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Cystic Nephroma in Adults. A Report of Two Cases and Review of the Literature

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We present two cases of cystic nephroma in a 55-year old and a 61-year old women. In both patients the results of ultrasound and clinical examinations were not characteristic enough to establish the precise preoperative diagnosis. Due to the age of the patients and the location of the lesions, possibility of clear cell carcinoma with cystic changes was considered. However, microscopic examination of postoperative specimens revealed benign nature of the tumors.

Introduction

Cystic nephroma (CN) is a rare benign cystic neoplasm composed of epithelial and stromal elements (def. WHO). This tumor has been described in the literature under wide variety of names: multilocular cystic tumor, renal multilocular cyst**,** multilocular cystic nephroma, benign polycystic nephroblastoma, renal cystadenoma or partial polycystic kidney [4, 9]. CN occurs primarily in the childhood within the first 2 years of life with male predominance (2:1). The second peak of incidence is in middle-aged persons, usually females (8:1) [9]. In children, CN may be considered as a part of the spectrum of Wilms' tumor and therefore should be separated from cystic partially differentiated nephroblastoma (CPDN) [9, 15]. A presentation in adults is almost always confused with a malignant renal neoplasm (renal cell carcinoma) [9, 13]. The recognition of this entity has a prognostic and diagnostic significance. CN shows no aggressive behavior and only surgical treatment is required [4]. However, regular monitoring by noninvasive techniques is advisable, because of the possibility of recurrence after non-radical surgery [4, 11]. A few cases of sarcoma developed in CN in adults were documented [2].

Case Descriptions

Patient I

A 55-year old woman (4370\2003) presented with a left loin pain lasting for four months. Ambulatory ultrasound examination showed tumor-like mass in the left kidney. On admission to the hospital physical examination revealed no abnormalities. Laboratory findings (serum electrolytes, kidney and liver function tests, urinalysis) were normal, except mild anemia. Ultrasound scan revealed a unilateral, multilocular cystic mass 6x6x5.5 cm, located in the central part of the left kidney and extended into the renal pelvis, obstructing the collecting system. Excretory urography, angiography and fine-needle aspiration biopsy (FNAB) were not performed. Due to the age of the patient and the location of the lesion, initial diagnosis of malignant renal neoplasm, probable clear cell carcinoma was formulated. Radical nephrectomy was performed. An excised specimen measured 10x6x4.5 cm. The tumor (diameter 6.5 cm) was located in central part of the left kidney. The lesion was clearly separated from the surrounding renal tissues, protruded into pelvicaliceal system and caused its obstruction. The patient has been followed up for 1 year with no recurrence so far.

Patient II

A 61-year old woman (686\2004) was referred to the hospital because of asymptomatic right renal mass found incidentally by abdominal ultrasound examination. Physical examination revealed no abnormalities. Laboratory findings (morphology, serum electrolytes, kidney and liver function tests, urinalysis) were unremarkable. Abdominal ultrasound showed a unilateral, complex cystic mass 5.5x5x5 cm in diameter, with enhanced septation, located in the right kidney. Neither renal pelvic nor vein involvement were demon-

strated. Excretory urography, angiography and fine-needle aspiration biopsy (FNAB) were not performed. Due to the clinical diagnosis of renal cell carcinoma, radical nephrectomy was performed. In the upper pole of the right kidney, the tumor 5.5 cm in diameter was found. The tumor was clearly separated from the rest of renal parenchyma and did not communicate with renal pelvis.

Macroscopic, histopathological picture and immunohistochemical findings of the tumors

Macro- and microscopic picture was identical in both cases. The cut surface of tumors showed multiple cysts (Fig. 1) of variable sizes up to 2 cm in diameter, that contained pale yellow, clear, serous fluid and did no communicate with one another. The septa dividing the cystic spaces were thin, sleek and translucent. Those cystic spaces were lined by a single layer of flattened or cuboid epithelium (Fig. 2). Hobnail cells were also present (Fig. 3). Some of the cysts were devoid of epithelium. The epithelial cells were supported by thick basement membrane. The fibrous septa tissue contained neither undifferentiated blastema nor embryonal renal tubules and gromeruloid structures (Fig. 4). There were no other noticeable elements such as cartilage, adipose tissue or skeletal muscle cells. The tumors compressed the renal parenchyma; as a result pseudocapsule was seen, which contained scattered, atrophic tubules.

Immunohistochemical studies were performed using the following antibodies: anti-keratin MNF116 (DAKO 1:100), monoclonal anti-EMA (DAKO 1:100), monoclonal anti-vimentin (DAKO 1:100), monoclonal anti-smooth muscle actin (DAKO 1:50), monoclonal anti-PCNA (DAKO 1:30), monoclonal anti-MIB-1 (DAKO 1:100), polyclonal anti-Wilms' tumor gene 1 (WT1) (Santa Cruz 1:200). Negative controls consisted of sections incubated with normal serum instead of the primary antibody. The normal kidney parenchyma served

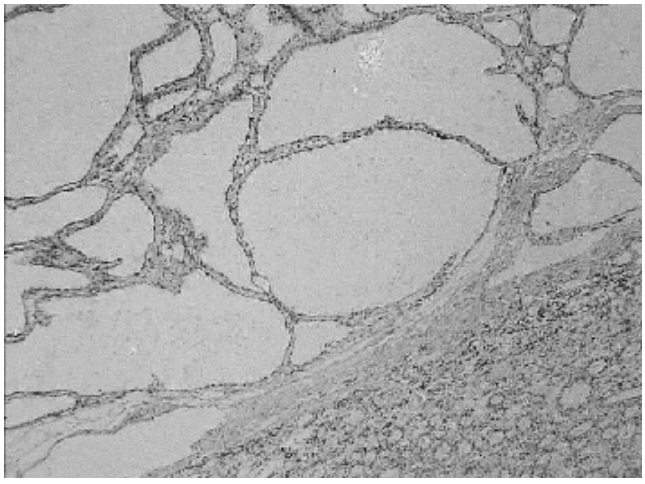

Fig. 1. Multiple cystic spaces and thin, fibrous septa are forming the tumor. HE. Magn. 200×.

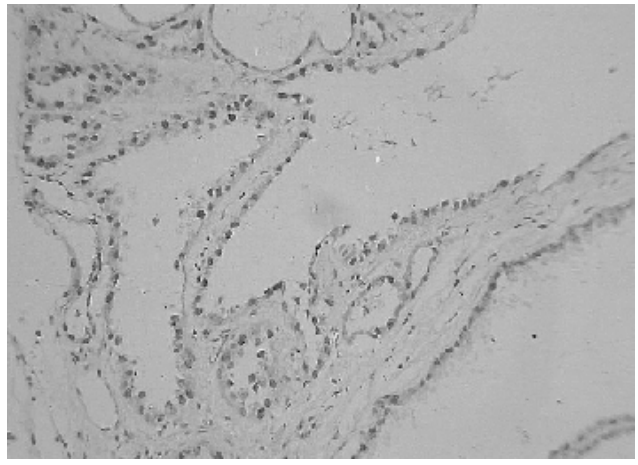

Fig. 2. Cystic spaces are lined by single layer of cuboid epithelial cells. HE. Magn. 400×.

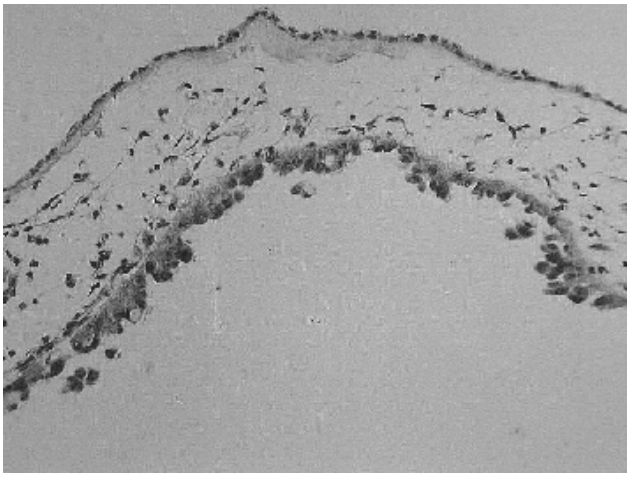

Fig. 3. Hobnail cells cover a part of the cystic space. HE. Magn. 400×.

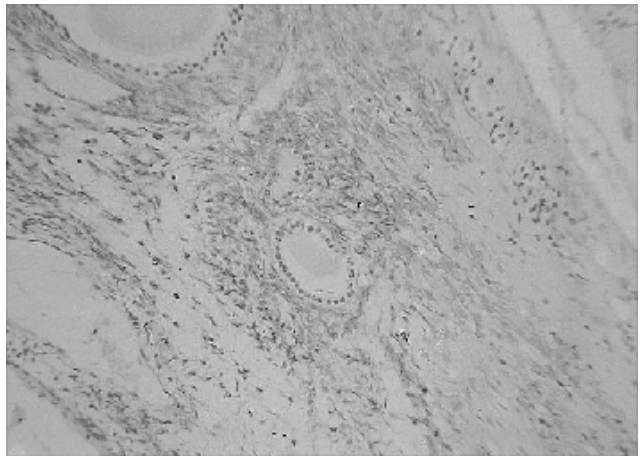

Fig. 4. A septum composed of fibrous tissue contains well-differentiated tubules. HE. Magn. 400×.

as an internal control. The secondary visualizing system included LSAB+ DAKO system.

All epithelial cells lining cystic spaces showed strong, cytoplasmic staining with anti-keratin antibodies and positive membranous immunoreaction with anti-EMA. The spindle cells of septa were positive for vimentin and some scattered fascicles of smooth muscle actin positive spindle cells were also found. Reaction with anti-MIB-1 and anti-WT1 were negative, while reaction with PCNA antibody showed positive nuclear staining of approximately 75% of the epithelial cells.

Discussion

CN was first described by Walter Edmunds in 1892 who named the condition cystic adenoma [10].

In Poland, the first description of CN was by Niemirowicz and Sporny in 1987 [16]. The neoplastic character of the lesion is nowadays well established. Some authors regarded CN as a developmental malformation rather than a neoplasm [18, 21]. Histological and immunohistochemical similarity of septal stromal cells to ovarian stroma led Steele et al. [20] to conclude that CN is a dysontogenic lesion resulting from müllerian tissue misplacement into the kidney. Other investigators suggest that CN is a hamartomatous malformation [9]. Friedman et al. [12] are of the opinion that CN originates from the collecting ducts.

Scanning electron microscopy showed that the epithelial cell of CN demonstrated short microvilli and long cilia and they closely resemble the epithelium of the collecting tubules [21].

A concept of neoplastic origin of CN was supported by Joshi and Beckwith [15], who suggested that the lesion is closely related to nephroblastoma and cystic partially differentiated nephroblastoma (CPDN). The progressive enlargement of CN in cases without surgical resection, supports an idea of the neoplastic process. A clonal proliferation of the epithelial cells in CN was recently shown by molecular biology methods [9].

The diagnostic criteria for CN were first formulated by Powell et al in 1951 [18] and then modified by Boggs and Kimmelstiel [3]. In 1989, Joshi and Beckwith [14] revised the histological criteria. These include: 1) CN is composed entirely of cysts and their septa; 2) the lesion forms a discrete, well demarcated mass; 3) the septa are an only solid portion of the tumor, conforming to the outlines of the cysts without solid expansible nodules; 4) the cysts are lined by flattened, cuboid or hobnail epithelium, and 5) the septa are composed of fibrous tissue in which well-differentiated mature tubules may be present. Poorly differentiated tissues and blastemal cells do not belong to the picture of CN and if present, the lesion should be classified as CPDN. According to Eble and Bonsib [9], the term CN covers two different diseases. The first one occurs in young children being a part of the spectrum of Wilms' tumor. Such tumors should be diagnosed as CPDN accordingly; irrespective whether elements of Wilms' tumor are found or not. The second one occurs in adults with no link to Wilms' tumor or nephrogenic rests and should be diagnosed as CN.

The lesion is usually unilateral and sporadic. Some unique bilateral CNs were reported [5, 11]. A familiar cluster of CN in association with pleuropulmonary blastoma has also been published [14]. CN may coexist with renal cortical adenoma and angiomyolipoma [19, 22]. A case of adenocarcinoma and some cases of sarcomas developing from CN in adults were presented [1, 2].

A few cases of CN were examined by fine-needle aspiration biopsy (FNAB) [8, 13]. The cytological smears included clusters and small group of epithelial cells with vacuolated or scant cytoplasm. Some of them showed a high nuclear/cytoplasmic ratio, the irregular contours of nuclei and prominent nucleoli. The background was proteinaceous or inflammatory but without necrosis. Hughes et al. [13] discussed the difficulties in distinguishing CN from cystic renal cell carcinoma in FNAB smears in adults. Drut [8] suggests that FNAB combined with modern visual techniques can be useful for preoperative diagnosis of CN in infancy. As a result, a patient can avoid preoperative chemotherapy.

Immunohistochemistry and lectin histochemistry analysis support the concept of a close relationship between CN, CPDN and nephroblastoma [6, 7]. Domizio et al. [7] showed immunoreaction for both desmin and vimentin in septal stroma. Davila et al. [6] revealed a strong reaction of epithelial cells for cytokeratin, and variably positive reaction for epithelial membrane antigen (EMA) and α–αntitrypsin. The cells were negative with proliferative cell nuclear antigen (PCNA). In our cases we found however, PCNA immunoreactivity in approximately 75% of the epithelial cells. Antibodies for collagen type IV react with basement membrane of the epithelium and membranes surrounding rudimentary tubules within septa [6].

Differential diagnosis of CN covers: polycystic kidney, hydronephrotic kidney, nephroblastoma, CPDN, renal cell carcinoma with cystic changes, clear cell sarcoma with cystic changes, cystic mesoblastic nephroma, angiomyolipoma and hamartoma of the renal pelvis [9]. Proper preoperative diagnosis by visual techniques or FNAB is often impossible or at least difficult especially in adults [13]. Treatment of CN is surgical by total, unilateral nephrectomy [4], recently however, a renal-sparing proce-

dure or even tumor resection only have been proposed as the standard of care, especially in cases with bilateral location [5, 11]. Follow-up should consist of visual techniques in regular intervals [11].

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