A case of Marfans syndrome with aminoaciduria

Sir,

Marfans syndrome is an autosomal dominant disease with a prevalence of 2-3 in 10,000 live births.[1] There have been very few reports of renal involvement in Marfans syndrome.[2,3] We report here a rare instance of aminoaciduria and phosphaturia associated with Marfans syndrome, a forme fruste of Fanconi syndrome.

A 30-year-old female was referred to our hospital with chest pain. On examination, she had marfanoid habitus. Chest roentgenogram revealed an enlarged mediastinum.

Computerized tomography scans revealed dissection of aorta Type B (Stanford Classification) without renal artery involvement.

Echocardiogram done revealed LV dysfunction. Aortic root was dilated to 45mm. There was mitral and aortic regurgitation. Serology for antinuclear antibody, anti-cardiolipin antibody and lupus anticoagulant was negative and serum creatinine was normal.

Examination revealed trauma-induced phthisis bulbi of the right eye and recurrent retinal detachment (rhegmatogenous) of the left eye with aphakia. There was also evidence of coarse chorioretinal atrophy on fundus examination of left eye suggestive of myopic disease. There was no positive family history or evidence of dural ectasia on MRI examination of the spines. Based on these, a diagnosis of Marfans syndrome was made in our patient.[4] Our patient satisfied the diagnosis of Marfans syndrome proposed by Rimoin *et al* in the absence of a positive family history by the presence of two major criteria (aortic dissection and aortic root dilatation) and the presence of more than two minor criteria (myopia, retinal detachment, mitral valve prolapse, skeletal deformities).[5]

Urine was negative for homocysteine. Screening for other inborn errors of amino acid metabolism like cystinuria, dibasic aminoaciduria and Hartnup disease was negative. Urine ninhydrin test for amino acids was positive and quantitative urine amino acid analysis revealed generalized aminoaciduria of the physiological type. Urine for glucose was negative. The 24h urine collection revealed proteinuria of 800 mg/24h (Normal < 150 mg/24h) and phosphaturia of 1100 mg/24h (Normal 10-15 mg/kg/24h). All other solutes in the urine like uric acid, glucose, calcium, sodium and potassium were normal. There was no past history of exogenous intoxications with metals, organic compounds or drugs to suggest the cause of proximal tubular dysfunction. Her serum calcium, magnesium, phosphate and arterial blood gas analysis was normal. X-ray was normal with no osteopenia.

Renal involvement in Marfans syndrome is distinctly rare.[2,3] There have been reports of reno-vascular hypertension and glomerular involvement. We report here a case with aminoaciduria and phosphaturia, a forme fruste of Fanconi syndrome. The patient was investigated for other evidence of Fanconi syndrome, which was found to be negative. The workup for other causes of aortic root dilatation like Ehlers-Danlos syndrome Type 4 (EDS) and familial aortic aneurysms was not done in view of the patient satisfying the criteria for Marfans syndrome convincingly, with no other suggestive features of these syndromes and also that EDS Type 4 only occasionally causes aortic dissection.

Fanconi syndrome is characterized by aminoaciduria, glucosuria and phosphaturia as cardinal features, while acidosis, hypouricemia, hypercalciuria, hypokalemia, polyuria and proteinuria are also commonly associated features.[6] In addition there are incomplete forms of Fanconi syndrome in which at least one of the cardinal features are missing.

The cause of aminoaciduria in Marfans syndrome as a forme fruste of Fanconi syndrome is very difficult to speculate. Probably, if the renal artery was involved in dissection, that could explain the findings as due to ischemia. But the renal artery was not involved in our case to explain the association. Probably, mutations in the fibrillin gene in Marfans syndrome produce defective binding regions in the epidermal growth factor-like domains, which could cause defective arrangement of transporters in the renal tubule cells. Probably, the proximal tubular cells perform the bulk of reabsorption of the glomerular filtrate, while the distal cells have less of these functions and so are not evident in an overt manner.

This is a new observation. There have been a few sporadic reports in some older papers,[7,8] but the real diagnosis of Marfans syndrome in these cases are in doubt. The clinical significance of this observation requires long-term follow-up and experimental studies.

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