Case Report

Caroli’s syndrome associated with medullary sponge kidney and nephrocalcinosis

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Key words: Caroli’s syndrome; computed tomography; medullary sponge kidney; nephrocalcinosis

Introduction

Congenital non-obstructive multifocal dilatation of the intrahepatic bile ducts (Caroli’s syndrome [1]) is a rare condition. Unlike true hepatic cysts, the cystoid ducts contain bile. Caroli’s syndrome can be present in a simple form with monolobar (often left lobe) or diffuse bile duct dilatation or in an associated complex form with additional extrahaepatic bile duct dilatations, congenital hepatic fibrosis, portal hypertension and cystic malformation of the pancreas, spleen or kidneys. Medullary sponge kidney, which was first described as a pathological entity in 1948 [2], consists of an ectasia of the terminal collecting ducts in the pericalyceal region of the renal pyramids with formation of small and large bilateral diffuse cysts. It is a benign condition with an excellent long-term renal prognosis. This case report presents the clinical and radiological findings of a patient with Caroli’s syndrome and unilateral preponderance of nephrocalcinosis due to medullary sponge kidney.

Case report

A 27-year-old male presented for the first time in his life with a 2-month history of recurrent right-upper-quadrant pain, nausea, vomiting and temperatures up to 39.8°C. He had lost 10 kg within 2 months, but had never had diarrhoea, jaundice, renal symptoms, arthralgias, or abdominal operations before. He was an intravenous drug addict (cocaine, heroin). History of family disease included his father who had died because of a ‘kidney tumour’. The desired examination of family members (mother, 1 brother) was refused.

On the initial physical examination, he had a tachycardia (112 b.p.m., regular rhythm) without pathological murmurs, and was normotensive. He presented with epigastric pain and an abdominal tenderness, but without hepatosplenomegaly, skin icterus, or oedema of the legs. The right renal area was painful. Additional pathological findings of the physical examination were absent. Laboratory investigations showed an increased erythrocyte sedimentation rate (95/120 mm n.W.), increased white cell count (15.3 x 109/l) without neutrophils, increased platelet count (708 x 109/l), decreased haemoglobin (11.3 g/dl, normochromic, normocytic), increased C-reactive protein (230 mg/l, normal <5 mg/l). There were disordered liver parameters with alkaline phosphatase (376 U/l, normal <170 U/l), gammaglutamyltransferase (103 U/l, normal <34 U/l) and hypoalbuminaemia (2.5 g/dl, normal >3.5 g/dl). Immunoelectrophoresis showed a polyclonal IgG-elevation. The creatinine clearance, urine sediment and arterial blood gas analysis were normal and there was no proteinuria. The urine concentrations of calcium (1.0 mmol/day, normal range 1.3–10 mmol/day), phosphate (20.2 mmol/day, normal range 23–48 mmol/day) and chloride (164 mmol/day, normal range 170–250 mmol/day) were slightly decreased, whereas the urine potassium, sodium, citrate and oxalate were within normal ranges. E. coli bacteria were found in the biliary fluid, which was taken from biliary ducts during endoscopic retrograde cholangiopancreatography (ERCP). Blood/urine/sputum cultures were sterile. All other routine laboratory and immunological parameters (ANA, C3, C4, HLA-B27, circulating immune complexes, anticiadilinip antibody, rheumatoid factor, ANCA, anti-GBM antibody, hepatitis A, B, and C, HIV) and serum/urine osmolality were within normal ranges or negative.

Ultrasound showed various cystic bile ducts throughout the whole liver. A hypoechoic intrahepatic area (3 cm diameter) was detected near the portal vein. The ductus hepatocholedochus was dilated and the gall-bladder was filled with multiple stones. The kidneys were enlarged (14 cm) and showed cystic formations. The left kidney had a reduced parenchyma.
Multiple calculi were found in the pyramids of the right and to a lesser extent of the left kidney.

The diagnosis of Caroli's disease was based upon an ERCP which showed multiple saccular dilated intrahepatic bile ducts without stone formation throughout the whole liver (Figure 1), a cholecystolithiasis, and extrahepatic choledocholithiasis. An endoscopic papillotomy (EPT) was performed and the choledochus stones were caught by a dormia cage. Putrid fluid was found after EPT.

A Tru-cut liver biopsy was performed under control of computed tomography. The histological evaluation showed ectactic intrahepatic bile ducts with concentrated biliary fluid without dysplastic changes of the mucosa or biliary glands. Acute inflammation with infiltration of neutrophil granulocytes, lymphocytes and macrophages and abscess formation were observed.

Computed tomography revealed multiple cystic dilatations of the intrahepatic bile ducts with a maximal diameter of 2 cm throughout the whole liver and a hypodense area near the portal vein within the porta hepatitis (3 cm pericholangic abscess in the liver segment IV, Figure 2.). The spleen and pancreas were without pathological findings and signs of portal hypertension were absent. Multiple calculi were found in both kidneys with predominance of the right kidney. The opacifications were seen in the pyramids.

Intravenous pyelogram showed the involvement of most calices with a brush-like appearance radiating out from the calices in both kidneys (Figure 3). The right kidney had a macrocalcification in its cortical parenchyma.

Additional technical examinations (gastroscopy, radiological examination of the chest and abdomen, transoesophageal echocardiography, electrocardiogram) were within normal limits. The final diagnosis was Caroli's syndrome with medullary sponge kidney and uncomplicated nephrocalcinosis. The clinical course improved tremendously with antibiotic therapy. However, in the following 3 months, the patient presented twice in our hospital with fever and abdominal pain. The ERCP revealed recurrent choledochus stone formation and the signs of an acute cholangitis.

Antimicrobial therapy led to rapid improvement.
Computed tomography showed that the pericholangic abscess became smaller. Because of the diffuse manifestation of the disease, a surgical intervention was not performed. In addition, the relapse of the disease with recurrent complications such as cholangitis and stone formation decreases the possibility of an effective surgical therapy. Therefore, regular evaluation of laboratory and liver function parameters were made in order to determine when a liver transplantation should be performed.

Discussion

Caroli’s syndrome belongs to the group of fibropolycystic liver diseases. It comprises a broad spectrum of hepatic, pancreatic and spleen abnormalities. Caroli’s syndrome may have the same renal malformations that are associated with isolated autosomal recessive congenital hepatic fibrosis (CHF). They range from ectatic medullary collecting ducts resembling medullary sponge kidney [3] to dilatation of both the medullary and cortical collecting tubules [4] and autosomal recessive polycystic kidney disease ARPKD. This associated form of Caroli’s syndrome is thought to be transmitted in an autosomal recessive pattern.

Interestingly, CHF [5] and Caroli’s syndrome [6] can be encountered in patients with autosomal-dominant polycystic kidney disease ADPKD, which was formerly thought to exclude this diagnosis. Several hypotheses such as modification of alleles/genes, or environmental factors, may serve as an explanation for this phenomenon. Medullary sponge kidney is a congenital condition which is usually not inherited, but often associated with inherited diseases. It presents with diffuse and bilateral cysts of the medullary portions of collecting ducts [7].

As in our patient, focal involvement or predominance of one kidney has been described. Caroli’s syndrome without CHF has no clear pattern of inheritance and is usually not associated with renal cystic disease as in this case report.

The pathogenesis of Caroli’s syndrome is unknown. Nakanuma [8] considered a disproportionate speed of growth of biliary epithelium and of the supporting connective tissue to be the reason. A ‘ductal plate malformation’ with an arrest in the normal organogenesis was also assumed [9]. These hypotheses might be used to suggest a common pathogenesis of cystic malformations of hepatic/renal ductal epithelial cells.

Disease manifestations of Caroli’s syndrome usually appear in childhood and young adults, but may also go unrecognized the whole life. The clinical course ranges from recurrent cholangitis without complications to proliferation of dilated small terminal intrahepatic canaliculi with cirrhosis and portal hypertension, induction of intracystic stones, hepatic abscesses and secondary amyloidosis or pancreatitis. Hepatic fibrosis is regarded as a premalignant factor and formation of malignant tumours (cholangiocarcinoma) have been described in 7% of cases [10].

Diagnostic tools are ultrasonography, endoscopic retrograde cholangiopancreatography, computed tomography (‘central dot sign’), transcutaneous hepatic biopsy, radionuclide hepatobiliary imaging, intraoperative cholangiography, and percutaneous transhepatic cholangiography [11]. In addition to the effective antibiotic therapy of cholangitis, endoscopic removal of stones and surgical methods such as Roux-Y hepatico-jejunostomy, lobar hepatectomy or liver transplantation seem to be of benefit [12,13]. Prophylaxis against infections by continuous administration of antibiotics and against stone formation with chenodoxycyclic acid can not be recommended.

The clinical course of medullary sponge kidney is generally benign with only rare progression to chronic renal failure. Complications by stone formation (almost 60% of the patients), urinary tract infection (30%), chronic pyelonephritis (10%), or nephrocalcinosis (50%, mostly calcium oxalate) are frequently found. Effective therapy of symptomatic patients with pyramidal nephrocalcinosis has been achieved by extracorporeal shock-wave lithotripsy [14]. Hypercalciuria and distal renal tubular acidosis, which are present in almost 40–90% of cases were not detected in our patient. The radiographic findings are essential for the diagnosis and include a wide spectrum of features such as papillary blush, linear radiations, medullary cyst formation, and nephrocalcinosis [7].

The present case report of Caroli’s syndrome shows that the detection of cystic liver disease warrants additional renal investigation and examination of the whole family is needed to determine the type of inheritance.

Acknowledgements. Christian Mrowka is supported by the Deutsche Forschungsgemeinschaft DFG grant Mr 15/1–1.

References

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Received for publication: 1.9.95
Accepted in revised form: 29.11.95