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Atypical Immune Dysregulation, Polyendocrinopathy, Enteropathy X-Linked (IPEX) Syndrome - Should We Consider Kidney Involvement As A Major Hallmark? A Clinical Case Presentation

George-Claudiu Costea[1], Rosa Bacchetta[3], Mihaela Gherghiceanu[2], Anca Elena Marin[1], Ovidiu Limoncu[1], Cristina Stoica[1]
[1]Department of Pediatrics-Nephrology, Fundeni Clinical Institute, Romania
[2]Department of Department of Ultrastructural Pathology, Victor Babes National Institute of Pathology, Romania
[3]Department of Division of Pediatric Hematology and Oncology, Stem Cell Transplantation and Regenerative Medicine, Center for Definitive and Curative Medicine Stanford, United States

Case Study : Secondary to FOXP3 mutations, IPEX syndrome is a heterogeneous entity with a wide range of symptoms- from dermatitis, diarrhea and endocrine abnormalities (that comprise the so-called typical form) to lesions in virtually every organ, without the classical triad, a situation generally known as the atypical form of the disease. From the few published cases in the literature, one can argue that renal involvement is not so common, the main pattern of injury being membranous nephropathy, though glomerulosclerosis was also reported. We hereby present the case of a 12 years-old male patient, born from a non-consanguineous family. He was diagnosed at 19 months of age with nephrotic syndrome, unresponsive to steroid therapy. Cyclosporine (CsA) was started, with gradual remission of the disease, but with minimal reminiscent proteinuria. After 5 years, CsA was discontinued, the patient developing progressive sub-nephrotic range proteinuria with minimal microscopic hematuria. A WES analysis revealed a hemizygous FOXP3 likely pathogenic variant (c.454+4A>G), along with a heterozygous COL4A4 VUS (c.5045G>A, p.Arg1682Gln), considered unlikely to induce a severe AD-Alport syndrome. A renal biopsy was performed, illustrating a membranous pattern of injury with moderate to severe tubular atrophy and interstitial fibrosis. The electron microscopy showed variations of the GBM's thickness in some areas, along with subepithelial dense deposits and podocyte lesions. We concluded that, in our case, the severe lesions observed are secondary to the autoimmune dysregulation that defines IPEX syndrome. It's our opinion that the COL4A4 variant would explain the variations in the GBM thickness but would not induce neither a membranous pattern of injury, nor the severe interstitial compartment lesions. As a few other cases, but increasing in number, reported worldwide, our case illustrates that one should consider IPEX nephropathy as a cause of early onset pediatric membranous glomerulonephritis, even in the absence of the classical IPEX triad.

Renal biopsy.jpeg