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LETTER TO EDITOR

Role of 2 putative genes in familial collagenofibrotic glomerulopathy

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Dear Editor,

In 2020, we published an article titled "Collagenofibrotic glomerulopathy-report of a rare renal disease with serial biopsies" in your journal.[1] It was subsequently made known to us that the patient in the previous report (A) has several siblings with chronic renal disease. One of her younger sisters (patient B) came for a renal biopsy which showed similar features. A diagnosis of collagenofibrotic glomerulopathy (CG) or type III collagen glomerulopathy was made for patient B, and familial or inherited disease was suspected. As such, whole exome sequencing was performed for patients A and B.

A heterozygous mutation of the complement factor H (*CFH*) gene (c.3446G>A, p.Arg1149Gln)) was detected in both patients. This mutation was interpreted as a variant of unknown significance by the reporting laboratory. In addition, patient A had a homozygous mutation in *NUP205* (c.1822A>T, p.Ile608Phe), while patient B manifested an identical heterozygous mutation of this gene; this was also classified as a variant of unknown significance. There is a single case report of a different homozygous mutation in the *NUP205* gene that is associated with steroid-resistant focal segmental glomerulosclerosis.[2]

The genetic results of our patients suggest that further attention should be given to the roles of *CFH* and *NUP205* in the pathogenesis of familial CG. Cases of CG described in the literature are mostly sporadic, with rare occurrences of familial cases in children[3] and adults.[4,5] Vogt *et al*. proposed a link between CFH deficiency (paediatric atypical haemolytic uraemic syndrome) and collagenofibrotic glomerulopathy.[6] Factor H is a protein that inactivates C3 in the alternative complement pathway. Deficiency of factor H leads to chronic uncontrolled activation of the alternative complement pathway but a direct link between factor H deficiency and type III collagen glomerulopathy has not been established. Following the publication of Vogt *et al*., we are unaware of a second case with this mutation in patients diagnosed with CG. It is also unclear if factor H deficiency is inherited in an autosomal dominant or recessive fashion.[6] With several siblings affected and given that our 2 patients both have heterozygous mutations, it seems likely we are dealing with an autosomal dominant mode of inheritance.

In summary, there is a paucity of data on the genetic basis of familial type III collagen glomerulopathy. This correspondence serves to highlight the putative role of 2 genes.

Keywords: collagenofibrotic, collagen type-III, glomerulopathy, familial, hereditary, genetic, genes

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