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Case Report

Cystic partially differentiated nephroblastoma in an adult: a case imitating the process of normal nephrogenesis along with corresponding WT1 expression

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Abstract: Cystic partially differentiated nephroblastoma (CPDN) is extremely rare in adults. Only 2 cases have been documented in the English literature. Herein, we present a third case of CPDN with unique morphological and immunohistochemical features. A 45-year-old man had a multicystic right renal mass, with a maximum diameter of 3 cm on magnetic resonance imaging. Being unable to rule out malignancy, partial nephrectomy was performed. The surgically resected specimen contained a multicystic mass, 3 × 3 × 2.5 cm in size, without an expansile solid nodule. Histopathological examination revealed nephroblastomatous elements without identifiable blastema; transition from cap-mesenchyme-like cells to an immature glomerulus was observed and maturing tubules and a glomerulus were present. Despite the lack of a blastema, the diagnosis of CPDN was the most appropriate. Immunohistochemical WT1 expression imitated the pattern of ongoing normal nephrogenesis. Therefore, we believe that the blastema disappeared because of maturation.

Keywords: Cystic partially differentiated nephroblastoma, adult, WT1, nephrogenesis, maturation

Introduction

Cystic partially differentiated nephroblastoma (CPDN) is a rare multicystic tumor of the kidney, usually presenting before the age of 2 years [1]. CPDN may be part of a spectrum, which includes cystic nephroma (CN) that is benign, CPDN that has low malignant potential, and cystic Wilms tumor (WT) that is malignant [1-3]. CPDN is considered to be a highly cystic WT lacking a expansile solid nodule, with immature to maturing nephroblastomatous epithelial and stromal elements, along with characteristic blastema [4].

In adults, only 2 cases of CPDN have been reported in the English literature [5, 6]. Owing to the extremely rare occurrence of CPDN in adults, several multicystic renal tumors including cystic renal cell carcinoma (RCC) and CN, which are more frequent in adults, should be excluded before concluding a diagnosis of CPDN [7]. Of importance, most cases of WT express the WT1 protein, a gene product of *WT1* located on chromosome 11p13 [8]. In cases of WT, stromal elements usually express WT1 [9]; however, in normal nephrogenesis, WT1 would not be expressed in stromal elements, but expressed in elements ranging from the blastema to the glomerulus [10].

Herein, we presented a third case of CPDN in an adult. While a characteristic blastema of CPDN was absent, the presence of immature nephroblastomatous elements strongly suggested the diagnosis of CPDN. As WT1 expression reminiscent of normal nephrogenesis was observed, we believe that tumoral nephrogenesis or maturation, ranging from the pre-existing blastema to the glomerulus, progressed, and the lack of blastema was owing to maturation.

Case report

A 45-year-old man without any complaints was referred to our hospital because a right renal

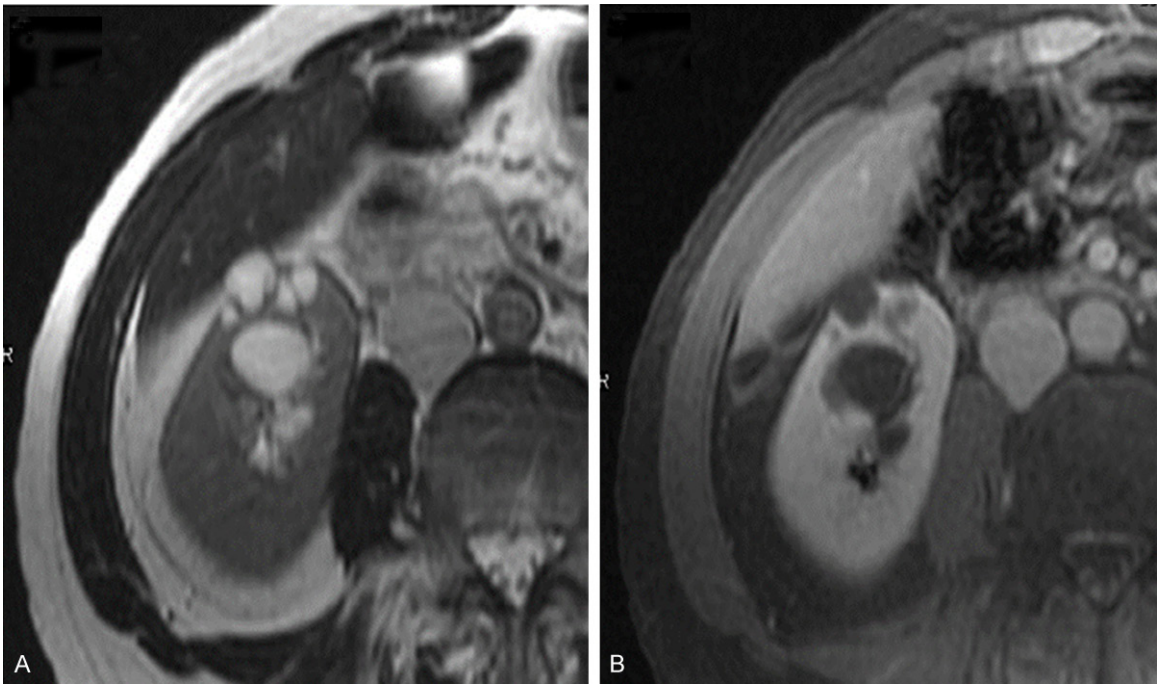

Figure 1. Magnetic resonance imaging. A. On a T2-weighted image, a renal mass with a maximum diameter of 3 cm can be observed, with multiple cysts present inside. B. On a contrast-enhanced T1-weighted fat-suppressed image, septa between the cysts showing enhancement similar to the normal renal parenchyma.

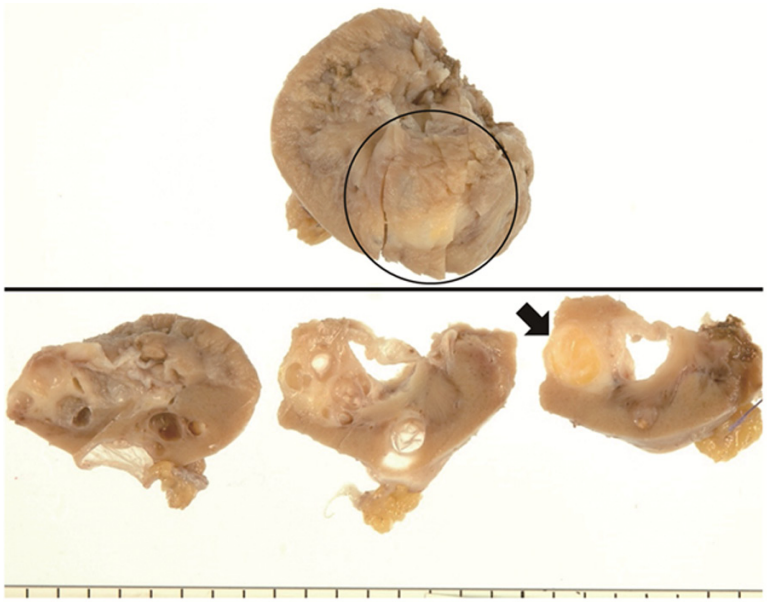

Figure 2. Macroscopic findings. The upper half of the figure shows the surgically resected specimen viewed from the inner side. The encircled area corresponds to the initial location of the mass. The lower half of the figure shows cut surfaces of the specimen; a multicystic tumor with fat is apparent, as indicated by the arrow. The tumor size was 3 × 3 × 2.5 cm. The cysts did not communicate with pyelocaliceal system.

mass was detected by using abdominal ultrasonography during a physical check-up. Laboratory test results were unremarkable. However, using magnetic resonance imaging, the mass, with a maximum diameter of 3 cm, was found to contain multiple cysts observed as high-intensity areas on a T2-weighted image (**Figure 1A**). Septa between the cysts showed enhancement similar to the normal renal parenchyma on a contrast-enhanced fat-suppressed T1 weighted image (**Figure 1B**). Cystic RCC and CN were included in the differential diagnosis, and partial nephrectomy was performed.

The surgically resected specimen revealed a mass, 3 × 3 × 2.5 cm in size, with multiple cysts on the cut surface (**Figure 2**, lower half); the cysts did not communicate with the pyelocaliceal system, when viewed from the inner side (**Figure 2**, circle). A yellowish area corresponding to fat was identified (**Figure 2**, arrow). No

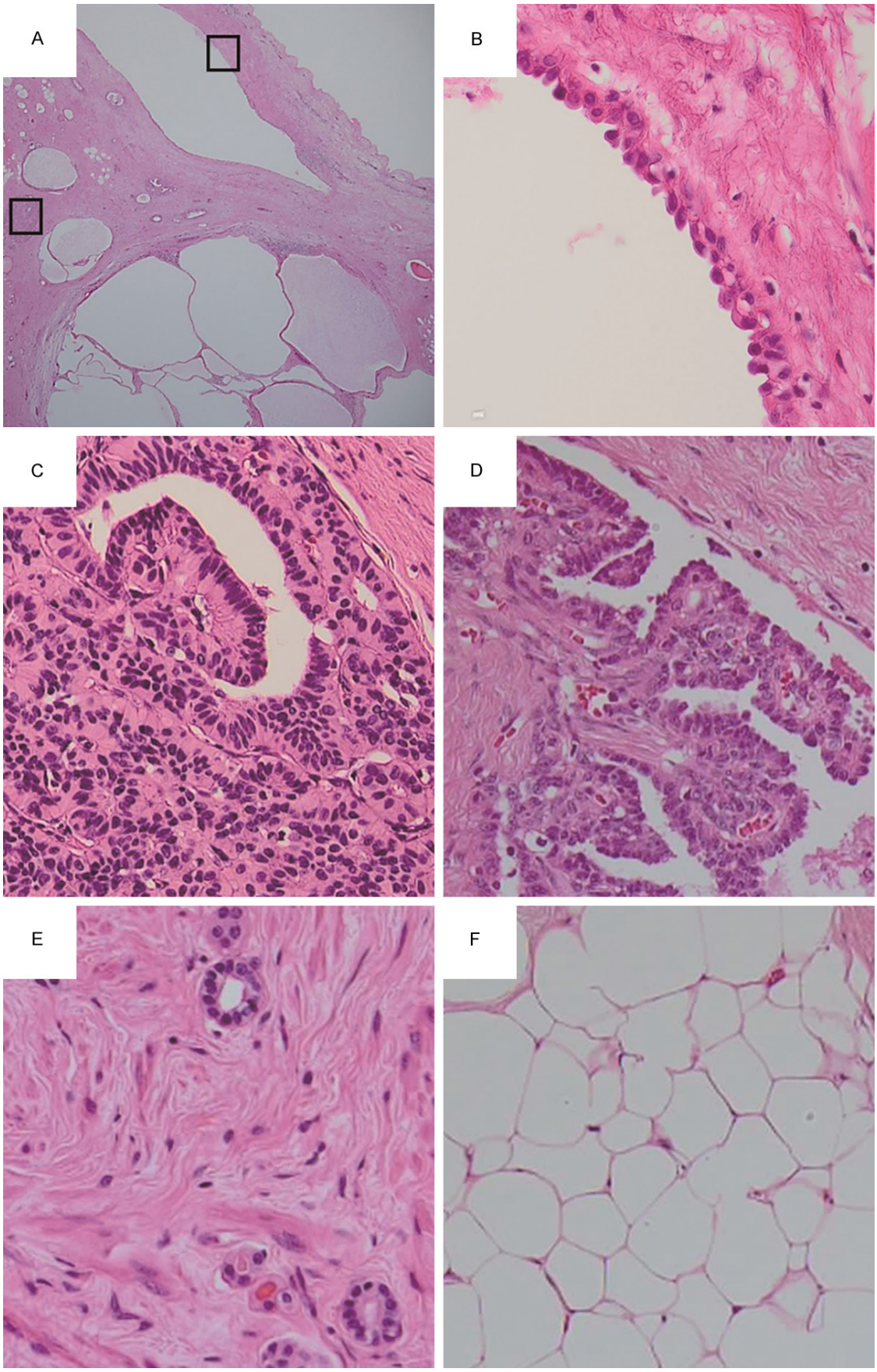
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Figure 3. Microscopic findings. (A) Low-power view of the tumor displaying nephroblastomatous elements in the septa of the cysts (× 12.5). (B) Boxed area above (A) showing a cyst wall covered by hobnail cells (× 400). (C) Boxed area on the left of (A) showing cap-mesenchyme-like cells, immature tubules, and an immature glomerulus with a stubby papilla (× 400). (D) A maturing glomerulus is observed (× 200). (E) Maturing tubules as well as maturing skeletal muscle cells are present (× 400). (F) Macroscopically identified fat is matured. Variability in the size of the cells can be observed, which is different from normal fat (× 400).

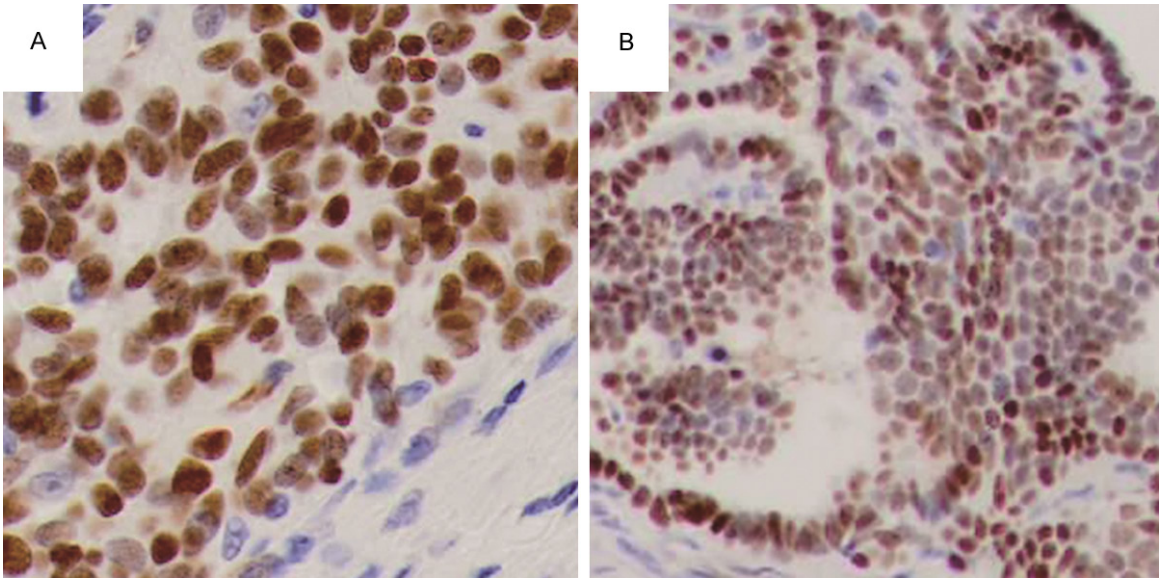

Figure 4. Immunohistochemical findings for WT1. A. Cap-mesenchyme-like cells and immature tubules showing nuclear positivity (× 400). B. A maturing glomerulus showing immunostaining with a nuclear pattern (× 200).

expansile solid area was observed. This macroscopic appearance suggested the possibility of cystic angiomyolipoma (AML) or CPDN.

Microscopic examination revealed nephroblastomatous elements in the septa of the cysts (**Figure 3A**). The cysts were covered by flattened or cuboidal to hobnail cells (**Figure 3B**). The nephroblastomatous elements ranged from immature to mature. The immature ne phroblastomatous elements included immature tubules and an immature glomerulus that were seemingly generated from cap-mesenchyme-like cells appearing to be undergoing mesenchymal-epithelial transition (**Figure 3C**). Maturing elements, a glomerulus (**Figure 3D**), tubules, and skeletal muscle cells (**Figure 3E**) were identified. Matured fat was macroscopically detected and differed from normal fat, as the size of the fat cells was variable (**Figure 3F**). Although a blastema was not observed, a diagnosis of CPDN was considered. Surgical margins were tumor-free, and the kidney background seemed to be unremarkable, without any nephrogenic rest.

Immunohistochemistry showed positivity for WT1 (6F-H2; Dako, Glostrup, Denmark) in the nucleus of the cap-mesenchyme-like cells and immature tubules (**Figure 4A**), as well as in the maturing glomerulus (**Figure 4B**). However, stromal elements were negative for WT1. Less than 1% of the cells were positive for Ki-67 (MIB-1; Dako).

The postoperative course was uneventful, and the patient has been recurrence-free for 2.5 years without adjuvant therapy.

Discussion

Cystic lesions of the kidney can be largely classified into two categories [11]. The first category is characterized by the presence of an isolated cystic mass not showing cystic changes in the renal parenchyma. Most of these lesions represent cystic tumors. While cystic changes may be encountered in most renal neoplasms, few tumor subtypes show cystic change as a defining feature involving the entire tumor. The second category is characterized by bilateral cystic changes and diffuse involvement of the

Table 1. Clinicopathological features of cystic partially differentiated nephroblastoma in an adult

Year	Age	Sex	Location	Blastema	WT1	Outcome
1999	45	M	Left kidney	+	-	no recurrence for 11 months without adjuvant therapy
2001	26	F	Left kidney	+	NA	no recurrence without adjuvant therapy
Our case	45	M	Right kideny	-	+	no recurrence for 30 months without adjuvant therapy

NA, not available.

kidneys without forming a discreet mass, which is based on hereditary or developmental predispositions. When identifying a renal cystic tumor in adults, differential diagnoses of cystic RCC, CN, and mixed epithelial and stromal tumor of the kidney (MESTK) are usually included [12]. As adult cases of CPDN or cystic WT are rare, these conditions are not usually considered [5, 6, 13]. CN and CPDN are identical on radiological and gross examination [11]; both these types are devoid of expansile solid nodules, characteristic of cystic WT [14]. Histopathological examination identifying blastema and/or nephroblastomatous elements rendered a diagnosis of CPDN, even though fat, suggestive of cystic AML [15], was present as was observed in our case.

Strictly defining CN after excluding MESTK with ovarian-type stroma [12], CN, CPDN, and WT may represent different stages in the evolutionary spectrum of the same entity, with CPDN being an intermediate between CN, which is benign, and WT, which is malignant [1-3]. The idea of spontaneous maturation of WT to a more differentiated form of cystic tumors such as CPDN and CN is reasonable, when considering the fact that neuroblastoma transforms into ganglioneuroma [1, 16]. The relationship between CPDN and WT is strengthened by the findings of hyperdiploidy or trisomy 12 in some CPDNs; both the findings are karyotypes also observed in some WTs [17]. However, CN and CPDN may not constitute a spectrum, because genetic analyses in a study cohort revealed that *DICER1* mutation is the major genetic event in the tumorigenesis of CN, but not in CPDN [18]. In addition, CN may harbor risk for malignant transformation [18], which has not been previously reported in CPDN.

Most cases of WT, but only one case of CPDN, express WT1, a gene product of *WT1* located on chromosome 11p13 [8]. *WT1*-mutant cases of WT contribute to only 10-15% of all WTs [19]. In cases of wild-type *WT1*, diffuse immunoreactivity was displayed in the cytoplasm of the stromal elements and blastema, while immunoreactivity in *WT1*-mutant cases was generally weaker and was confined to the stromal elements [9]. In the present case showing nuclear expression of WT1 in epithelial-oriented components, stromal and/or cytoplasmic immunopositivity was not observed, which was different from usual patterns of WT. In normal kidneys, the main role of WT1 is nephrogenesis through epithelial differentiation from blastema [8]. A unique feature of our blastemal-lacking CPDN was nuclear expression of WT1, limited to a cap-mesenchyme-like structure, immature tubules, an immature glomerulus, and a maturing glomerulus, suggesting imitation of normal nephrogenesis [10]. Although blastema were present in the 2 reported cases of CPDNs in adults (**Table 1**), one case lacked WT1 expression [5] and the expression of WT1 in the other case was not described [6]. Considering the normal-nephrogenesis-like pattern of WT1 expression in our case, we believe that tumoral nephrogenesis or maturation, ranging from a pre-existing blastema to the glomerulus, progressed, and the lack of blastema was owing to maturation that was postulated even in WT and was observed in neuroblastoma [1, 16].

CPDN shows little or no capacity for invasion [7]. As CPDN does not recur or metastasize and it seems to have a benign course, simple nephrectomy would be recommended [3]. However, 2 cases in children presenting with intra-abdominal recurrence without metastasis were documented; one case recurred possibly because of incomplete resection [1] and the other owing to rupture of cysts [20]. Although complete resection was achieved in our case, it is preferable to perform regular follow-ups.

In conclusion, this is the third reported case of CPDN in an adult. A unique feature of this case was the absence of a blastema and the presence of other immature to mature nephroblastomatous elements. WT1 expression in our case was different from typical cases of WT, as the expression pattern of WT1 imitated normal nephrogenesis in our case. This expression

pattern supported the ongoing maturation of our CPDN and would likely result in the disappearance of blastema.

Disclosure of conflict of interest

None.

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