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ART IN THE WARD

A 39 year-old man with acroparesthesia and uncommon renal arterial lesions. What is the diagnosis?

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Case description

A 39 year-old man was referred to our nephrology department because of incidentally-discovered renal failure and proteinuria. Past medical history consisted of a long-lasting history of warm temperature-triggered burning pain in the extremities, diagnosed as erythromelalgia, for which pain management required an intrathecal catheter. His older brother had congenital hearing loss, and his mother had a stroke at the age of 62. Upon admission, results of the physical examination were unremarkable except for the presence of bilateral ankle edema. Laboratory investigations showed progressive renal failure with increased serum creatinine at 248 µmol/L versus 108 µmol/l two years prior to the current admission to the renal unit. Serum albumin was 3.5 g/dL, the urine albumin-to-creatinine ratio was 3.5 g/g and urinalysis did not show hematuria or leukocyturia. Renal ultrasound revealed two dedifferentiated 90-mm and 100-mm kidneys without hydronephrosis or renal cyst. Hemoglobin 1Ac and fasting glycemia were normal. Antinuclear antibodies, cryoglobulinemia, C3 and C4 complement levels were normal. Tests for human immunodeficiency, hepatitis B, and hepatitis C viruses were negative. Serum and urinary protein electrophoresis did not reveal monoclonal gammopathy. A kidney biopsy was performed for light microscopy and immunofluorescence (IF) analysis and revealed mainly fibrotic lesions with numerous glomeruli showing focal segmental glomerulosclerosis (Fig. 1) without obvious or specific lesions to guide a precise diagnosis. IF staining was negative on the glomeruli.

Case solution

However, after careful analysis of the kidney biopsy, renal interlobular arteries showed vacuolized endothelial cells and foamy media smooth muscle cells. More importantly, in the media the pathological smooth muscle cells were often replaced by beaded necrotic and hyalin deposits (Fig. 2). These histological lesions, together with a long-lasting history of acroparesthesia strongly suggested the diagnosis of Fabry disease, that was further confirmed by alpha-galactosidase A activity dosage at 1.4 nmol/h/mg (normal 104–236), and mutation of the Galactosidase Alpha (GLA) gene resulting in enzyme deficiency. In Fabry disease, renal biopsy often shows lacy lipid inclusions, commonly found in podocytes, distal tubules, interstitial fibroblasts and endothelial cells [1]. Renal arterial involvement is a relatively frequent but poorly recognized and likely underestimated lesion. The main known features involve an overloaded aspect of endothelial and smooth muscle cells with lacy lipid inclusions. However, hyaline deposits within the media are less well understood and often inaccurately described. Our case highlights the histopathologic challenges and diagnostic delays sometimes present in patients with Fabry disease, with respect to the often nonspecific clinical and laboratory symptoms [2]. Such arterial lesions involving kidney large-caliber arteries should prompt a search for Fabry disease, especially when renal biopsy shows mainly scarring and fibrotic lesions without suggestive glomerular changes. The diagnosis of these rare genetic nephropathies is crucial because it allows, on the one hand, to propose genetic screening and medical follow-up of the other family

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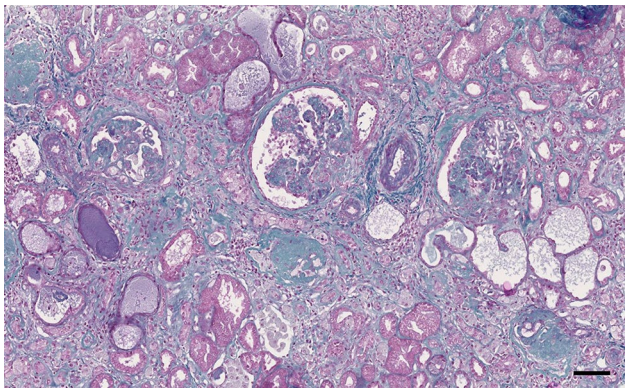

Fig. 1 Renal biopsy with Masson Trichrome staining showing mainly fibrotic lesions with numerous glomeruli showing focal segmental glomerulosclerosis (colour figure online)

members, and on the other hand, within the framework of Fabry disease, to allow access to a specific treatment by enzyme replacement therapy [3].

Declarations

Conflict of interest Authors have disclosed no conflicts of interest.

Ethical statement Reporting of this case was approved by the institution.The patient provided written informed consent.

References

1. Fogo AB, Bostad L, Svarstad E et al (2010) Scoring system for renal pathology in Fabry disease: report of the International Study Group of Fabry Nephropathy (ISGFN). Nephrol Dial Transplant 25(7):2168–2177

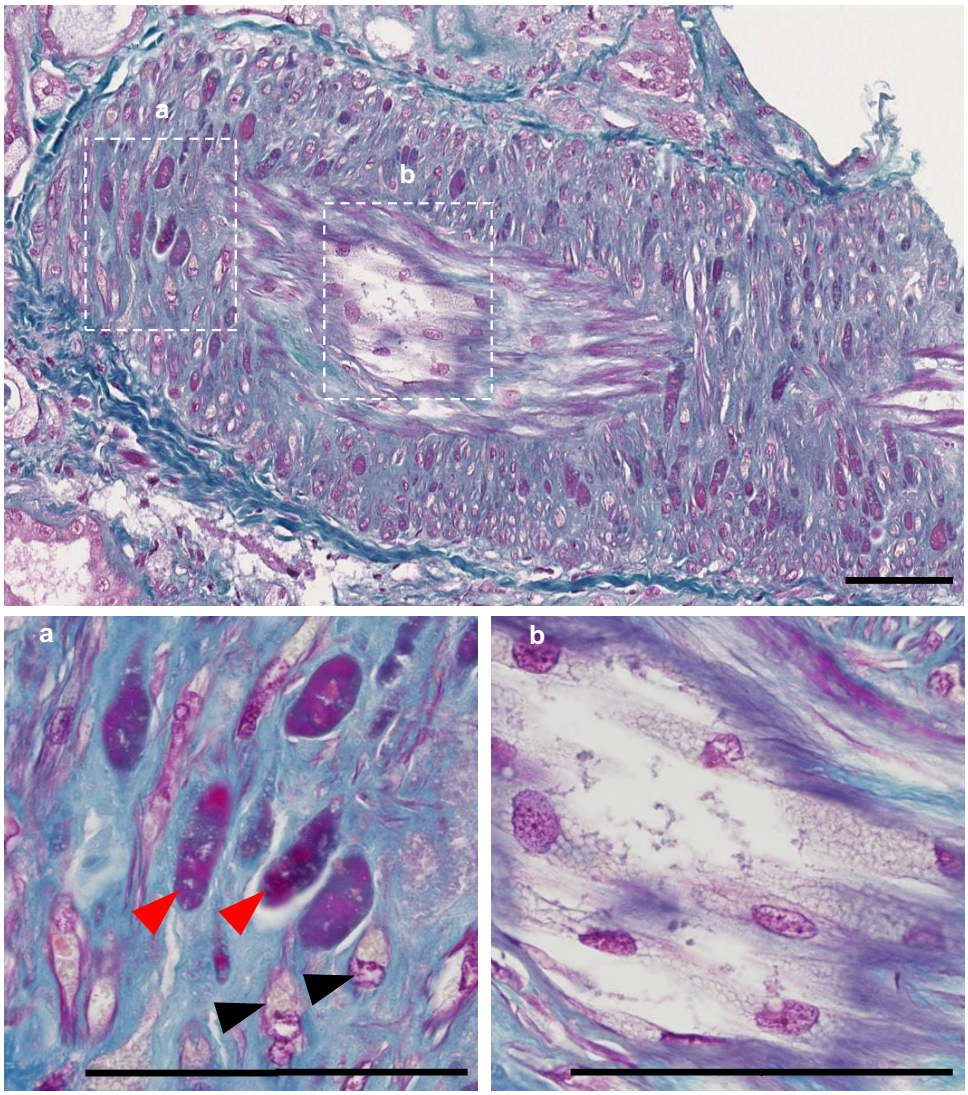

Fig. 2 Kidney biopsy with Masson Trichrome staining, showing a renal interlobular artery with vacuolized endothelial cells (1b) and foamy media smooth muscle cells (1a, black arrowhead). In the media, the pathological smooth muscle cells were often replaced by beaded necrotic and hyalin deposits (1a, red arrowhead). Scale bars 100 µm (colour figure online)

2. Lidove O, Kaminsky P, Hachulla E et al (2012) Fabry disease "The New Great Imposter": results of the French Observatoire in Internal Medicine Departments (FIMeD). Clin Genet 81(6):571–577
3. Schiffmann R, Hughes DA, Linthorst GE et al (2017) Screening, diagnosis, and management of patients with Fabry disease: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. Kidney Int 91(2):284–293