Localized cystic disease of the kidney: case report and review of the literature

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Abstract Localized cystic disease of the kidney (LCDK) is a benign and non-progressive renal anomaly that may initially be confused with autosomal dominant polycystic kidney disease (as in the index case) or cystic neoplasms. It is best diagnosed with contrast-enhanced CT scan demonstrating the characteristic features of an unencapsulated mass of smooth-walled cysts with enhancing renal parenchyma between them. It is most often an incidental finding, but may present with flank pain or haematuria. Hypertension and renal impairment are uncommonly associated with LCDK. A complete physical examination and comprehensive family history are important to exclude other acquired or inherited causes of cystic kidney disease and to avoid unnecessary diagnostic procedures or nephrectomy. We describe a case manifesting many of the typical features of the condition and review previously published cases to describe the natural history and presentation of this rare entity.

Keywords Cystic · Disease · Kidney · Localized · Unilateral

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Introduction

Localized cystic disease of the kidney (LCDK) is a rare disorder of unknown etiology that must be distinguished from other cystic renal disorders such as autosomal dominant polycystic kidney disease (ADPKD) and cystic neoplasms. It is characterized by the presence of an unencapsulated conglomeration of cysts, separated by developmentally normal renal parenchyma, that affects all or part of one kidney [1, 2]. We describe a case displaying many of the salient features of the condition and analyze the previously published cases.

Case report

A 62-year-old male was reviewed for hypertension, mild chronic kidney disease and a background of cystic kidney disease of uncertain etiology. At age 53 years he had presented with mild impairment of kidney function and hypertension. At that time, ultrasound and CT scan demonstrated a grossly enlarged multicystic right kidney (measuring 24 cm bipolar length) with a left kidney that contained two simple-appearing cysts but was otherwise normal (Fig. 1). Post-contrast scans showed only a tiny area of normally enhancing renal tissue in the anterior right kidney. A DTPA scan at that time showed that the right kidney contributed only 6 % of total glomerular filtration, with overall DTPA clearance of 96 mL/min. The patient was diagnosed with ADPKD and treated for hypertension. He was then lost to nephrology follow-up before re-referral to our clinic at age 62 years.

His medical history included a seronegative inflammatory arthritis (which involved the joints of his hands, ankles and knees) and responded well to prednisolone and

Fig. 1 Two images from a contrast enhanced CT of the patient at age 53 years. **a** Grossly enlarged cystic right kidney with an otherwise normal left kidney (with the exception of a single simple cyst). **b** Red arrows demonstrate lines of normally enhancing renal parenchyma within the cystic right kidney

maintenance sulfasalazine) and obesity (body mass index 32.5 kg/m^2). His regular medications were sulfasalazine, prednisolone (2.5 mg daily), olmesartan, hydrochlorothiazide and diltiazem. He drank approximately 140 g of alcohol per week and did not smoke cigarettes.

His mother and father lived to their ninth and eighth decades respectively, and were not affected by kidney disease. He had two brothers and a son who also did not suffer from kidney disease. At the time of his diagnosis of ADPKD, screening of his first-degree relatives had not revealed cystic kidney disease.

On examination, his right kidney was not ballotable and there were no signs of uremia. Urinalysis was unremarkable. Twenty-four-hour urine protein excretion was 0.18 g/day and creatinine clearance 84 mL/min.

The patient was referred to a medical geneticist who agreed that LCDK was the most likely diagnosis. An MRI brain did not reveal any evidence of the potential

intracranial manifestations of ADPKD or tuberous sclerosis. Repeat renal tract ultrasound confirmed innumerable cysts in the right kidney (bipolar length 24 cm) and a left kidney containing two cysts, as before, one of which was large (11 cm diameter) and septated.

The patient continues to have regular surveillance follow-up with his nephrologist. Twelve years after his initial diagnosis, he is asymptomatic from his kidney disease and his kidney function remains unchanged.

Discussion

LCDK is a rare disease and its prevalence is unknown. Sporadic case reports appeared in the latter part of last century under various descriptions. The first large case series were reported in the early part of this century and the term localized cystic disease of the kidney was chosen to emphasize the distinction between this entity and ADPKD [3, 4]. Bisceglia and Cretí identified 54 cases published between 1964 and 2005 [5] and a literature search identified a further 22 cases published since 2005 (these papers are summarized in Table 1 of the Supplementary Material). All 76 cases plus the case reported here are considered together in the following discussion.

The median age at diagnosis was 40 years (range 0–83) with a male preponderance (65 %). Follow-up periods extended up to 30 years and there were no reports of progression of disease or malignancy. Where the presenting symptom could be determined ($n = 71$), the most common presentation was incidental (41 %) followed by flank pain (28 %), hematuria (21 %) and a palpable abdominal mass (10 %). In a number of cases, the presentation was due to trauma revealing previously asymptomatic disease.

Urinary tract infection and nephrolithiasis appear uncommon. There were two reported cases of uncomplicated urinary tract infection and one case of proven pyogenic cyst infection. Asymptomatic renal stones were identified in the affected portion of the kidney in two cases and one patient had symptomatic nephrolithiasis.

There was one report of intractable flank pain, hematuria and hypertension (in a patient with LCDK of the lower pole of his right kidney) which responded to partial nephrectomy and a case of polycythemia associated with LCDK, which also resolved after nephrectomy.

Hypertension was reported in 9 (13 %) cases with a median age of 53 years, but including two young children (10 months and 3 years). Of the five patients who underwent nephrectomy, hypertension resolved in three with the result not reported in the other two.

Among cases in which specific mention was made of serum creatinine or glomerular filtration rate ($n = 29$),

impairment of renal function was reported in 24 % however, no cases of advanced chronic kidney disease (eGFR < 30 mL/min) were reported. As with our case, most of these patients had concurrent hypertension and it was unclear to what degree the impairment in kidney function could be attributed to LCDK. Our case is unusual in that renal scintigraphy demonstrated reduced function in the affected kidney. Few cases describe measurement of differential renal function however, in most cases (5/7) no such difference was identified (whether assessed qualitatively by excretion of contrast during contrast enhanced CT or quantitatively by DTPA scan). Only two other cases describe a reduction in differential function. Our case was also complicated by low-level proteinuria, which in the context of hypertension and reduced functional nephron mass in the affected kidney, raises the possibility of the eventual development of progressive loss of renal function or secondary focal sclerosing glomerulosclerosis. This highlights the prudence of long-term follow-up of patients with LCDK.

The pathogenesis of LCDK is unknown. Histologically the affected area is indistinguishable from ADPKD, with smooth walled cysts of flat or cuboidal epithelium containing straw-coloured fluid [2, 6, 7]. The renal parenchyma between the cysts is developmentally normal, although it may appear distorted, and sometimes atrophied, presumably by the local mass effect of multiple cysts. All sections of the nephron can be affected, including the glomerulus [7]. This has given rise to the hypothesis that LCDK is due to a somatic mutation of PKD1 (the gene responsible for most cases of ADPKD) [8]. However, this attractive explanation is complicated by the apparent lack of progression in cyst size and number over time, contrary to the typical natural history of ADPKD. An unspecified developmental abnormality is now assumed to be the cause. The presence of simple cysts in the contralateral kidney, as seen in the presenting case, has not previously been reported and bilateral LCDK has not been described. We hypothesise the coincidental development of acquired simple cysts.

The diagnostic test of choice is contrast-enhanced CT scan of the renal tract. This demonstrates the characteristic non-enhancing cysts with normally enhancing renal parenchyma within the intervening bands of tissue. Calcification in the cyst walls and hyperdense cysts suggestive of cyst hemorrhage appear to be common. Pertinent negative findings include the absence of mural irregularities and the lack of encapsulation [6]. An algorithm facilitating radiological diagnosis has been published [9]. The differential diagnosis of cystic lesions of the kidney centers on ADPKD and a number of congenital and neoplastic conditions—especially multicystic dysplastic kidney, cystic

Wilm's tumor or renal cell carcinoma, cystic nephroma, von Hippel-Lindau disease and tuberous sclerosis.

LCKD is distinguishable from ADPKD by its localized nature and by the absence of family history, progression to end-stage kidney disease and characteristic abnormalities in other organ systems [3]. Multicystic dysplastic kidney is a congenital anomaly that may cause cystic change in one or more segments of one kidney. However, as this is due to abnormal differentiation of metanephric elements in utero, this is accompanied by ureteropelvic malformations and abnormal renal lobes [2, 8].

Neoplasm is a frequent concern and one of the main benefits of the characterization of LCDK is that it allows these patients to confidently forgo nephrectomy. In addition to renal cell carcinoma (RCC) (which presents with multiple cysts in 5 % of cases), one must also consider multilocular cystic nephroma and cystic Wilm's tumor. All of these lesions are surrounded by a capsule or pseudocapsule, they displace normal renal tissue and do not contain internal bands of normally enhancing parenchyma [10]. Two autosomal dominant inherited conditions associated with multiple renal cysts and neoplasms are tuberous sclerosis and von Hippel-Lindau disease. Both, however, are associated with a phenotype of multiple benign tumors in other organ systems. Other rare conditions that present with unilateral renal cystic lesions include renal lymphangiomas (*hygroma renalis*) and hydatid cyst [5, 7].

In conclusion, LCDK is a rare, benign, non-progressive entity, best diagnosed with contrast-enhanced CT demonstrating the characteristic features of an unencapsulated mass of smooth-walled cysts with enhancing renal parenchyma between them. It is often diagnosed following an episode of flank pain or hematuria, but may be detected as an incidental finding. Hypertension and renal impairment are uncommon but have been reported. A complete physical examination and comprehensive family history are important to exclude other acquired or inherited causes of cystic renal disease and to avoid unnecessary diagnostic procedures.

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