Renal amyloidosis in cystic fibrosis: role of colchicine therapy

Cystic fibrosis (CF) is the most common autosomal-recessive condition affecting the white population, with an incidence ranging between 1:2500 and 1:1800 births. It is caused by a mutation in the CFTR gene, encoding the polyprotein CF transmembrane conductance regulator (CFTR), which functions as an ATP-responsive chloride channel in the apical membrane of epithelial cells. Pathologic changes related to CFTR mutations mostly affect secretory cells, resulting in low secretion volume and increased viscosity and promoting mucosal obstruction in the lung, pancreas, biliary tract, sinuses and reproductive tract [1].

Patients with CF currently show a continuing improvement in their life expectancy, an improvement that allows for better multidisciplinary monitoring and earlier therapeutic interventions. Owing to their longer life expectancy, an improvement that allows for better multidisciplinary monitoring and earlier therapeutic interventions. Owing to their longer life expectancy, CF patients present complications that were not recorded before [2]. This is illustrated by the following report of two cases of renal AA amyloidosis in women with CF.

Case 1

In the first patient, CF was diagnosed at the age of 2 years (genotype ΔF 508/ΔF 508) with pulmonary symptoms and failure to thrive. She has a history of a chronically impaired digestion and of infections of the respiratory tract, infections treated with high-dose intravenous antibiotics. Diabetes mellitus (DM) was diagnosed at the age of 28 years. When she was 41 years old, she developed oedema and nephrotic syndrome. Laboratory data revealed proteinuria 8 g/day and glomerular filtration rate 74 mL/min. Kidney biopsy disclosed SAA amyloidosis. She was commenced on oral colchicine, 1 mg/day progressively increased to 2 mg/day. After 1 year of this treatment, proteinuria is 3 g/day and renal function is slightly improved, with a creatinine clearance of 83 mL/min. A moderate reduction in SAA protein concentration (from 325 to 229 mg/L) was observed.

Case 2

In the second patient, CF was diagnosed at the age of 21 years (genotype ΔF 508/N) owing to her family history. Pulmonary infections required intravenous antibiotics every 3 months. DM was diagnosed at the age of 38 years. At the age of 41 years, she developed proteinuria of 1.4 g/day with decreased renal function (glomerular filtration rate 50 mL/min). Light microscopy (Figure 1) and immunohistochemistry revealed renal amyloidosis of the SAA type. Oral colchicine was commenced at 1 mg/day. After 1 year, the disease stopped progressing. Creatinine clearance was 56.6 mL/min and proteinuria was 2 g/day. SAA protein decreased from 1250 to 110 mg/L.

Discussion

Inflammation-associated systemic amyloidosis (AA) is a known complication of chronic infection and of inflammatory and neoplastic diseases. AA is due to an imbalance between the production and the degradation of serum amyloid A protein (SAA), leading to its accumulation and deposition in various organs [3]. Amyloidosis is a surprisingly rare complication of CF, given the chronic inflammatory nature of the condition and the fact that all patients eventually develop marked bronchiectasis. Whilst it has been suggested that undetected cases may explain the apparent rarity of the association, this has not been verified by retrospective pathological studies. It is probable that in the past, the short life expectancy of patients with CF did not allow enough time for the development of amyloidosis. The median life expectancy of children born with CF has now improved considerably. With this longer survival the pattern of complications will predictably change. Amyloidosis complicating CF is likely to be seen with increasing frequency [4].

In any event, renal amyloidosis should be suspected in patients with CF and proteinuria and must be investigated by kidney biopsy.

Colchicine therapy, which is the standard of care in familial Mediterranean fever complicated by secondary (AA) amyloidosis, seems to be also effective in CF-induced amyloid disease.

There are only two cases reported in the literature, cases in which colchicine was used to treat renal amyloidosis in patients with CF [5]. In one, manifestations of nephrotic syndrome were prevented without any evidence of renal insufficiency (time of follow-up was not specified). In the second patient, colchicine delayed for 18 months the apparent onset of renal insufficiency.
Our data confirm this scarce literature and make a point of commencing colchicine treatment without delay when a diagnosis of renal AA amyloidosis is made in a patient with CF.

Conflict of interest statement. None to declare.

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References
1. Yahiaoui Y, Jablonski M, Hubert D et al. Renal involvement in cystic fibrosis: diseases spectrum and clinical relevance. Clin J Am Soc Nephrol 2009; 4: 921–928.
2. Montagnac R, Sanlaville F, Soto B et al. Renal disease in cystic fibrosis. Néphrol Thér 2009; 5: 550–558.
3. Mc Laughlin AM, Crotty TB, Egan JJ et al. Amyloidosis in cystic fibrosis: a case series. J Cyst Fibros 2006; 5: 59–61.
4. Gaffney K, Gibbons D, Keogh B et al. Amyloidosis complicating cystic fibrosis. Thorax 1993; 48: 949–950
5. Kuwertz-Bröking E, Koch HG, Schulze Everding A et al. Colchicine for secondary nephropathic amyloidosis in cystic fibrosis. Lancet 1995; 345: 1178–1179.

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