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Letters to the Editor

Autosomal recessive polycystic kidney disease diagnosed in a 39-year-old woman with kidney failure and cramps☆

Poliquistosis renal autosómica recesiva diagnosticada en mujer de 39 años con fallo renal y calambres

Dear Editor,

Autosomal recessive polycystic kidney disease (ARPKD) is a rare hereditary disease with an estimated incidence of 1:10,000 to 1:40,000.[1,2] It is due to a mutation in the *PKHD1* gene that codes for a protein called fibrocystin or polyductin which is responsible for differentiating between kidney and bile duct tubules.[1] It is characterised by kidney cysts with progressive kidney function deterioration and biliary dysgenesis that causes congenital liver fibrosis.[2,3] Subtypes can be established according to the age of presentation and severity of the disease: prenatal, neonatal, childhood and young adult.[3] The most severe cases with nephromegaly and Potter's syndrome are described in the first year of life,[4] while those detected in adolescence are less symptomatic and kidney function deteriorates later. Nevertheless, there are few published articles describing patients that were diagnosed as adults.

A 39-year-old woman with no relevant medical history was seen in the emergency room for cramping in her legs during the last 6 months, but that had been more severe during last week. It was associated with asthenia, hyporexia, and 20 kg of weight loss during the last year. She denied taking NSAIDs or other drugs. No fever, photosensitivity, skin lesions, arthralgia, or other symptoms of systemic disease. Physical examination was normal, except for a blood pressure of 93/61 mmHg. The blood tests showed creatinine 5.53 mg/dl, urea 386 mg/dl, sodium 127 mEq/l, potassium 5.3 mEq/l, magnesium 1.2 mg/dl, calcium 6 mg/dl, PTH 672 pg/ml, haemoglobin 8.4 g/dl, pH 7.28, bicarbonate 13.6 mmol/l, pCO_2 29 mmol/l and anion GAP 19. Urinalysis: proteinuria 310 mg/day, natriuria 186 mEq/day, calciuria 86 mg/day, magnesuria 48 mg/day, with no glycosuria, haematuria, or leukocyturia. Anaemia and smear tests were normal. Immunological and serum test were normal. The TSH, cortisol, ACTH, and ADH hormones were normal, but renin and aldosterone were elevated. Abdominal ultrasound: kidneys decreased in size with poor corticomedullary differentiation, cortex thinning, and predominant bilateral simple medullary cysts under 1 cm, with no lithiasis or hydronephrosis (Fig. 1). Cystic dilations of the intrahepatic bile ducts were observed as an incidental finding on the ultrasound and confirmed with magnetic resonance cholangiopancreatography, which are indicative of Caroli's disease (Fig. 2).

After intravenous magnesium, calcium, potassium, and bicarbonate treatment, the cramps resolved. She was prescribed salt supplements to normalise her blood pressure. At discharge: creatinine 4.5 mg/dl, sodium 133 mEq/l, potassium 3.7 mEq/l, calcium 7.1 mg/dl, magnesium 2.2 mg/dl, pH 7.34 and bicarbonate 24 mmol/l. Oral salt supplements were considered necessary. Family screening of her parents, siblings, and children, with kidney ultrasound and blood tests was normal. There was no genetic relationship between her parents. The confirmatory diagnosis was obtained using genetic testing that detected the mutation in the *PKDH1* gene; furthermore, the presence of associated tubulopathy was ruled out. After four months, the patient began peritoneal dialysis.

ARPKD is a paediatric disease with kidney and liver symptoms, with few cases published of adult-onset. The differential diagnosis was first made as autosomal dominant polycystic kidney disease (ADPKD) that, although rarely, can sometimes be associated with Caroli's disease.[5] It was discarded because her kidneys were not increased in size and the kidney cysts were sub-centimetre in size. Other hereditary cystic

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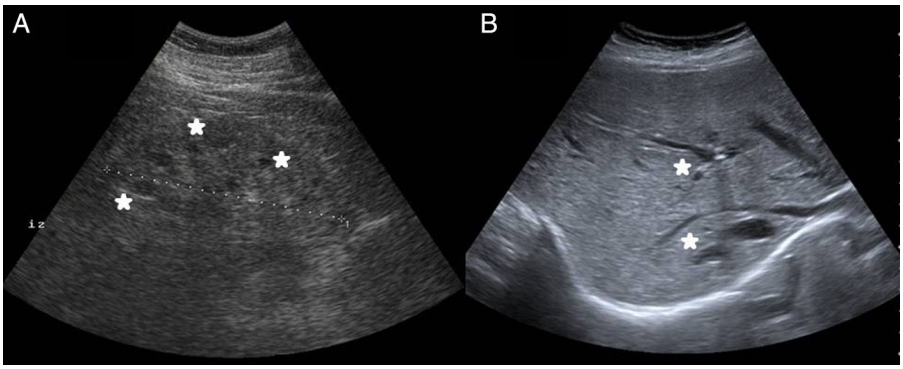

Fig. 1 – Ultrasound (A) Cortical kidney sinus cysts. (B) Cystic dilation of the intrahepatic bile ducts.

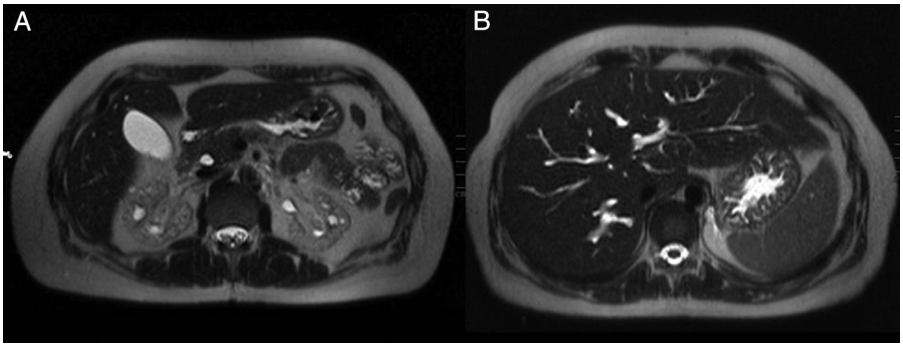

Fig. 2 – Magnetic resonance cholangiopancreatography: (A) Bilateral kidney cysts. (B) Caroli's disease in the liver.

nephropathies were also excluded: cystic medullary kidney disease, nephronophthisis, disease caused by a mutation in the *HNF1b* gene, tuberous sclerosis, Von Hippel-Lindau disease, as well as acquired cystic kidney disease: simple cysts, acquired cystic disease, or Cacchi-Ricci disease.

In our case, the tubular changes, hypomagnesaemia, natriuresis, and polyuria, with cramping symptoms were the guiding symptoms. Although associated electrolyte changes have been described,[6–8] this is the first case of ARPKD in the literature that started with symptomatic hypomagnesaemia. Moreover, other concomitant tubulopathies, such as Gitelman syndrome that could explain the findings of hyperreninism and hyperaldosteronism secondary to hypomagnesaemia, were ruled out by the genetic testing. In our patient, these could be due to the increased urinary excretion of sodium, water, and magnesium due to disfunctioning tubular cells.

There is a progressive deterioration of kidney function and more than half of the patients need renal replacement therapy before the age of 20 years.[1,9] Hypertension is a factor of poor prognosis, it starts during the first months of life and improves with age.[2,7] The patient did not present with a history of hypertension and during admission she had low blood pressure, probably due to her salt-wasting nephropathy, which could have favoured the benign progression of this case.

In conclusion, ARPKD is a disease of the childhood, but it should not forgotten that it can start in adults with more moderate clinical manifestations. This disease should be suspected in adults with end-stage chronic kidney disease, radiological findings that are compatible with the diagnosis (millimetre medullary kidney cysts, dilation of the intrahepatic bile ducts), and associated symptomatic electrolyte disorder.

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A rare cause of diarrhea in patients with focal segmental glomerulosclerosis

Una causa poco frecuente de diarrea en pacientes con glomeruloesclerosis focal y segmentaria

Dear Editor,

Focal segmental glomerulosclerosis (FSGS) symbolizes a common histologic pattern of glomerular injury associated with numerous disease mechanisms. Ulcerative colitis (UC) represents one of the types of inflammatory bowel disease, which occurs in genetically predisposed individuals. The coexistence of these two diseases is an unexpected condition. Lately, case reports have been published documenting the development of nephropathy after treatment of ulcerative colitis with mesalamine or sulphasalazine. In cases in the literature, this coexistence has been identified as associated with 5-ASA therapy.[1–5] In this case, we report the ulcerative colitis occurring in a patient with focal segmental glomerulosclerosis not affiliated with 5-ASA therapy.

A 66-year-old man, with a 3-year history of focal segmental glomerulosclerosis, was admitted with bloody and mucoid diarrhea which had been for lasting for 10 days. There was no fever, nausea, vomiting or infection. There was no feature in the patient's history except diarrhea. Physical examination also was normal. Laboratory investigation demonstrated impaired renal function and proteinuria due to focal segmental glomerulosclerosis. Renal function test which is similar to the old values showed serum creatinine level of 3.15 mg/dl (0.8–1.3), BUN level of 89 mg/dl (17–43) and 24-h urine protein level of 1876 mg/day (<200). In addition, his erythrocyte sedimentation rate (ESR) was 79 mm/h (<20) and C-reactive protein (CRP) was 6.66 mg/dl (<0.4). A large amount of leukocytes and erythrocytes was seen in the stool microscopy. Stool cultures were detected negative twice. Colonoscopy revealed that there were to exudates of millimetric ulcers descending colon, sigmoid colon and rectum. The colon biopsy confirmed the diagnosis of ulcerative colitis.

The patient was started on mesalamine. His symptoms showed marked improvements after starting mesalamine treatment. After treatment, laboratory investigation demonstrated; creatinine level of 3.7 mg/dl (0.8–1.3), BUN level of 116 mg/dl (17–43), ESR level of 38 mm/h (<20), CRP level of 0.319 mg/dl (<0.4), and 24-h urine protein level of 2099 mg/day (<200). There were no abnormalities suggestive of nephrotoxicity in patients due to mesalamine, while acute phase reactants declined. The decline in ESR and CRP levels is thought to be in favor of improving ulcerative colitis activation.

A focal segmental glomerulosclerosis after ulcerative colitis treatment with mesalamine and sulfasalazine has been reported in the literature.[1] Additionally in the literature, there have been several minimal changes in the disease following the treatment of inflammatory bowel disease with mesalamine or sulfasalazine.[2–6] A case report has been published of nephrotic syndrome due to Crohn's disease with mesalamine treatment.[7]

In this case, we discuss about the developed ulcerative colitis in a patient who was followed for focal segmental glomerulosclerosis. Unlike previously reported cases, mesalamine and sulfasalazine have no effect on the togetherness of the two diseases. Although primary and secondary FSGS forms are defined based on the underlying cause, the podocyte damage is a common result eventually. Some genetic factors affect the inflammation which is the main cause of development of the ulcerative colitis. An unknown cause such as genetic, environmental or infections except drugs may be factors in the etiology of these two diseases. Furthermore, an unknown cause can facilitate the development of nephrotoxicity after mesalamine and/or sulfasalazine treatment. In our case, the patient's renal function did not change significantly after mesalamine treatment.