

### Biopsy-proven giant cell arteritis in an elderly woman diagnosed 11 years earlier with microscopic polyangiitis: two different vasculitides in the same patient separated in time

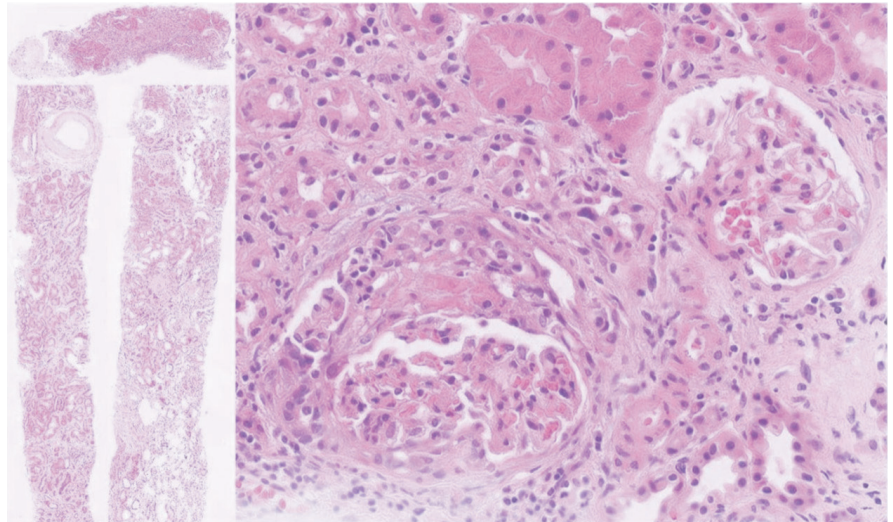
Sirs,

Renal involvement, showing a pauci-immune focal crescentic glomerulonephritis, is typical of microscopic polyangiitis (MPA) but absent in giant cell arteritis (GCA).

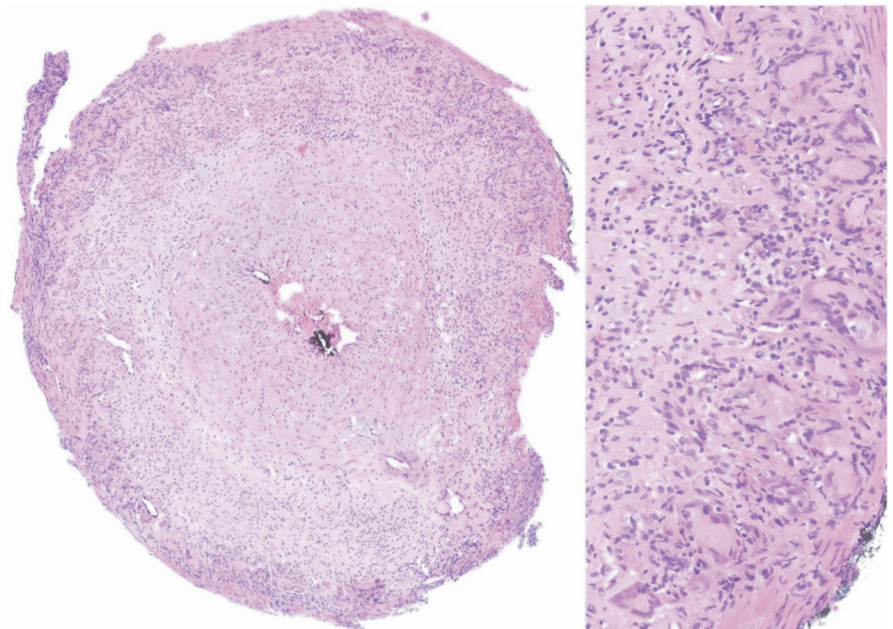
MPA patients may show inflammation in the temporal artery (1). However, they have typical necrotising vasculitis findings such as the presence of fibrinoid necrosis with polymorphonuclear leukocyte infiltration without giant cells. This is not the case for GCA characterised by the absence of fibrinoid necrosis and the presence of internal elastic lamina rupture with mononuclear infiltration, intimal hyperplasia, and multinucleated giant cells in at least 50% of patients (2).

We describe an elderly woman who was diagnosed with antineutrophil cytoplasmic antibodies (ANCA)-associated MPA in the kidney and eleven years later with biopsy-proven GCA. Although the development of renal limited MPA several years after a diagnosis of biopsy-proven GCA has been described (3), to the best of our knowledge, the independent development of GCA several years after a diagnosis of limited-renal MPA has not previously been reported.

A 65-year-old woman with unremarkable past history was referred to the Nephrology clinic in July 2011 because of urinary protein-to-creatinine ratio (UPCR) of 0.50 g/g and blood creatinine of 1.70 mg/dl. She had no hypertension, headache, asthenia, dyspnoea, weight loss, skin lesions, arthralgia, or other symptoms. She denied gross haematuria, foamy urine, urolithiasis, non-steroidal anti-inflammatory drug (NSAID) intake or recurrent urinary tract infection. A year earlier, her blood creatinine level was 1.00 mg/dl. A month later (August 2011), she was admitted to the hospital due to vomiting and abdominal pain. Laboratory results showed acute kidney injury with a blood creatinine level of 2.80 mg/dl, UPCR 0.50 g/g and haematuria (40 red blood cells per high power field (RBC/HPF); reference: 0 to 5). Renal ultrasound excluded hydronephrosis. She received treatment with 0.9% saline solution intravenously without improvement in renal function. The immunological panel revealed positive ANCA by indirect immunofluorescence with a p-ANCA pattern and a titer of 1/20. ELISA test also showed positive antimyeloperoxidase (anti-MPO) antibodies-195 U/ml (reference range: 0 to 3.5). Renal biopsy showed 14 glomeruli, 8 (57%) of them completely sclerosed. In six other glomeruli, three



**Fig. 1.** Renal biopsy showing normal glomeruli on the right and renal crescent formation with fibrinoid necrosis on the left. Note the presence of chronic damage to the interstitium in the upper left.



**Fig. 2.** Temporal artery biopsy showing transmural inflammation of the temporal artery. Note the presence of giant cells in the detail on the right.

had crescents (two fibrous crescents and the other fibroepithelial crescent) with occasional polymorphonuclear leukocytes in some capillary lumens. The interstitial fibrosis/tubular atrophy score was <5%. Direct immunofluorescence did not show binding of any antiserum antibodies (IgG, IgA, IgM, C1q, C3, Kappa or lambda). This biopsy was consistent with pauci-immune focal crescentic glomerulonephritis (Fig. 1). A diagnosis of limited-renal MPA was made. She was treated with intravenous pulses of methylprednisolone (500 mg day for three consecutive days), followed by oral prednisone, starting at a dose of 1 mg/kg/day (60 mg/day) and subsequent tapering plus intravenous cyclophosphamide 850 mg monthly for four doses (August to November 2011). After the fourth dose of

cyclophosphamide, blood creatinine level had decreased from 2.80 mg/dL to 0.90 mg/dL, haematuria from 40 to 0 RBC/HPF, UPCR from 0.50 to 0.13 and anti-MPO levels from 195 to 3.7 U/mL. Then, maintenance treatment was started with mycophenolate mofetil 2 g/day and prednisone was tapered to 5 mg/day. In November 2018, mycophenolate mofetil was replaced with rituximab (two 1-gram IV infusions separated by 2 weeks given every 6 months) and prednisone was discontinued. Courses of rituximab were given until October 2021. During all the treatment, no clinical relapses were detected; creatinine levels were steady between 0.80 and 1.00 mg/dl without haematuria.

In June 2022, she began to report headache with a poor response to NSAIDs. She com-

plained of left frontal headache (visual analogue pain scale 7 out of 10). However, she denied jaw claudication, symptoms of polymyalgia rheumatica, fever, anorexia, weight loss or loss of visual acuity. Cranial MRI did not show abnormalities. Five months later, in December 2022 at the age of 77, she was admitted to hospital due to hypertensive urgency (200/100 mmHg) and horizontal binocular diplopia. Blood pressure was treated with oral captopril and amlodipine. Brain computed tomography showed no abnormalities, and binocular horizontal diplopia was attributed to ischaemia of the left sixth cranial nerve. A temporal artery biopsy showed fragmentation of the internal elastic lamina, partial obliteration of the lumen and granulomatous inflammation, with presence of mononuclear inflammatory infiltrate, and multinucleated giant cells (Fig. 2). These findings were consistent with GCA. Treatment with prednisone 40 mg/day was started. In addition, tocilizumab 162 mg subcutaneously every week was given to allow for the gradual taper of prednisone.

Cases of ANCA-associated vasculitis and temporal arteritis without the typical histopathological characteristics of GCA have been reported, so they can be considered as ANCA-associated vasculitis with involvement of large vessels (4, 5). The “true” concomitant association of biopsy-proven GCA and MPA is rare, but has certainly also been described (6).

We present a unique case of presence of two well-differentiated systemic vasculitides separated in time in the same patient. The age of presentation of each vasculitis in this patient is in line with the peak incidence of these pathologies in Spain. The incidence of biopsy-proven GCA in Spain is 101.3 per million inhabitants aged 50 and over, with an increase in the annual incidence rate with advancing age up to a maximum of 231.6 in the 70–79 age group (2). The annual incidence of MPA in Spain is much lower, being reported as 7.91/million people for the total population (7). Like other ANCA-associated vasculitides, MPA showed a peak incidence in the age group of 55–64 years in the Spanish population (7).

One issue that must be addressed is the management of this patient once the second vasculitis –GCA– has been diagnosed. The use of tocilizumab in patients with GCA has been supported by clinical trials and open-label studies based on daily clinical practice (8, 9). However, one point of possible concern is whether tocilizumab can prevent the potential risk of MPA relapses. In this regard, Sakai *et al.* reported on two patients with MPA and reviewed the clinical evidence on tocilizumab in patients with ANCA-associated vasculitis (10). They described that clinical remission was obtained in 15 of 17 patients (88.2%) with primary and secondary ANCA-associated vasculitis, especially MPA, evaluated in the review (10).

This unique case supports the need for follow-up of patients with well-established systemic vasculitis. Careful evaluation for the presence of clues to the presence of a condition other than the underlying primary disease is recommended.

R. FERNANDEZ-PRADO<sup>1</sup>, MD\*

A. GARCÍA-FERNÁNDEZ<sup>2</sup>, MD\*

A. AVELLO<sup>1</sup>, MD

E. HERAS-RECUERO<sup>2</sup>, MD

P. CANNATA<sup>3</sup>, MD

M.A. GONZÁLEZ-GAY<sup>2,4</sup>, MD, PhD

<sup>1</sup>Division of Nephrology, IIS-Fundación Jiménez Díaz, Madrid;

<sup>2</sup>Division of Rheumatology, IIS-Fundación Jiménez Díaz, Madrid;

<sup>3</sup>Department of Pathology, IIS-Fundación Jiménez Díaz, Universidad Autónoma of Madrid;

<sup>4</sup>Medicine and Psychiatry Department, Universidad de Cantabria, Santander, Spain.

\*These authors shared first authorship.

Please address correspondence to:

Miguel Ángel González-Gay

Division of Rheumatology,

IIS-Fundación Jiménez Díaz,

Av. de los Reyes Católicos 2,

28040, Madrid, Spain.

E-mail: miguelaggay@hotmail.com

ORCID iD: 0000-0002-7924-7406

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