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Case Report

Pseudoglandular myxoid adrenocortical adenoma with positive epithelial markers: a case report and review of the literature

Ming-He Bai, Li-Yun Liu, Meng Zhao, Qian Wu, Xiao-Juan Zheng, Ji-Xian Wang, Zhi-Yong Zhang

Department of Pathology, Tangshan Gongren Hospital, Tangshan, China

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Abstract: Myxoid adrenal cortical adenoma with a pseudoglandular structure is a special histological variant and is extremely rare. We report about a 32-year-old Chinese woman with a right adrenal mass during a routine physical examination. The cut surface of the mass had a vague nodular, which gross appearance was pale, yellowish, and semitransparent. Histologically, the region is mostly characterised by pseudoglandular pattern with myxoid stroma. They are filled with clear cells or eosinophilic cells, as well as semitransparent regions, in which anastomosing small eosinophilic cells arranged in pseudoglandular, cord-like, or wreath-shaped structure float in the mucous pool. Immunohistochemical staining shows Melan-A, vimentin, and CD56 were positive and CK (AE1/AE3) were nucleus-side staining. A small number of tumor cells were positive for alpha-inhibin and synaptophysin, ki-67 labeling index was 3%. EMA, chromogranin A, WT-1, and P63 were negative. This report aimed to emphasize pseudoglandular patterns with mucus secretion which could occur in adenomas of the adrenal cortex, nucleus-side positive for CK is remarkable. However, this type may have malignant potential, so regular follow-up is needed.

Keywords: Myxoid adrenal cortical adenoma, pseudoglandular pattern, CK, nucleus-side

Case presentation

A 32-year-old Chinese woman discovered a painless mass in her right adrenal gland in a routine physical examination in Nov., 2018. There were no additional abnormal findings, such as obesity and hypertension, and neither biochemical nor physical signs of endocrine pathology. By viewing the results of the contrast-enhanced test, an irregular mass of soft-tissue's higher density that approximately 4.0 cm×3.5 cm in size was found in the right adrenal gland. After the injection of the contrast medium, the lesions showed obvious homogeneous enhancement. The MRI of the right adrenal area displayed a slightly lower T1 nonuniformity and a slightly higher T2 nonuniformity. By the contrast, the opposite phase didn't exist significant reduction of contrast signal. The boundary was clear, and the maximum diameter was about 4.1 cm. It was clear that the local right adrenal tissue's development could be seen. After the patient's admission, right adrenal mass resection by the laparoscope was performed under general anesthesia. Then, the specimen was sent for pathological examination. Shortly afterwards, she recovered quickly.

Pathological examination

Grossly, the surgical specimen of the adrenal gland was measured about 5×4×3 cm. The mass was a vague nodule which was 4.5×3.5×3 cm in size and its cut surface partly showed faint yellow, semitransparent in myxoid areas, as well as partly golden yellow.

Histologically, the tumour was enveloped by fibrous capsule. It was characterised by pseudoglandular structure in myxoid background. The tumor cells were arranged in irregularly anastomosing cords-like, nest patterns, and pseudoglandular architecture with occasional microcystic dilatations floating in pools of myxoid material. The shapes of these cells were small and round, oval, or polygonal. In some areas, most of the tumor cells had a moderate

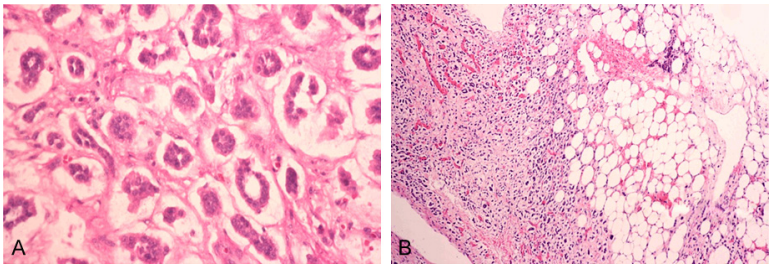

Figure 1. Tumor cells are arranged in irregularly anastomosing cords, nest patterns and pseudoglandular architecture with occasional microcysts floating in pools of myxoid material. Cells are small and round, oval, or polygonal. Cytoplasm contains granular and weakly eosinophilic material. Regular nuclei with dispersed chromatin had visible nucleoli but lacking atypia and pleomorphism (A); The tumor extends to the periadrenal adipose tissue (B) (hematoxylin and eosin).

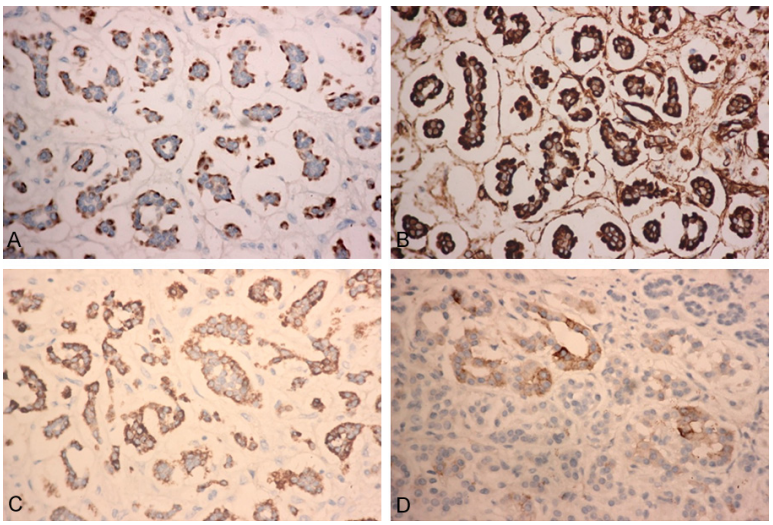

Figure 2. Immunohistochemistry of pseudoglandular myxoid adrenocortical adenoma including perinuclear positivity for cytokeratin (AE1/AE3) (A), vimentin (B), and melan-A (C). Focal positivity for synaptophysin (D).

amount of clear vacuolated cytoplasm and contained tiny granular and weakly eosinophilic material. They had regular nuclei with dispersed chromatin. Part of the nuclei had visible nucleoli but lacked atypia. In the myxoid area the tumor cells neither had dysplasia nor cell pleomorphism (**Figure 1A**). Mitotic figures and necrosis were not observed. The tumor infiltrated into the periadrenal adipose tissue areas (**Figure 1B**). Residual adrenal cortex was found surrounding the tumor. No necrosis or signs of invasive growth were observed.

Immunohistochemical findings

Tumor cells were positive for CK (AE1/AE3) and apparently nucleus-side staining (**Figure 2A**). Tumor cells were also positive for Vimentin (**Figure 2B**), Melan-A (**Figure 2C**) and CD-56, focal positive for inhibin-α, and synaptophysin (**Figure 2D**). EMA, chromogranin A, WT-1, P63 were negative.

Discussion

Myxoid adrenal cortical adenomas are very rare. However, pseudoglandular arrangements in tumors of the adrenal cortex have rarely been mentioned. Papotti et al. reported 14 adrenocortical tumors with variably abundant myxoid component. Myxoid changes are identified most frequently in malignant or borderline adrenocortical tumors [1]. Adrenal cortical adenoma is a benign neoplastic proliferation of adrenal cortical tissue. Most adrenal adenomas occur on one side and clinical symptoms are diverse. The tumors can be classified into two groups: functional and non-functional tumor according to the secretion situation of endocrine hormone. Excessive cortisol secretion could cause Cushing syndrome. Excessive secretion of aldosterone can cause primary aldosteronism or Conn syndrome [2]. Non-functional adrenal adenomas show no clinical symptoms. Myxoid adrenocortical adenomas are usually filled with extracellular myxoid materials, which is very necessary to differentiate from metastatic mucinous adenocarcinoma in the adrenal gland. Under an existing related study, it seemed relatively straightforward to distinguish myxoid adrenal cortical tumor from other adrenocortical ones by the histopathology and immunohistochemical findings. Surgical resection of the mass is the primary way.

Here, we have described a case of pseudoglandular myxoid adenoma of the adrenal gland. Gelatinous areas can be seen grossly, which exactly indicates an extensive myxoid transfor-

mation. As the occurrence of myxoid changes is limited to the focal areas in some cases, the situation mentioned is not the rule [3]. Microscopically, the patterns of these neoplasm cells take on irregular clusters, nests, trabeculae, anastomosing cords, or rare pseudoglands [4]. Pseudoglandular areas contain mucin type material that exists mainly in extracellular matrix not in cytoplasm and show Alcian blue and PAS staining. Myxoid material might represent a degenerative process or a product of stromal fibroblasts and tumor cells [5]. The tumor cells have a moderate amount of eosinophilic and hyaline cytoplasm. The material has never been found in the cytoplasm of neoplasm cells, so the origin of myxoid material is unknown.

Immunohistochemical expressions have revealed adrenal cortex markers are positive, namely inhibin α, Melan-A, and vimentin. Synaptophysin and CD56 can also be positive. Synaptophysin often express in adrenal medulla but in this case it expressd focally in adrenal cortex tumour. CKpan is negative or focal weak positive. EMA, S-100, and CgA are negative [6]. Immunohistochemical staining of neoplastic cells floating the myxoid component has confirmed an adrenal cortical origin. Vimentin is expressed primarily in cells of mesenchymal origin. In addition it is also expressed in the adrenal cortex including human adrenocortical carcinomas. Synaptophysin is a marker of neuroendocrine cells which express primarily in adrenal medullary cells, but adrenocortical carcinoma cells can also express this protein. Inhibin α is expressed in suprarenal cortex within the zona reticularis and gonadal stromal cells. Inhibin α has been more prominent in human adrenocortical carcinomas that secrete sex hormones. Notably, in this study CK (AE1/AE3) expressed mainly in the nucleus side. This phenomenon has not seen in previous studies and may represent typical characteristics.

Differentiation of benign from malignant in adrenocortical tumors is often difficult. Endocrine neoplasms of other organs can affect them. The criteria for malignancy proposed by Weiss in 1984 and restudied in 1989 [7] includes the combination of the following 9 features: nuclear grade, mitotic figures greater than 5/50 HPFs, atypical mitoses, clear cells comprising 25% or less of the tumor, a diffuse architecture, microscopic necrosis, as well as invasion of venous, and sinusoidal and capsular structures. Malignant adrenal cortical neoplasms tend to be larger and heavier than its benign counterparts.

The differential diagnosis of myxoid adrenocortical neoplasms also includes metastatic and primary tumors with myxoid changes, such as chordoma, chondrosarcoma, liposarcoma, myxoid leiomyosarcoma, and malignant fibrous histiocytoma [8]. Chordomas may be the most difficult to recognize from myxoid adrenocortical tumors. It has much more sparse cells than myxoid adrenocortical tumors. Keratin is strong positive staining in chordomas and abundant smooth endoplasmic reticulum [9]. Liposarcomas have distinct adipocytes and S-100 protein is positive. Myxoid leiomyosarcomas consist of spindle and epithelial cells, which usually express muscle markers such as desmin and smooth muscle actin. When pseudo glandular areas are prominent, a well-differentiated metastatic adenocarcinoma is to be taken into account first, since pulmonary, breast, and other rarely glandular carcinomas may metastasize to the adrenal gland. Unlike the nuclei of mucinous adenocarcinoma, nuclei of myxoid adrenocortical adenoma are usually located in the central portion of the cytoplasm instead of compressed to the periphery. Strong cytokeratin expression is usually helpful to identify a metastatic carcinoma. Myxoid adrenocortical adenomas need to differentiate diagnosis from adrenal pheochromocytoma.

Immunohistochemical features can be useful. Adrenal pheochromocytoma tumor cells express CgA and support cells at the periphery of tumor cell nests express S100. Careful histopathologic examinations of the tumors and a battery of immunohistochemical staining are critical to identify these lesions. The presence of clear to eosinophilic cytoplasm, variable amounts of lipid vacuoles, and positive immunostaining in synaptophysin and inhibin α are all essential diagnostic features to myxoid adrenocortical tumors. Post-renal adenoma is a rare benign tumor originating from the kidney which riches in mucin-like background and duct-like structure. Most of the posterior renal adenoma comprising acinus, glandular duct, and the nipple shows CDH17 membrane posi-

tive, which is a sensitive and highly specific marker to posterior renal adenoma [10].

To conclude, pseudoglandular myxoid adrenocortical adenoma is tended to be misdiagnosed in virtue of its rare and distinctive histological features. The biomarkers associated with adrenal cortex are quite useful in difficult cases. Recognition of this entity would be beneficial for both pathologists and clinical doctors to avoid misdiagnosis and unnecessary treatment.

Disclosure of conflict of interest

None.

Address correspondence to: Zhi-Yong Zhang, Department of Pathology, Tangshan Gongren Hospital, 27 Wenhua Road, Lubei District, Tangshan 063000, China. Tel: +86-315-3722441; E-mail: 1073810505@qq.com

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