D-penicillamine induced membranous glomerulonephritis in a child with Wilson's disease

Dear Editor,

Wilson's disease (WD) is a rare autosomal recessive disorder of copper homeostasis with a prevalence of 30 affected individuals per million population. Treatment is based on oral chelating agents such as D-penicillamine. Despite its effectiveness, D- penicillamine presents significant adverse effects. Among them is proteinuria and nephrotic syndrome[1].

An 11 year- old boy was admitted with persistent transaminasaemia. According to his medical history, physical examination, laboratory and histological findings of the liver biopsy and genetic evaluation he was diagnosed to have WD. Treatment with D-penicillamine was started initially on the dose of 250 mg twice daily and forty days later of 500 mg in the morning and 250 mg in the evening. Fourteen months later, a routine urinalysis revealed proteinuria without haematuria. Proteinuria was measured at 2.1 gr/24h, with blood total protein 5.4g/dl, albumin 3.0g/dl and normal renal function. Immune investigation revealed normal findings. A percutaneous renal biopsy was performed and displayed findings consistent with membranous glomerulonephritis. The daily dose was gradually reduced until its total cessation and treatment with trientine was initiated. Upon tapering of D-penicillamine, proteinuria was reduced and disappeared when the child was still on 250 mg. A year later, the child is free of proteinuria with normal renal function.

D-penicillamine is a sulfur containing aminoacid that chelates copper and promotes its urinary excretion. Among its adverse effects are proteinuria and nephrotic syndrome[1,2]. It has been supported that proteinuria can occur at any time, from six weeks to five years after D-penicillamine initiation, with a median time of seven months. The meantime from the first occurrence of proteinuria to nephrotic level proteinuria range from few weeks to several years. A percentage of 60%-70% of the patients who present proteinuria may develop nephrotic syndrome if the treatment is continued[3]. After stopping D-penicillamine, proteinuria may gradually decrease, however 40% of the patients continue having proteinuria with no evidence of progressive renal disease[3].

Moreover there have been reported few cases of anti-myeloperoxidase, anti-neutrophil cytoplasmic antibody(ANCA)-positive rapidly progressive glomerulonephritis developed during D-penicillamine treatment in patients with rheumatoid arthritis or systemic sclerosis[4,5]. However in both diseases, ANCA-associated glomerulonephritis has been described even in the absence of the D-penicillamine. In a recent case report ANCA- associated glomerulonephritis was described in a patient treated with D-penicillamine for WD[5].

We would like to emphasize the importance of routine renal evaluation of patients with WD on D-penicillamine therapy. In case of renal involvement cessation of D-penicillamine therapy and substitution by trientine is strongly recommended.

References

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Key words: Wilson's disease, D-penicillamine, child, proteinuria

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