Interesting Case

Dialysis-associated acquired cystic kidney disease imitating autosomal dominant polycystic kidney disease in a patient receiving long-term peritoneal dialysis

Daniel Neureiter¹, Helga Frank², Ulrich Kunzendorf², Rüdiger Waldherr³ and Kerstin Amann¹

¹Department of Pathology, ²Department of Internal Medicine/Division of Nephrology, University of Erlangen and ³Practice for Pathology, Heidelberg, Germany

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Introduction

Acquired cystic kidney disease (ACKD) is frequently observed in patients with end-stage renal failure or who are on long-term dialysis, independent of the cause of the renal failure [1]. Criteria for the diagnosis of ACKD are: (i) the presence of at least one to five kidney cysts confirmed by means of ultrasound or computer tomography (CT); and (ii) pathologically, an extension of cysts involving >25% of the renal parenchyma [2]. Usually the end-stage kidneys are of a small to normal size and the renal cysts are <0.5 cm in diameter [3]. These findings differ fundamentally from the morphology of autosomal dominant polycystic kidney disease (ADPKD) [2]. Nevertheless, in some cases the differential diagnosis is clinically difficult due to an uncommon macroscopic presentation.

Here we present a 36-year-old male patient, who had end-stage renal failure from IgA-nephropathy and had developed a large, completely cystic, transformed, ADPKD imitating kidney after 6 years on continuous ambulatory peritoneal dialysis (CAPD).

Case

A 36-year-old man with a history of peritoneal dialysis renal replacement therapy was referred to our hospital because of acute flank pain on the left hand side. This was a strong hollow pain which did not spread but nevertheless continued for a few hours after the patient had been admitted. There were no signs of fever, vomiting or abnormalities of bowel movement. One week before admission, the patient had suffered from a cold with a slight cough.

Renal failure with a nephrotic syndrome and a proteinuria of 5 g per day had first been discovered at the age of 30. At that time, the creatinine clearance was markedly reduced (25 ml/min) and the patient was hypertensive. The patient had no family history of kidney disease. A kidney biopsy at the time led to a diagnosis of glomerular sclerosis with mesangial immunoglobulin A deposition and IgA nephropathy (Berger’s disease). Six months later, the patient developed uraemic symptoms and CAPD therapy was started.

In 1996, the patient’s right kidney had to be surgically removed due to a paranephric abscess. The histological examination of the removed kidney confirmed the presence of an IgA nephropathy with complete sclerosis of nearly all glomeruli. A cystic transformation of this kidney was not observed.

Remarkable in the patient’s past history was an atrial septum defect (ostium secundum defect), which had been successfully closed percutaneously using a clamshell device in 1995.

On admission, the patient was normotensive (140/90 mmHg), the heart rate was normofrequent, the respiratory rate was 18 breaths per minute and there were no signs of fever. His skin was pale and he showed no peripheral oedema. Auscultation revealed a pericardial rub and little moist rales over both lungs. Palpation of the left flank was very painful without any palpable expansive tumour in this region. His peristalsis was normal and the entry zone of the peritoneal catheter showed no cutaneous irritation or signs of local infection. The patient was totally anuretic.

Laboratory results

Laboratory results revealed the uraemic state (creatinine 14 mg/dl, BUN 106 mg/dl), there was a
normochromic and normocytic anaemia (haemoglobin 7.1 g/dl, haematocrit 22%), reduced reticulocyte count and normal platelet count. Electrolytes, LDH- and lactate-levels and acid-base balance were normal. Infection parameters were slightly elevated (leucocytes $10.7 \times 10^9$/µl, blood sedimentation 25/41 mm, CRP 63 mg/l).

Ultrasonography showed a greatly enlarged left kidney (17 cm in length, 7.5 cm in width) with a strongly intensified density of the kidney parenchyma and multiple cystic formations around the whole circumference of the kidney. The cysts were of different sizes ranging from 0.3 to 6 cm in diameter and there were various dense echo reflexes inside the cystic formations. No other abnormalities were found in the abdomen; in particular no tumour, no other cysts or free fluid. A subsequent computer tomogram of the abdomen (Figure 1a) confirmed these ultrasonographic findings and provided evidence that the enlarged left kidney contained numerous cyst formations with diameters of up to 4 cm. Signs of abscess or infection were absent. Echocardiographic examination proved a circular echo-free pericardial effusion without haemodynamic consequences. This finding was interpreted as a uraemic pericarditis due to the end-stage renal disease state.

On account of a further decrease in the haemoglobin concentration and assuming that bleeding of a renal cyst was causing the severe flank pain, the patient was then referred to our urology consultant. As a result of this, the nephrectomy of the left kidney was carried out, the post-operative course being without complications. The peritoneal dialysis catheter was removed at the same time and haemodialysis therapy was started.

Macroscopic findings (Figure 1b)

We found an extremely enlarged kidney with a weight of 890 g and a size of $17.0 \times 12.5 \times 10.0$ cm. On the cross-section, multiple cysts in the cortex and medulla could be seen with a diameter varying in general from 0.1 to 4.5 cm. The cysts nearly completely replaced the renal parenchyma. The cysts’ wall occasionally showed solid-polyloid lesions up to 0.3 cm in diameter, which were yellow-brown in colour. The content of the cysts was haemorrhagic in most of the cases; sometimes bleeding extended into the perirenal space. None of the cysts were infected and the surface of the kidney appeared granular.

Microscopic findings (Figure 1c–f)

The renal parenchyma was almost completely replaced by multiple cysts of varying diameters forming a communicating system. The insides of many of these cysts showed not only amorphous eosinophil material, but also fresh haemorrhagic masses without any signs of acute inflammation.

Morphologically, two kinds of cysts could be detected. The majority of cysts was small and lined by a single layer of a flat or cuboidal epithelium (Figure 1c). Microvilli were present at the apical cell pole (Figure 1c, arrows). Dilated tubuli creating small neo-cysts were noted in many areas of the kidney (Figure 1c, asterisks). In close contact with these neo-cysts, huge cysts could be seen with solid complexes of a highly hyperplastic interdigitated epithelium and sometimes with microvilli (Figure 1d, arrows). This epithelium showed distinct signs of cellular atypia such as prominent and hyperchromatic nuclei. Mitoses were occasionally visible (Figure 1e, arrows). By using immunohistochemistry these hyperplastic cells expressed cytokeratins as markers of epithelial differentiation (cytokeratins Lu-5, Dianova®) and vimentin as a marker of mesenchymal differentiation (vimentin, Dako®). In addition, one papillary adenoma was noted (Figure 1f).

Between the multiple cysts the sparse remaining parenchyma showed areas of disseminated fibrosis only with sclerosed glomeruli, interstitial lymphoplasmacytic infiltration as well as arterio- and arteriolosclerosis. Typical residues of the underlying IgA-nephropathy such as mesangial IgA- or C3q-deposits were not observed when using monoclonal antibodies (Dako®).

Discussion

Since the autopsy study of Dunnill et al. in 1977, many clinical and morphological studies of acquired cystic kidney disease (ACKD) in patients with end-stage renal disease on long-term dialysis have been published [1–4]. Conclusions include the following.

- The incidence of ACKD varies from 10 to 95%. Men are more often afflicted with ACKD than women, and blacks more than Caucasians.
- Prevalence, size and number of cysts correlate with the duration of dialysis, but not with the original renal disease. No significant difference between the incidence of ACKD after haemodialysis and CAPD has been shown.
- Typical complications of ACKD are intra- and pericystic bleeding, macrohaematuria, rupture with retroperitoneal haemorrhage and a higher risk of malignant transformation than in normal kidneys.
- In most ACKD cases the kidneys are of a small- to normal-size. Renal cysts are typically small (up to 0.5 cm in diameter) and have been observed in the cortex and the medulla.
- Prolonged ischaemia, toxic effect of uraemic substances and oxalate-enhancement were discussed as promoters for cystic transformation in ACKD.
In our case a patient with end-stage renal disease due to IgA nephropathy and state of nephrectomy showed an enlarged residual kidney with large cysts imitating ADPKD. Only a few cases have been described in the literature regarding developing ACKD with large renal cysts resembling ADPKD [5–10]. In these cases, age, sex, underlying renal diseases as well as dialysis method (i.e. haemodialysis or CAPD) and the length of the dialysis treatment turned out to be highly heterogeneous. It should be pointed out that in all of these cases the diagnosis of ACKD was made on the basis of renal biopsies and a negative family history. Clinically, however, ACKD and ADPKD could not be distinguished by either sonography or CT scan.

Fig. 1. Abdominal computer tomogram (a) and macroscopic feature (b) showing an enlarged kidney with multiple cysts replacing the kidney, and fresh intracystic bleeding partly expanding to the perirenal space. The microscopic appearance (haematoxylin–eosin staining) of the ACKD demonstrates the dynamics of building new cysts (c, asterisks) and shows the whole spectrum of the epithelial plasticity from a single to multiple layers of 'normal' epithelium with microvilli (c, arrows), at the top in most cases, to a high hyperplastic 'atypical' epithelium with hyperchromatic and atypical nuclei (arrows indicate microvilli (d) and mitoses (e)). In addition, one papillary adenoma was found (f). Magnification: (c–e) ×40; (f) ×20.
But what was the evidence for ACKD in our patient? The onset of cystic kidney disease and the age of the patient argue for the diagnosis of ADPKD. A hereditary transmission, typical of ADPKD, could not be proven for our patient, since there was no history of renal disease in the patient’s family. The history of an atrial septum defect is of particular interest since this has been described as associated with ADPKD [11]. The possibility of a spontaneous ADPKD mutation could not be definitely ruled out, however. With respect to ACKD cases in particular, those with papillary lesions and heterogeneous chromosomal abnormalities, which could also affect the known genetic ADPKD defects, have been observed [12].

The main reasons for the pathological diagnosis of ACKD in our patient were the typical histological changes in the renal cysts, which could be seen throughout the whole kidney. The cysts were covered by a single line of a flat or cuboidal epithelium or by solid complexes of high hyperplastic atypical epithelium. However, in the majority of cases microvilli were observed at the apical pole of the epithelial cells, identifying the cells as derived from the proximal tubulus. Analysis of cyst fluid as well as histochemical and scanning electron microscopy studies showed that in ACKD, most of the cysts derive from the proximal tubuli [2,13]. In addition, we found multifocal areas of highly hyperplastic epithelium with typical signs of cytological atypia (e.g. bizarre and hyperchromatic nuclei or mitoses) but without evidence of malignancy, such as infiltrative growth or clear cells. Epithelial hyperplasia of cysts is frequently seen in end-stage dialysis kidneys, leading to the term ‘atypical cysts’ [14]. Furthermore, there is an increased association between ‘atypical cysts’ and renal cell adenoma or renal cell carcinoma, especially papillary tumours [14]. In our patient’s kidney one papillary renal cell adenoma was present. In contrast, simple cysts are typically lined by a single layer of flat or cuboidal cells. Furthermore, in ADPKD the cysts are derived from various parts of the nephron, and the epithelium of the cysts is mostly cuboidal to columnar; these cells are less often hyperplastic than in ACKD and renal malignancy is quite rare in ADPKD [15].

Moreover, another argument for the diagnosis of ACKD and against ADPKD in this case is the fact that the former removed right kidney had no cystic transformation.

Summary

The typical histological features of epithelial hyperplasia in the cysts, the lack of any family history of renal disease (such as in ADPKD), the fact that there was no cystic transformation in the previously removed right kidney and the lack of extrarenal signs of other genetic cystic disease (such as hepatic cysts or tuberous sclerosis) led to the final diagnosis of ACKD.

Patients with end-stage renal failure receiving long-term dialysis treatment occasionally develop very large cystic kidneys imitating ADPKD.

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References


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