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LETTERS TO THE EDITOR

Rheumatoid arthritis and ANCA-associated vasculitis - an unusual overlap successfully treated with rituximab

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Dear Editor,

Rheumatoid arthritis (RA) is among the most common inflammatory arthritis[1]. Despite a well-established association between RA and other autoimmune conditions, its overlap with anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) remains relatively rare[2]. Herein, we present a patient with long-standing RA who developed AAV with a rapidly progressive renal failure during the disease course.

An 83 years-old man, with a background history of dyslipidaemia, arterial hypertension, and benign prostatic hyperplasia, had been under the care of our Rheumatology Department for more than 30 years following a diagnosis of erosive RA with positive rheumatoid factor and anti-citrullinated protein antibodies. He had lost follow-up in the prior two years, precipitated by the clinical disruptions caused by COVID-19. However, in his last appointment, he was in clinical remission under deflazacort 6 mg/day, methotrexate 10 mg/week, and sulfasalazine (SSZ) 1500 mg/day, which he maintained throughout his period of absence.

After the two-year lapse in follow-up, he returned to our Rheumatology clinic. On physical examination, he had no swollen or tender joints but presented with symmetrical oedema of the lower limbs and increased arterial pressure (152/68 mmHg). Laboratory results showed normocytic normochromic anaemia (haemoglobin 9.5 g/dL), increased erythrocyte sedimentation rate (51 mm/h) and C-reactive protein (0.72 mg/dL), rise in serum creatinine (from a previous SCr 0.82 mg/dL to 1.48 mg/dL), and active urinary sediment (leucocytes 52/mcgL; erythrocytes 290/mcgL). The patient was referred to our Nephrology team and later admitted due to the rapidly progressive course of renal involvement. Laboratory revaluation showed haemoglobin 10.0 g/dL, SCr 2.5 mg/dL, active urinary sediment (leucocytes 72/mcgL; erythrocytes 941/mcgL), and proteinuria 1200 mg/24h. Immunology revealed positive myeloperoxidase-ANCA (622 UQ) and negative proteinase 3-ANCA, anti-dsDNA, and antinuclear antibodies. Serum amyloid A and complement fractions were within normal range. Laboratory workup for infections was negative. Chest and perinasal sinus computed tomographies were unremarkable. Renal biopsy revealed crescentic pauci-immune glomerulonephritis (Figure 1). Upon further inquiry, the patient revealed that he had been experiencing hearing impairment for the past year, prompting an audiogram examination that confirmed bilateral sensorineural hearing loss. Additionally, he reported an unintentional weight loss of 5 kg, accounting for 7% of his body weight. Microscopic polyangiitis (MPA) diagnosis with renal and ear involvement was established with a Birmingham Vasculitis Activity Score (BVAS) of 20. The patient was started on rituximab 1g (days 0 and 14) and oral prednisolone 60 mg/day following the PEXIVAS low-dose glucocorticoid protocol[3]. At 2-month follow-up, BVAS was 0, and improvement of renal function was observed: SCr 1.99 mg/dl, and urinary sediment with erythrocyturia (54/mcgL) and no leukocyturia. Presently, after 18 months of follow-up, the patient is on 5 mg of prednisolone/day and maintenance therapy with 1g of rituximab every 6 months, which we decided to keep long-term due to his RA. BVAS is 0, and he has no arthritis. Laboratory assessment showed negative MPO-ANCA and improved renal function (SCr 1.31 mg/dL; proteinuria 500 mg/24h). However, his hearing impairment unfortunately persisted.

Despite extensive research on both RA and AAV, their co-occurrence remains scarcely documented[4,5]. Consistent with our case, the majority of published reports indicate that AAV develops following RA, with MPA being the most prevalent subtype. Renal involvement is frequently observed; however, compared to cases of AAV without RA, these patients tend to exhibit fewer

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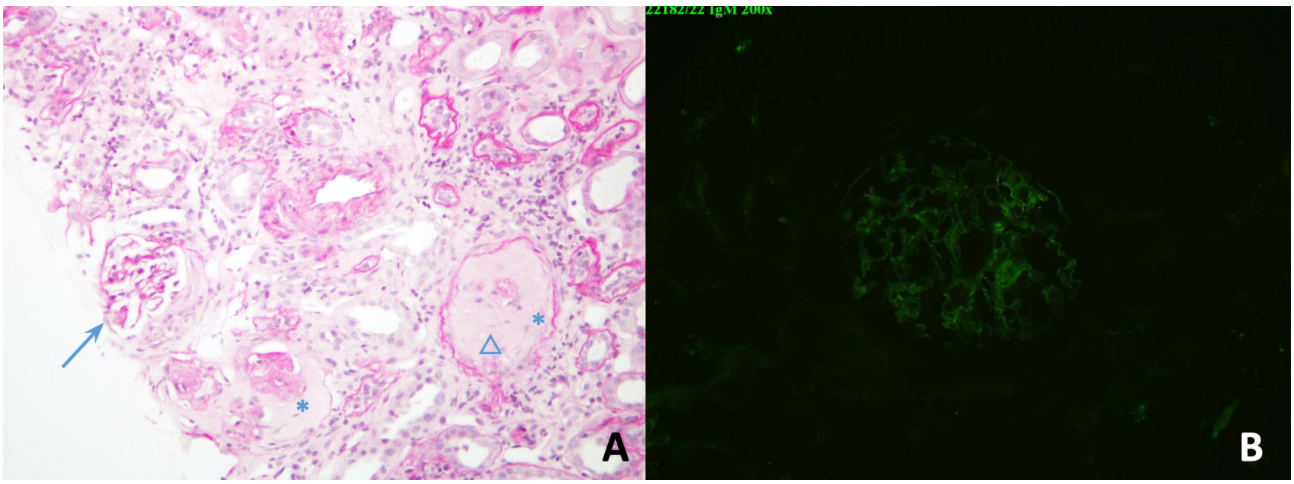

Figure 1. Renal biopsy. A – Fragment showing one glomerulus with a fibrocellular crescent (arrow) and two globally sclerosed glomeruli (*), one with Bowman's capsule destruction (Δ) [PAS 200x], B – Trace IgM deposition on capillary walls [Immunofluorescence IgM 200x].

extrarenal manifestations[6]. Additionally, unlike in our case, hearing loss is a rare feature of this association, previously reported only in two cases of granulomatosis with polyangiitis (GPA)[7,8]. The female sex is also more commonly affected, and the time between RA- and AAV-onset is usually below 10 years, with very rare reports above 30 years[5]. Treatment with SSZ has also been associated with the onset of GPA, but more research is needed to establish the same parallelism with our case[9]. In summary, our case report highlights the potential overlap between RA and AAV, successfully treated with rituximab.

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