Thin Glomerular Basement Membrane in a Kidney Transplant of an Alport's Syndrome Patient: A Case Report

S. Santos[a,d,*], S. Marques[b,d], T. Golper[c], A. Langone[c], and A.B. Fogo[c,d]

[a]Department of Nephrology, Centro Hospitalar do Porto, Porto, Portugal; [b]Department of Nephrology, Hospital São João, Porto, Portugal; [c]Department of Medicine, Division of Nephrology, Vanderbilt University Medical Center, Nashville, Tennessee, USA; and [d]Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

ABSTRACT

Alport syndrome (AS) and thin basement membrane lesions are caused by various mutations in type IV collagen genes. Although AS is considered a rare disease, thin basement membrane is a frequent pattern, especially in families with a history of persistent hematuria. We report a patient with a diagnosis of AS who developed end-stage kidney disease (ESKD) and received a kidney transplant from a living unrelated donor. The graft biopsy specimen surprisingly showed a pattern of thin basement membranes.

GLOMERULAR diseases after transplantation are generally divided into recurrences of the original disease that affected the recipient's native kidney and de novo diseases. This differentiation may be difficult, because less than one quarter of recipients have biopsies before transplantation. In addition, some patients labeled as having de novo disease have donor-origin lesions [1].

Alport syndrome (AS) and thin basement membrane lesions are caused by various mutations in type IV collagen genes, and are common causes of persistent familial hematuria. Mutations in the gene coding for the α5 chain of collagen IV cause X-linked AS, whereas mutations in genes for α3 and α4 chains cause autosomal-recessive (AR) and autosomal-dominant types of AS. The carrier state of ARAS frequently manifests as benign familial hematuria presenting morphologically with only thin basement membranes [2].

The prevalence of thin basement membrane lesion may be estimated from the frequencies of glomerular hematuria, and the prevalence of carrier state of ARAS. These approaches suggest that thin basement membrane lesion affects more than 1% (but <10%) of the population, making it the most common inherited renal lesion [3].

Transplants from living donors with thin basement membrane lesion, including carriers of X-linked AS, remain controversial because the risks remain unknown. Effects of this phenotype on allograft function are unclear [4]. In affected families with mutations in type IV collagen genes, kidney transplantation from living donors who are genetically unrelated represents the better choice for both patient and donor [5].

We report an original case of a patient that in the first biopsy had a dual diagnosis of AS and superimposed immune complex-mediated C3 dominant glomerulonephritis, developed end-stage kidney disease (ESKD), and underwent kidney transplantation from a living unrelated donor. The graft biopsy showed a surprising pathological diagnosis. To our knowledge a similar case has not been described before.

CASE REPORT

A 20-year-old Indian man presented to his primary care physician in July 2007 with history of leg swelling worsening over a month, with serum creatinine 2.7 mg/dL and hematuria and proteinuria measured by dipstick. He also had hypertension, was started on nifedipine 30 mg/d, and was referred to nephrology. At admission he reported foamy urine intermittently; he denied gross hematuria, dysuria, abdominal pain, nausea, vomiting, rash, arthralgia, myalgias, shortness of breath, or headaches. He also denied use of nonsteroidal anti-inflammatory drugs (NSAIDs), herbal supplements, or illicit drugs. There was a positive family history for kidney disease; one of two maternal uncles had received a kidney transplant. Physical examination revealed blood pressure of 164/102 mm Hg, and 1+ edema of bilateral lower extremities. Serum creatinine level was 3.52 mg/dL, blood urea nitrogen (BUN) was 29 mg/dL, hemoglobin was 11.6 mg/dL, and spot urine protein/creatinine ratio was 5.5 g/g, with 21–50 red blood cells (RBCs). Serological work-up included normal complement levels, negative hepatitis B and C serological test results, negative antinuclear antibodies, anti-

*Address correspondence to Sofia Santos, MD, Department of Nephrology, Centro Hospitalar do Porto, Largo Prof. Abel Salazar, Porto 4099-001, Portugal. E-mail: sofia.fersantos@gmail.com

0041-1345/17
https://doi.org/10.1016/j.transproceed.2017.07.006

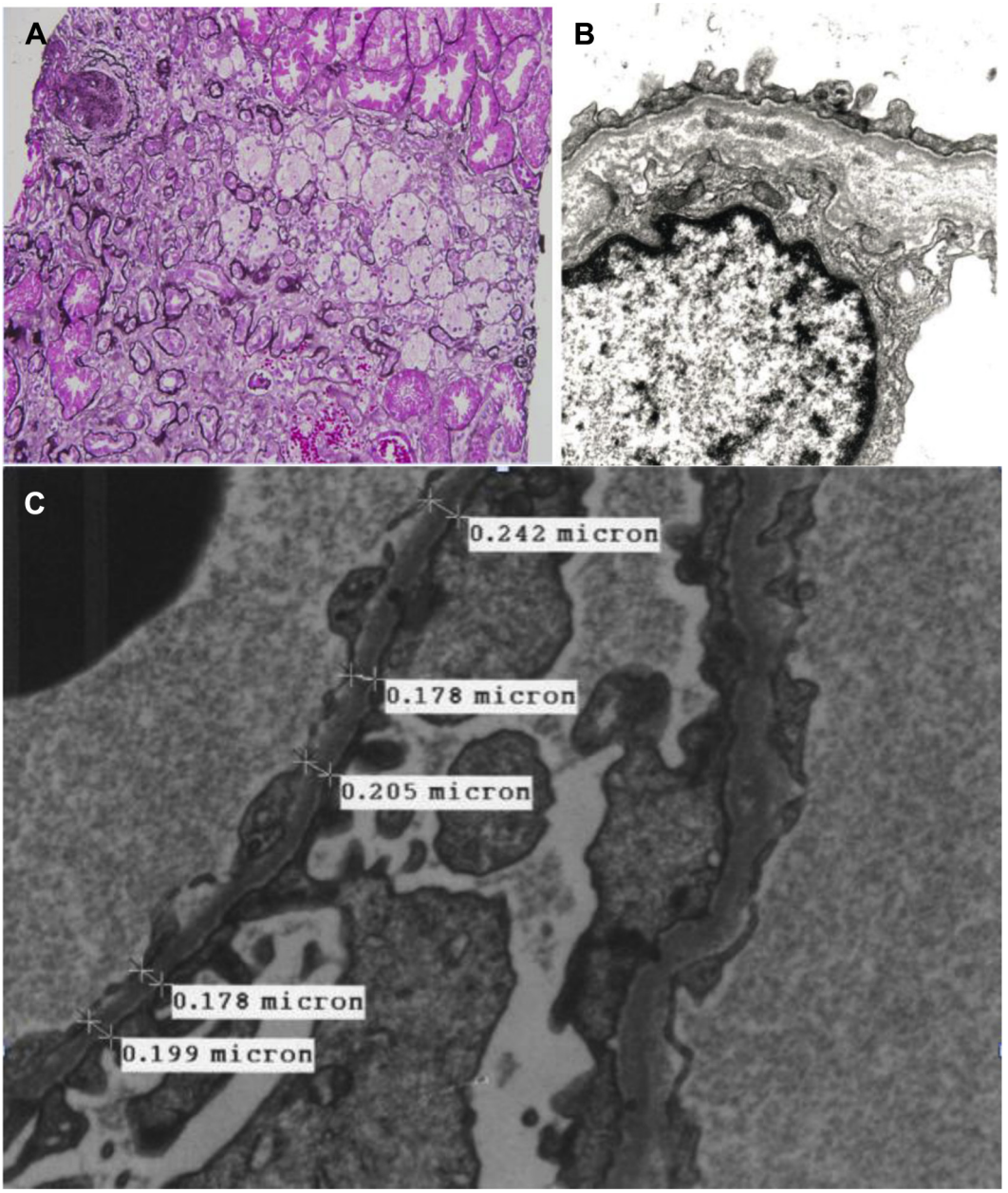

Fig 1. **(A)** The native kidney biopsy shows extensive tubulointerstitial fibrosis and globally sclerotic glomeruli, with numerous clusters of interstitial foam cells, characteristic but not pathognomonic of AS (periodic acid-Schiff stain; original magnification x200). **(B)** There was segmental thickening of the GBM with lucencies, basket-weaving, and lamellation in the native kidney, characteristic of AS (transmission electron microscopy; original magnification x13 000). **(C)** The transplant biopsy specimen shows thin areas of the GBM, with no lamellation or basket-weaving (transmission electron microscopy; original magnification x21 500).

neutrophil cytoplasmic antibodies (ANCA), and anti-glomerular basement membrane (anti-GBM) antibody. Renal ultrasound showed kidneys with normal size, diffusely bilaterally echogenic with no mass or hydronephrosis. A renal biopsy was performed; 16 glomeruli were present, 13 of which were globally sclerosed, 1 segmentally sclerosed, with mild increase in mesangial matrix and cellularity in nonsclerosed glomeruli. One glomerulus showed an early fibrocellular crescent but there was no fibrin, necrosis, or endocapillary hypercellularity of glomerular tufts. There was 80%–90% interstitial fibrosis with proportional tubular atrophy with a moderate interstitial lymphocytic infiltrate in scarred areas and numerous clusters of interstitial foam cells (Fig 1). There were occasional proteinaceous casts but no crystals or tubular necrosis. There were moderate hyalinosis of arterioles, moderate intimal fibrosis of interlobular arteries, and mild intimal fibrosis of large arteries. Immunofluorescence showed 3+ C3-dominant and