

รายงานผู้ป่วย

Myxoid adrenal cortical carcinoma associated with Cushing's syndrome.

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Yenrudi S, Maneesri S, Kasantikul V. Myxoid adrenal cortical carcinoma associated with Cushing's syndrome. Chula Med J 1994 Jan 38(1) : 33-38

A 48-year-old woman presented with a nine-month history of hypertension followed by clinical features of Cushing's syndrome. Bilateral suprarenal masses were detected pre-operatively with excretory urography and ultrasonography. The left adrenal tumor was resected together with the left kidney. The pathological diagnosis was myxoid adrenal cortical carcinoma. The nature of the tumor cells was verified by immunohistochemical and electron microscopic studies. Such myxoid carcinoma in association with clinically active steroid production is unusual and appears unique in our experience.

Key words : Myxoid, Cortical Carcinoma, Cushing's Syndrome

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Received for publication. December 8, 1993.

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เสาวณีย์ เย็นฤดี, สุภางค์ มณีศรี, วีระ กษานติกุล. มะเร็งของต่อมหมวกไตชนิดที่สร้างสารมิกซอยด์ และมีกลุ่มอาการ คushing. จุฬาลงกรณ์เวชสาร 2537 มกราคม; 38(1) : 33-38

ผู้ป่วยหญิง อายุ 48 ปี มีอาการความดันโลหิตสูงมา 9 เดือน หลังจากนั้นมียกลุ่มอาการCushing ร่วมด้วย excretory urogram และ ultrasound พบก้อนที่บริเวณต่อมหมวกไตทั้ง 2 ข้าง ได้ทำการผ่าตัดก้อนรวมต่อมหมวกไตและไตซ้าย ผลการวินิจฉัยทางพยาธิวิทยาเป็นมะเร็งของต่อมหมวกไตชนิดที่มีสาร myxoid ในก้อนร่วมด้วย มะเร็งที่มีพยาธิสภาพดังกล่าวมา ร่วมกับการสร้างฮอร์โมนชนิด steroid เป็นปรากฏการณ์ที่ยังไม่เคยพบมาก่อนเลย

Adrenal cortical carcinoma is a rare malignant neoplasm.⁽¹⁾ May et al. classified the lesion, based on hormone production, as functioning and non-functioning tumor.⁽²⁾ The former lesion predominantly affects women while the latter neoplasm occurs more frequently in men. Most patients with adrenal cortical carcinoma often present with abdominal symptoms such as fullness, indigestion, pain, or mass. Several cases were accompanied by hormone abnormalities including elevated urinary or serum steroid, and features of Cushing's syndrome.⁽³⁾ Computerized tomographic (CT) findings often detect a central area of low attenuation, irregular contrast enhancement or calcification.⁽⁴⁾ Pathologically, functioning and non-functioning tumors are indistinguishable.⁽⁵⁾ The histological features of such neoplasms are variable.⁽⁶⁾ The tumors may exhibit the alveolar or trabecular patterns of the normal adrenal gland as well as a diffuse and sheet-like appearance. The neoplastic cells may be either lipid-rich or lipid-poor. Ultrastructurally, numerous large abnormal mitochondria, with mostly tubular or lamellar cristae and parallel pattern of rough endoplasmic reticulum (RGR), have been described.⁽⁷⁾ We present here a case of clinically functional adrenal cortical carcinoma with abundant extracellular myxoid substance. Such a feature is unusual and has been rarely described in the literature. Additionally, the nature of the tumor cells has been verified by immunohistochemical and electron microscopic studies.

Case report

A 48-year-old woman had a history of persistent hypertension for nine months. She had been treated elsewhere. Eight months later, she developed clinical features of Cushing's syndrome. The patient was then hospitalized at Chulalongkorn Hospital.

Examination revealed blood pressure of 210/120 mmHg. Truncal obesity, "buffalo hump" and "moon face" were observed. The remaining physical findings were unremarkable. Her fasting plasma glucose ranged from 248 to 390 mg%. Urinalysis was positive for sugar. Plasma cortisol level was 31 µgm% (normal 7-25 µgm%) in the morning and 31.5 µgm% (normal 2-9 µgm%) in the evening. Dexamethasone suppression tests, either at standard low dose or high dose, were unsuppressible. An excretory urogram disclosed a large left suprarenal mass. Additionally, the ultrasonogram demonstrated a 11.3x7.6 cm inhomogeneous echomass in the same area. Furthermore, a similar lesion was also noted in the right adrenal gland.

The patient underwent left adrenalectomy and nephrectomy. After surgery, she received hydrocortisone supplement, anti-hypertensive drugs, and other supportive measures. The condition gradually improved and she was sent home 12 days later.

The gross specimen consisted of an irregular brownish mass without capsule which was surrounded by a thin layer of adrenal tissue. The variegated cut surface showed a gray-white mucinous area mingled with meaty-

brown tissue and foci of necrosis (Fig. 1). The kidney was free of tumor involvement. Microscopically, clusters of neoplastic cells were arranged in alveolar pattern. Many large tumor cells had eosinophilic cytoplasm while some showed vacuolated cytoplasm (Fig. 2). The nuclei were vesicular with prominent nucleoli. Mitoses were often noted. Additionally, abundant intercellular mucoid material was enhanced by alcian blue and also showed positivity with Mayer mucicarmine stain (Fig. 3). Immunostains showed diffuse positivity for alpha-1-antitrypsin in tumor cells as well as focal positivity for keratin, but were negative for epithelial membrane antigen, vimentin and chromogranin. Ultrastructurally, the tumor cells contained lipid droplets and a parallel array of rough endoplasmic reticulum (Fig. 4). Coarse chromatin was seen as small clumps in the nuclei. Neurosecretory granules were not seen. Based on light and electron microscopic findings, the final pathological diagnosis was adrenal cortical carcinoma.

Discussion

Generally, adrenal cortical carcinoma is difficult to distinguish from adrenal cortical adenoma, renal cell carcinoma, and pheochromocytoma.⁽⁵⁾ We excluded the possibility of the tumor being an adrenal cortical adenoma because of its size, the presence of necrosis, the marked pleomorphism of the neoplastic cells and the presence of mitoses. Although some degree of pleomorphism and mitoses can be seen in benign adrenal adenoma, they are more conspicuous in adrenal cortical carcinoma, as noted in our example. Concerning renal cell carcinoma, the tumor characteristically expands and distorts the renal calyces, while adrenal cortical carcinoma usually displaces rather than distorts the kidney. Furthermore, the ultrastructural finding of parallel pattern of RER provided evidence against renal cell carcinoma. The absence of neurosecretory granules also indicated that the present tumor was not a pheochromocytoma.

The histological feature of myxoid appearance, which was clinically active in steroid production in our example, is unusual. Tang et al. have described a myxoid adrenal cortical carcinoma in a 41-year-old woman, but the lesion was clinically inactive with regard to hormone secretion.⁽⁵⁾ Fung et al. suggested that the myxoid material could be produced by the stromal cells upon neoplastic stimulation.⁽¹⁰⁾ However, such myxoid substance could represent a degenerative process within the tumor.

With regard to the immunohistochemical study, a high percentage of the neoplastic cells contain vimentin which is an intermediate filament of mesenchymal cells.⁽⁵⁾ However, such filament was absent in our case. This is probably related to the fact that the tumor may have lost its original mesenchymal properties while many of them remained. It should be noted that neoplastic cells often show positivity to keratin, as observed in the present lesion. This finding indicates that adrenal cortical carcinoma is an epithelial or epithelial-derived tumor.^(5,11)

Because a majority of adrenal cortical carcinoma metastasizes to the lung, liver, adjacent organs and bone, we suggest that the opposite adrenal cortical lesion could thus represent evidence of a metastatic tumor.^(3,12) The ultrasonogram's finding of a hypoechoic mass in the right adrenal gland tends to support this view. Luton et al.

observed that prognosis was poor in patients having metastatic tumor at the time of diagnosis.⁽¹²⁾ Early diagnosis thus is essential for curative therapy. Currently, radical surgery is the single modality of management for cure or prolonged survival.⁽¹³⁾



Figure 1. An irregular adrenal mass showing necrosis and hemorrhage.

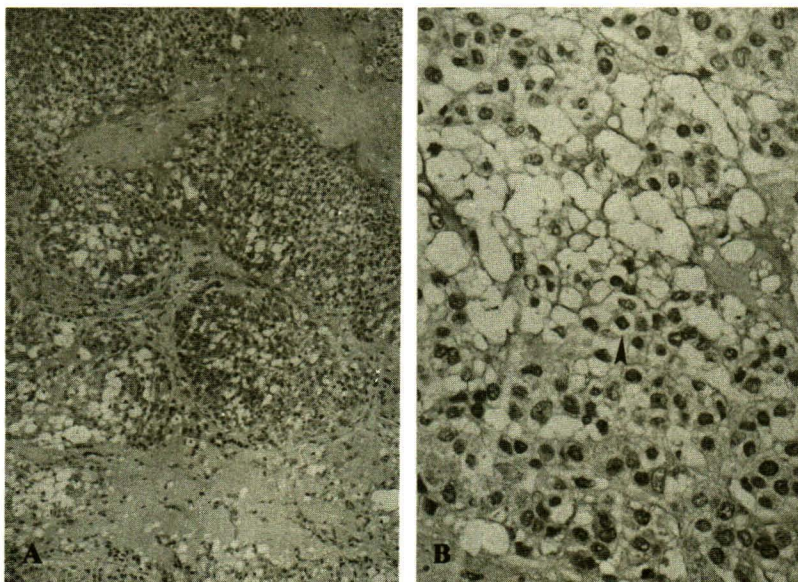


Figure 2. A. Tumor cells arrange in cords mimicking normal adrenal cortical structure. H&E x 100. B. Vacuolated cytoplasm in neoplastic cells, arrow. H&E x 400.

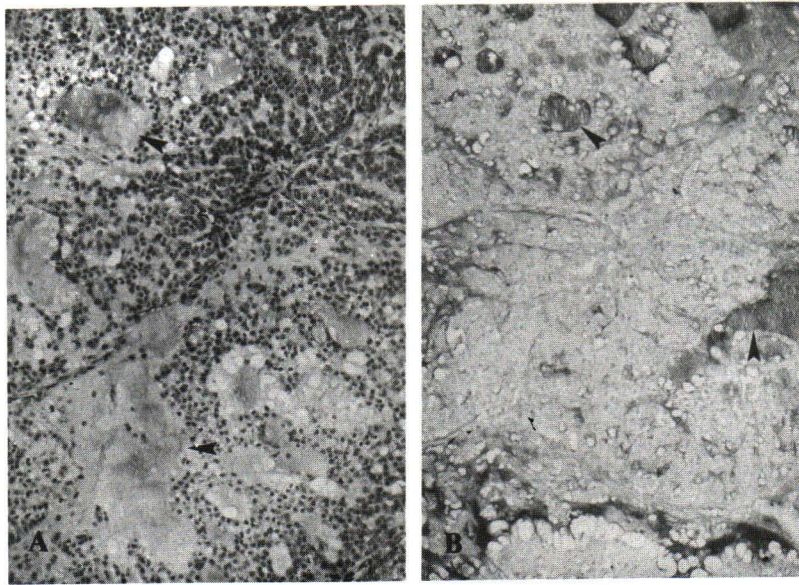


Figure 3. A. Cords and trabeculae of tumor cells with abundant intercellular mucin, arrows. H&E x 100
B. Arrows indicating mucin, Alcian blue x 400

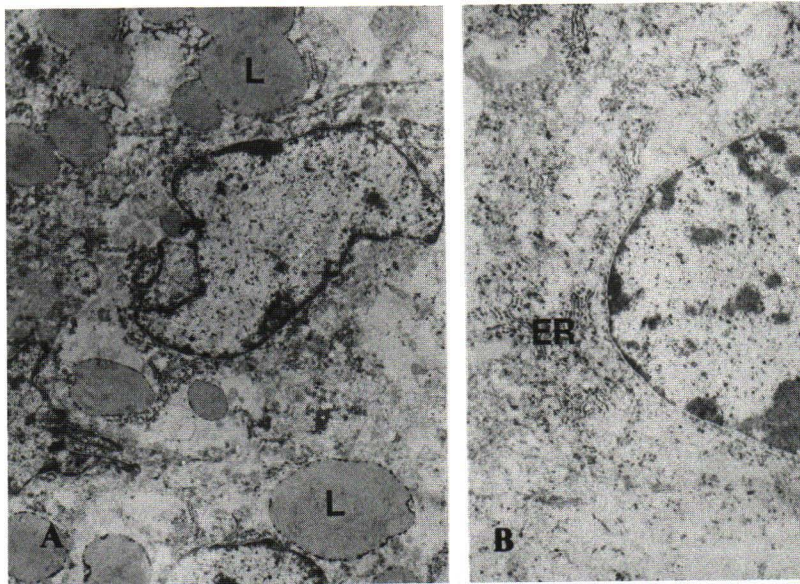


Figure 4. A. Tumor cells showing intracytoplasmic lipid globules, L. Uranyl acetate lead citrate x 60,000
B. Parallel RER near the nucleus of the tumor cell, ER. Uranyl acetate lead citrate x 76,000

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