Nephropathy associated with Charcot-Marie-Tooth disease: Importance of Genetic Testing.

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Introduction: When both polyneuropathy and nephropathy are diagnosed in young individuals, targeted genetic testing for rare syndromes should be pursued. Mutations in the INF2 gene are the leading cause of autosomal dominant focal segmental glomerulosclerosis (FSGS) [1]. These mutations are associated with Charcot-Marie-Tooth disease (CMT). Only a handful of cases have been reported where CMT disease is linked to kidney damage of different origins (such as membranous nephropathy) caused by other mutations (like MPZ gene)[2]. Autosomal dominant intermediate Charcot-Marie-Tooth disease (CMT) type E is extremely rare, with a prevalence of less than 1 in 1,000,000.

Case presentation: A 40-year-old woman was diagnosed with stage 3b chronic kidney disease, non-nephrotic range proteinuria, general ailments and polyneuropathy. Due to reduced kidney size, a renal biopsy was not possible. Given the extensive family history of kidney disease (father, brother, sister) genetic testing was conducted. A pathogenic heterozygous variant of the INF2 gene, associated with autosomal dominant glomerulosclerosis and autosomal dominant CMT disease, was identified. Additional neurological examination confirmed the diagnosis.

Discussion: INF2 gene mutation and nephropathy usually present clinically as nephrotic syndrome, because this is the most common clinical manifestation of FSGS [3,4], though atypical variants exist, as in our case. Literature reports several cases of sensorimotor neuropathy and proteinuric illness, with histopathology showing minimal change disease as well [2]. Without a kidney biopsy, genetic testing is crucial for identifying the disease, especially with a family history of kidney issues.

Conclusions: Genetic screening in case of family anamnesis or finding of rare forms of glomerulopathies is important, because in the case of inheritance, treatment with immunosuppressants is not applied [2]. INF2 gene mutation screening should be applied to all those with steroid-resistant nephrotic syndrome or renal failure of unknown etiology at a young age.

References:

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