12] Lu HS, Gan MF, Chen HS and Huang SQ. Adrenal myelolipoma within myxoid cortical adenoma associated with Conn's syndrome. J Zhejiang Univ Sci B 2008; 9: 500-505.

[13] Zhang J, Sun J, Liang Z, Gao J, Zeng X and Liu T. Myxoid adrenocortical neoplasms: a study of the clinicopathologic features and EGFR gene status of ten Chinese cases. Am J Clin Pathol 2011; 136: 783-792.

[14] Zeng Z, Wu HX, Zhan N, Huang YB, Wang ZS, Yang GF, Wang P and Fu GH. Prognostic significance of USP10 as a tumor-associated marker in gastric carcinoma. Tumor Biology 2014; 35: 3845-3853.
[15] Zeng Z, Zhou Z, Zhan N, Yuan J, Ye B, Gu L, Wang J, Jian Z and Xiong X. USP10 expression in normal adrenal gland and various adrenal tumors. Endocr Pathol 2015; 26: 302-308.
[16] Aubert S, Wacrenier A, Leroy X, Devos P, Carnaille B, Proye C, Wemeau JL, Lecomte-Houcke M and Leteurtre E. Weiss system revisited: a clinicopathologic and immunohistochemical study of 49 adrenocortical tumors. Am J Surg Pathol 2002; 26: 1612-1619.
[17] Gupta D, Shidham V, Holden J and Layfield L. Value of topoisomerase II alpha, MIB-1, p53, E-cadherin, retinoblastoma gene protein product, and HER-2/neu immunohistochemical expression for the prediction of biologic behavior in adrenocortical neoplasms. Appl Immunohistochem Mol Morphol 2001; 9: 215-221.
[18] Volante M, Sperone P, Bollito E, Frangipane E, Rosas R, Daffara F, Terzolo M, Berruti A and Papotti M. Matrix metalloproteinase type 2 expression in malignant adrenocortical tumors: diagnostic and prognostic significance in a series of 50 adrenocortical carcinomas. Mod Pathol 2006; 19: 1563-1569.
[19] Iino K, Sasano H, Yabuki N, Oki Y, Kikuchi A, Yoshimi T and Nagura H. DNA topoisomerase II alpha and Ki-67 in human adrenocortical neoplasms: a possible marker of differentiation between adenomas and carcinomas. Mod Pathol 1997; 10: 901-907.
[20] Zhang J, Wang C, Gao J, Sun J, Zeng X, Wu S and Liang Z. Adrenal cortical neoplasms: a study of clinicopathological features related to epidermal growth factor receptor gene status. Diagn Pathol 2014; 9: 19.
[21] Wang CP, Zhang J, Gao J, Liu PP, Wu SF, Zeng X and Liang ZY. [Clinicopathologic features and expression of epidermal growth factor receptor and vascular endothelial growth factor in adrenocortical tumors]. Zhonghua Bing Li Xue Za Zhi 2012; 41: 686-690.
[22] Normanno N, De Luca A, Bianco C, Strizzi L, Mancino M, Maiello MR, Carotenuto A, De Feo G, Caponigro F and Salomon DS. Epidermal growth factor receptor (EGFR) signaling in cancer. Gene 2006; 366: 2-16.