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Cystic fibrosis of pancreas and nephrotic syndrome: a rare association

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Cystic fibrosis (CF) is a genetic disease with autosomal recessive inheritance and is common in Caucasian people. The prevalence of this disease is between 1/2,000 and 1/3,500 live births, and the incidence varies between populations. Although the CF transmembrane conductance regulator gene is expressed in the kidneys, renal involvement is rare. With advances in the treatment of CF, life expectancy has increased, and some previously unobserved disease associations are now seen in patients with CF. It is important to follow patients with CF for possible abnormalities that may accompany CF. In this paper, we present two rare cases of CF accompanied by nephrotic syndrome.

Key words: Cystic fibrosis, Nephrotic syndrome, Child

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Introduction

Cystic fibrosis (CF) is a recessively inherited genetic disease that decreases quality of life and is more commonly seen in Caucasian people. CF occurs due to defective epithelial cell chloride channels caused by mutations in the CF transmembrane conductance regulator (*CFTR*) gene[1]. Nephrotic syndrome (NS) is more common in children than adults. NS is a clinical syndrome characterized by massive proteinuria and hypoalbuminemia due to increased permeability of the glomerular capillary membrane.

Because several systems are involved in CF, clinical symptoms show a heterogeneous distribution[2]. The gastrointestinal system, reproductive system, and sweat glands are affected in patients with CF, and CF also causes progressive lung disease, which is still the most important cause of morbidity and mortality[3]. Early diagnosis and appropriate treatment are very effective in reducing long-term morbidity from CF.

The lungs are generally affected by CF, while pancreatic involvement is seen in 85–90% of cases[4,5]. The *CFTR* gene is usually expressed in the kidneys; however, renal involvement is not very common in patients with CF[6]. Patients that experience urinary system involvement most commonly have nephrolithiasis and cough related mechanical urological problems[7,8]. Urolithiasis in CF may result from enteric hyperoxaluria caused by fat malabsorption and the lack of intestinal oxalate degrading bacteria as *Oxalobacter formigenes*. Additional renal manifestations occasionally reported in children and teenagers include amiloid protein A (AA) type amyloidosis, membranoproliferative glomerulonephritis, and postinfectious glomerulonephritis[9-11]. The number of CF-NS associated cases is limited in the literature[10,12]. In this report, we present two rare cases of both NS and CF in children.

Case reports

Case 1

A nine-year-old male patient diagnosed with CF, lung disease, and pancreatic insufficiency had been monitored for three years. A gradual increase in the ratio of decline in the urine and complaints of swelling of the face and both ankles had begun two years previous. Physical examination revealed the following: temperature, 36.8℃; pulse, 92/min; blood pressure, 109/71 mmHg (95th percentile); edemas in both lower extremities and the sacral region; and more prominent edemas around the face. Other system examinations were normal. Liver function tests, viral hepatitis panel results, alpha-1 antitrypsin levels, and abdominal ultrasonography were normal but sweat test was 98 mmol/L (chloride concentration).

At that time he was detected hypoalbuminemia and proteinuria on a random urine sample. Complement factors 3 and 4 were normal, antinuclear antibody was negative, serum urea was 11 mg/dL, triglyceride was 175 mg/dL, total cholesterol was 230 mg/dL, creatinine was 0.6 mg/dL, and albumin was 0.5 g/dL in diagnosis time and 24-hour urine collection revealed nephrotic range proteinuria (>960 mg/m^2/day).

The patient began steroid therapy following NS diagnosis. At follow-up, the patient was found to have steroid-resistant NS, and a renal biopsy was performed under light microscopy and immunofluorescence microscopy. The renal biopsy showed mesangial proliferation without AA. Partial remission was achieved using low-dose steroids (15 mg/day prednisolone, for a period 1 year) and cyclosporine A therapy (3 mg/kg/day; for a period 4 months). Serum albumin and total protein levels in serum were 3.2 g/dL, 5.5 g/dL after treatment, respectively. Renal biopsy was the second time in the last 6 months. Serum Amyloid A protein was negative. At the moment, our patient has treated with 0.5 mg/kg/every other day prednisone and his proteinuria (30 g/day) has continued. The patient is still in partial remission.

The patient's radiological imaging showed destruction around the peripheral airways, and bronchiectasis was detected. Pulmonary function tests provided the following values: forced expiratory volume in 1 second (FEV_1) 78% and forced vital capacity (FVC) 85%; FEV_1/FVC values were low. The patient was treated with recombinant human DNase, followed by treatment with inhaled bronchodilators and pulmonary rehabilitation.

Case 2

A two-year-old male patient was referred to Dicle University Department of Pediatric Pulmonology Unit. In history, he had diagnosed as CF due to chronic diarrhea, while he was two months of age. During follow-up, no pulmonary involvement was observed; however, eight months prior to this study a decrease in urine volume was detected, as well as, edemas in the patient's face and bilateral lower extremities.

The patient's medical history included an upper respiratory tract infection two weeks prior. Physical examination revealed the following: temperature, 36.8℃; pulse, 84/min; blood pressure, 94/50 mmHg (50th percentile); and edemas in the patient's face and bilateral lower extremities. Other system examinations were normal.

Laboratory examinations results revealed the following in diagnosis time; sweat test was repeated 122 mmol/L, liver function tests and complement factors 3 and 4 were normal, antinuclear antibody was negative, albumin was 0.6 mg/dL, total cholesterol was 220 mg/dL, urea was 16 mg/dL, and creatinine was 0.4 mg/dL. Twenty-four-hour urine collection was found nephrotic proteinuria (>960 mg/m^2/day) and the patient was diagnosed with NS and started oral corticosteroids 2 mg/kg/day, 6-week therapy and achieved remission. The patient was regarded as minimal change disease. The patient is still in remission and being followed for NS.

Discussion

Early diagnosis, intensive antibiotic therapy and developments in supportive treatment have extended the life expectancy for CF patients by reducing mortality and morbidity. Due to the increase in patient lifespans, previously unobserved disease associations have been detected. Renal involvement in CF patients is rare, but recently, renal pathologies such as glomerulosclerosis, mesangial proliferation, nephrocalcinosis and microscopic hematuria, tubular damage, fibrillary glomerulonephritis[13], and amyloidosis[9] have been reported.

The first case in this report was monitored for three years. The patient's biopsy revealed mesangial proliferation. The patient was diagnosed with steroid-resistant NS, and cyclosporine treatment was initiated in addition to prednisolone treatment. As a result of treatment, the patient is in partial remission. The second patient was diagnosed with NS when he was 1.5 years old, and since he did not have hematuria-hypertension. Systemic amyloidosis with renal involvement has been reported in some patients with CF[14]. Secondary amyloidosis is in fact a complication of chronic inflammatory processes such as tuberculosis and bronchiectasis, and it is conceivable that this condition may develop in patients with CF which is characterised by chronic and recurrent respiratory infections[10]. Renal amyloidosis is a cause of NS. The prognosis of patients with CF and AA amyloidosis is generally poor, with nearly all patients dying within 1 year of clinical presentation[15]. In second patient; there was no need for a renal biopsy because of responded to steroid therapy and renal functions returned to normal.

There is a widespread belief that kidneys are not affected by CF. NS may be randomly associated with CF, or it may be a complication of CF. CF patients may develop kidney disease due to nephrotoxic agent exposure, immune complexes circulating in the serum due to recurrent pulmonary infections, or nephrotoxic antibiotics, such as aminoglycosides. Regular patient follow-up will allow full systemic evaluation and early diagnosis of accompanying complications, especially renal disorders. CF patients must undergo urine tests and evaluations for possible renal disorders, including proteinuria.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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