Nephronophthisis Is an Important Differential Diagnosis of Nonspecific Interstitial Nephritis in Adults

To the Editor: We read with great interest the case report by Choi *et al.*[1] of a patient with nonspecific interstitial nephritis (IN) in whom a diagnosis of NPHP3 was made 30 years later. We emphasize the importance of including nephronophthisis in the differential diagnosis of IN in adults, even in the absence of polyuria.

We report 2 nonconsanguineous families with chronic IN and a late diagnosis of nephronophthisis. In the first family, the youngest brother was diagnosed fortuitously at age 21 years with chronic kidney disease associated with low-grade proteinuria (1 g/d). Kidney biopsy result revealed nonspecific IN with extended fibrosis. He reached kidney failure at age 27 years. His 31-year-old brother was investigated as a potential kidney donor. This checkup revealed chronic kidney disease (estimated glomerular filtration rate 50 ml/min per 1.73 m^2) with mild proteinuria (250 mg/d). In both brothers, genetic testing results showed a recurrent compound heterozygosity in *NPHP1* gene NM_001128178.3(NPHP1):c.[1027G>A];[(?_-94)-(*455_?)], p.[Gly343Arg];[p.0].[2]

In the second family, the youngest brother was kidney transplanted at age 36 years with a history of polyuria from childhood and mildly proteinuric chronic kidney disease. His elder brother started dialysis at age 57 years with a presumed diagnosis of lithium-induced chronic IN. Genetic testing results revealed a novel double heterozygosity in the *NPHP4* gene NM_015102.3(NPHP4):.1354G>T(;)(452+1_453-1)_(517+1_518-1)del, p.(Glu452*)(;)(p.?) in both brothers. Interestingly, no extrarenal features or kidney cysts were present in any of the patients.

Nephronophthisis is an autosomal recessive disease and the most prevalent genetic cause of pediatric kidney failure. Homozygous *NPHP1* deletions are reported as the cause of kidney failure in 0.5% of adults.[2,3] Our cases highlight the importance of including nephronophthisis (associated with mutations in >20 different genes) in the differential diagnosis of IN in adults, even in the absence of extrarenal manifestations. In both our families, the propositus initially had no family history of kidney disease. Importantly, genetic testing should cover all relevant genes, as shown by the case of Choi *et al.*[1] and our 4 cases.

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Response to "Nephronophthisis Is an Important Differential Diagnosis of Nonspecific Interstitial Nephritis in Adults"

The Authors Reply: We thank Gillion *et al.*[1] for their interesting contribution in response to our article[2] that