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Adrenal Rest Presenting as a Renal Cyst. A Case Report

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The report presents a 42-year old female patient, in whom a cyst of the left kidney was diagnosed. The clinical presentation and gross picture suggested a simple cyst. The lesion was removed surgically; in the cyst wall, histology revealed structures identical to normal adrenal cortex. Based of this observation, the final diagnosis was established as the so-called adrenal rest. Such lesions are not uncommon in the kidney, but what was extraordinary in the described case was the macroscopic presentation. Thus, in differential diagnosis of cystic lesions of the kidney one should also take into consideration adrenal developmental abnormalities. This may be of particular importance in cystic clear cell renal carcinomas, the structure of which is well known to resemble the adrenal cortex.

Introduction

Adrenal rests (AR's) or adrenal rest tumor is a tumor consisting of ectopic adrenal cortex tissue. The lesion is relatively common, detectable in as many as 20% of post-mortem examinations. In the kidney, AR can be found in 6% of general population. The site of AR appearance is closely related to the migration of primordial adrenal cells in the course of organogenesis, and thus it is regarded a developmental abnormality. Usually, AR's appear in the form of nodules or discs, yellow-orange in color and at times surrounded by a layer of fatty tissue. In the majority of cases they are asymptomatic and only accidentally detected. If detected, often they need to be differentiated from neoplastic lesions. The endocrine activity of AR generally does not affect the hormonal homeostasis. Nevertheless, AR may undergo considerable enlargement in the case of massive adrenal damage, in Nelson's syndrome, in ACTH overproduction and in patients with congenital adrenal hyperplasia (CAH). In such cases the lesion may markedly increase, an adenoma, and in rare instances carcinoma may develop. The present report describes AR, which clinically mimicked a simple renal cyst. To date no such case has been reported [2, 3, 8].

A Case Description

In September 2002, a 42-year old female patient was admitted to the Department of Urology, University Hospital of Cracow, for a surgical treatment of a cyst situated in the left kidney. A previous transabdominal ultrasonography revealed an oval fluid-filled space, approximately 90mm in diameter, situated in the upper pole of the left kidney. Based on this finding the diagnosis of a cortical cyst was established. No urinary retention was noted in the pyelocalyceal system and no hyperechogenic concretions. The right kidney and the remaining abdominal organs were echographically normal. In order to achieve a more precise visualization of the lesion, an abdominal CT scan was performed. Between the left phrenic dome and the upper pole of the left kidney, an encapsulated fluid-filled space was visualized, measuring 7.1x7.9cm. The upper kidney pole was flattened, and the entire organ was slightly displaced downwards. No significant lesions were noted in other abdominal organs, large vessels and retroperitoneal space. Urinalysis, urinary bacteriology, blood cell count, hemostatic system and biochemical tests were within normal limits. Serology for HBV, HCV and HIV was negative. Therefore, the patient was qualified for the operation. A cystic lesion from the left kidney was removed. The postoperative period was uneventful and the patient was discharged in good general condition. She is presently followed-up as an outpatient.

The material was fixed in 10% buffered formalin; the samples were routinely processed and embedded in paraffin. Four- μ m thick sections were stained with hematoxylin-eosin and immunostained using routine techniques and Dako Immuno-stainer (DAKO, Denmark). Antigen unmasking was performed in a microwave oven (3x5 minutes, 750W) in citrate buffer (pH 6.0). The following primary antibodies purchased from DAKO (Denmark) were used: anti-Ki-67 (clone MIB-1) diluted to 1:50, cytokeratin (MNF116) diluted to 1:100, EMA (E29) diluted to 1:100, vimentin (V9) diluted to 1:100 and synaptophysin (polyclonal) diluted to 1:100. Secondary antibodies and other reagents from the ENVISION and ENVISION+System kits were used (DAKO, Denmark).

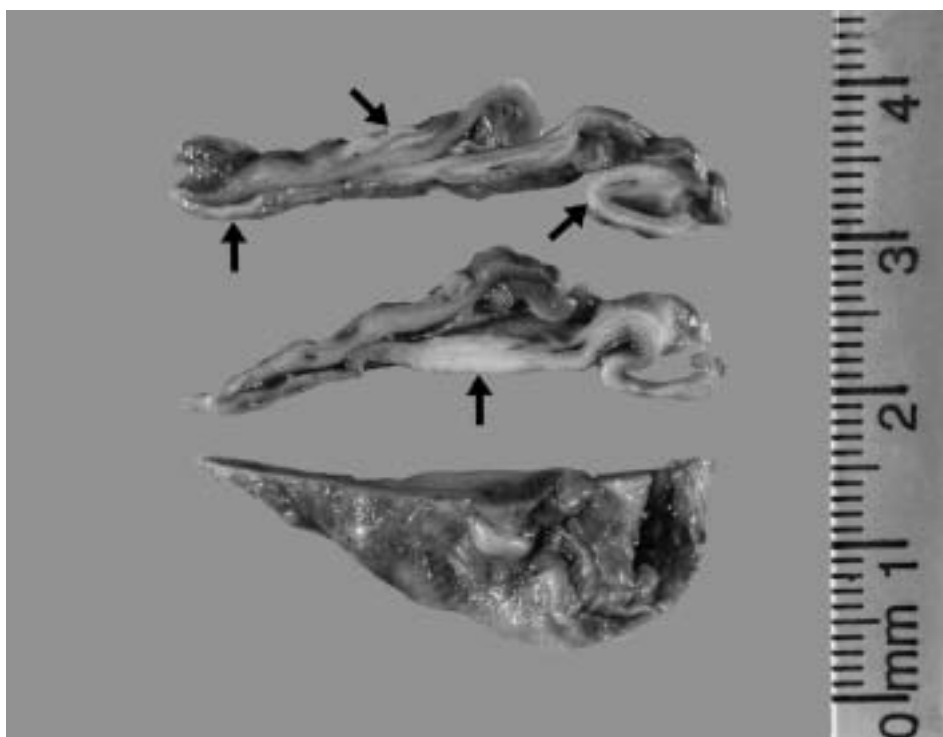


Fig. 1. The cyst with yellowish nodules (arrows) corresponding to adrenal cortical tissue.

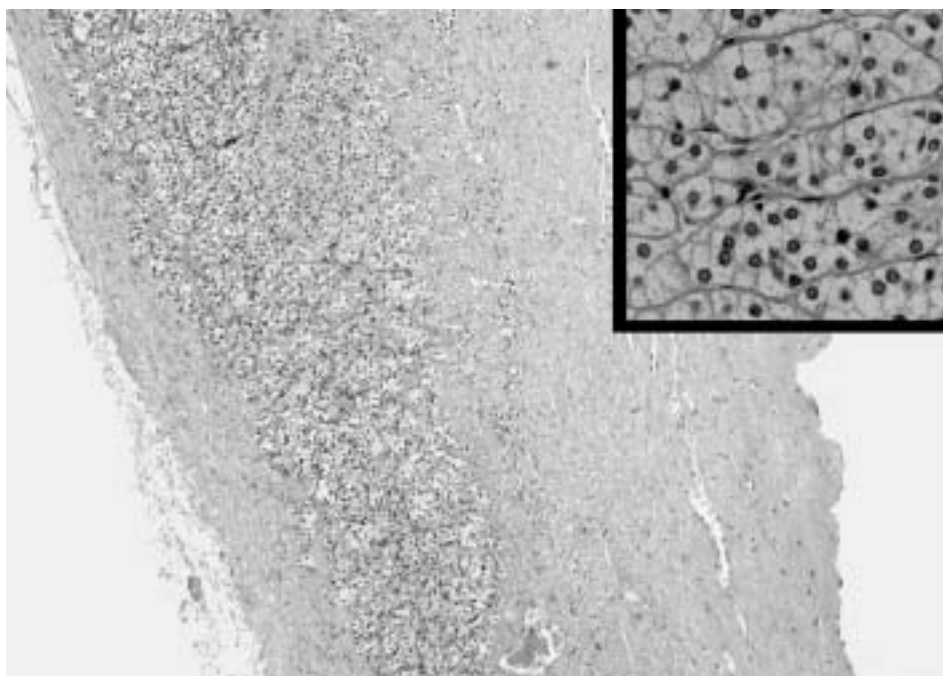


Fig. 2. Groups of cells with clear, foamy cytoplasm amidst fibrous tissue. HE. Lens magn. 10x, insert: 60x.

Gross examination revealed flat tissue fragments up to 5cm in size, that constituted the wall of the dissected cyst. The external surface was smooth, while yellowish 5 - 7mm nodules were prominent on the inner surface. The cyst wall was 3 - 4mm thick and was brownish-gray in color. Yellowish, well-delineated foci were scattered throughout (Fig. 1). On histologic examination the cyst wall was composed of fibrous tissue, with bands and clusters of cells with clear, slightly foamy cytoplasm, distinct boundaries and small, uniform nuclei (Fig. 2). Immunohistochemically, the cells were positive for vimentin and synaptophysin, while the reactions

for cytokeratin and EMA were negative. The clear cells showed no mitotic activity, and no Ki-67-positive cells were found. Histological findings allowed for defining the foci as structurally adrenal and the diagnosis of AR was established.

Discussion

The adrenal gland is formed of two germ layers: the cortex originates from the mesoderm, while the medulla from the ectoderm. The cortical bud (CB) develops in the beginning of the 5th week of gestation as symmetric cell

clusters that migrate from the mesoderm that lines the coelomic cavity. The CB cells aggregate on both sides of the dorsal mesentery and subsequently move towards the upper pole of the developing kidney and medially to the forming gonad. Inside the CB, a capillary network forms, and CB cells intensively proliferate and begin to arrange themselves in parallel trabeculae. In this way fetal cortex is formed. At the end of the 5th week of gestation, CB becomes surrounded by several layers of small epithelial cells arranged in clusters and arches, containing hyperchromatic, densely packed nuclei. These cells form the ultimate cortex. After birth, the fetal cortex undergoes a rapid involution. As early as 7 - 10 days after birth it is almost entirely disorganized and becomes displaced by the band of ultimate cortex cells, which in-growth from the periphery to the center. The adrenal medulla is formed by the cells of the sympathetic trunk bud at the end of the 5th week of gestation. These cells migrate with sympathetic nerve fibers along blood vessels deep into the fetal cortex.

AR's usually constitute small clusters of cells identical to adrenal cortex' and are found in various locations. They are most commonly observed in the retroperitoneal space fatty tissue in the proximity of the adrenal, near the upper renal pole, along testicular or ovarian vein, along the testis descent path, in the tail of the epididymis, broad ligament of the uterus or in the ovarian region. Isolated cases of AR appearing at other, distant locations, such as the liver, lungs and central nervous system, have been also described. AR is believed to be the result of CB cells displacement to an ectopic locations in the course of fetal development. In some cases other congenital malformations may be concomitantly present. Imaging studies show AR's as fat-rich, well-vascularized masses. Macroscopically, they are solid, usually small, characteristically yellowish nodules. Histologically, AR usually shows a three-layer structure, similar to normal adrenal cortex; yet a medullary component is almost never seen [2, 3, 8, 11].

In the majority of cases, AR is asymptomatic and does not cause hormonal imbalance. In some instance AR may evoke the symptoms of Cushing syndrome. In such patients, surgical excision of the tumor is recommended, what usually restores the hormonal balance. Rarely, AR's become symptomatic in patients with CAH. In such instance, AR's may markedly enlarge and assume a significant endocrine function. In consequence, clinical manifestations develop, in particular resulting from the compression of neighbouring organs. In males with CAH, symptomatic AR most frequently occurs within the testis, at times bilaterally. Some reports describe lesions up to 4.0cm in diameter. In symptomatic AR in patients with CAH, replacement hormonal therapy is usually effective and surgical treatment is not necessary [6, 10].

AR-type nodules are usually detected by ultrasonography or other imaging studies incidentally. The visualization of such a lesion necessitates a differential diagnosis, especially ruling out of neoplastic lesions. The histological structure of AR, identical with that of normal cortex, i.e. composed of clear cells with distinct boundaries, determines the direction of the work-up. Lesions situated close to the eutopic adrenal necessitate differentiation from adrenal cortex tumors; in the testis Leydig cell tumor has to be considered, while in the liver hepatocellular carcinoma has to be excluded. The kidney is a common location of AR. As is perfectly known, the very most common form of renal carcinoma is conventional renal cell (clear cell) carcinoma (RCC), with the structure resembling that of normal adrenal gland. This fact makes necessary an accurate differential diagnosis. The characteristics that discriminates between RCC and adrenal are the presence of cellular atypia in the former, predominantly seen as hyperchromasia and irregular nuclei, and more organized architecture in the latter. In some cases immunohistochemistry may be useful. The characteristic ICH pattern of RCC is the simultaneous expression of vimentin and epithelial markers. Adrenal cortical cells usually do not show the presence of cytokeratins and EMA, but are positive for markers of endocrine differentiation as synaptophysin, as well as inhibin. These reactions are not, however, wholly specific. Antibodies that react specifically with RCC cells have also been developed [4, 5, 7, 9]. In the present case, the gross presentation was misleading and mimicked a simple cyst. For a cystic lesions, the exclusion of cystic RCC is of clinical significance. This is a rare form of renal cell carcinoma, usually presenting as a multilocular cyst with a relatively thick wall containing foci of well differentiated clear-cell carcinoma. In our case the diagnosis of AR was established because of the absence of atypia and the organoid structure of the lesion. This diagnosis was confirmed by the immunohistochemical panel.

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