Extracranial subcutaneous nodules in giant cell arteritis: response to baricitinib

Sirs,

Giant cell arteritis (GCA) is a granulomatous vasculitis of large and medium-sized vessels, classically presenting with cranial ischaemic manifestations. Cutaneous involvement is uncommon and usually limited to ischaemic lesions of the scalp or tongue. In contrast, extracranial subcutaneous nodules are exceptionally rare and may be mistaken for infection, malignancy, or other inflammatory conditions (1, 2).

We report an 84-year-old woman with polymyalgia rheumatica treated with long-term low-dose prednisone (5 mg/day) and methotrexate (10 mg/week) who was admitted for left hemicrania headache and blurred vision. Ophthalmologic evaluation was compatible with anterior ischaemic optic neuropathy. Inflammatory markers were elevated. Ultrasound showed a temporal artery 'halo sign', and temporal artery biopsy confirmed GCA. High-dose glucocorticoids were started, and subcutaneous tocilizumab (162 mg weekly) was introduced as steroid-sparing therapy with good initial control, leaving a residual visual deficit (3, 4). After two years on tocilizumab, treatment was discontinued because of recurrent respiratory infections and urinary-source sepsis. Two months later, she developed erythematous lesions with palpable, non-tender subcutaneous nodules on the dorsum of the right hand and along the right forearm (Fig. 1). Laboratory tests supported relapse (C-reactive protein 22.9 mg/dL; erythrocyte sedimentation rate 72 mm/h) with mild normocytic anaemia (haemoglobin 11.2 g/dL). Given her age and prior immunosuppression, infection was carefully considered. However, skin biopsy demonstrated granulomatous vasculitis consistent with GCA, and microbiological cultures were negative for bacteria, mycobacteria and fungi; an infectious work-up (including serologies and interferon-γ release assay) was negative, supporting vasculitic nodules as a manifestation of relapse. Because the patient declined further parenteral therapy and after individualised benefit-risk discussion, we initiated off-label baricitinib 4 mg/day. Within one month, inflammatory markers normalised and the nodular lesions progressively resolved (Fig. 2). At 12 months, she remains in clinical remission on baricitinib with low-dose glucocorticoids, without thrombotic or infectious complications.

Previous reports of cutaneous or subcutaneous nodules in GCA are scarce, with fewer than ten patients described in the literature (5-8). Overall, two main clinical patterns can be recognised. The first corresponds to erythema nodosum-like lesions, typically presenting as tender, erythematous nodules predominantly affecting the lower limbs. Interestingly, in several cases these lesions preceded the onset of classical cranial or systemic manifestations of GCA, sometimes by several months, suggesting that they may represent an early or sentinel manifestation of the disease. The second pattern includes localised atypical subcutaneous nodules occurring at unusual anatomical sites, such as the supraclavicular, supraorbital, or cervical regions, which may also represent the initial manifestation prompting diagnostic evaluation. Across both patterns, histopathological confirmation has been central to diagnosis, with skin biopsies consistently demonstrating granulomatous vasculitis involving sub-

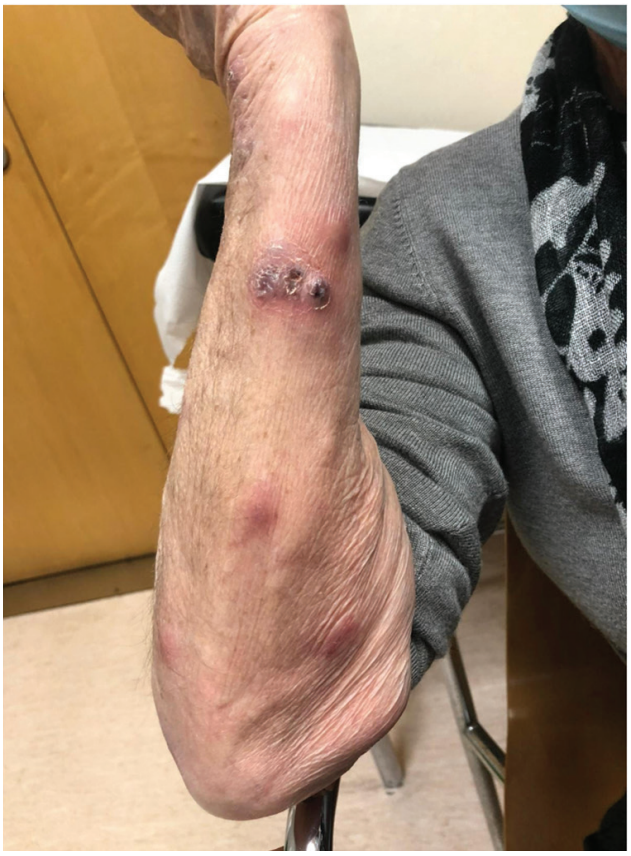

Fig. 1. Before treatment.

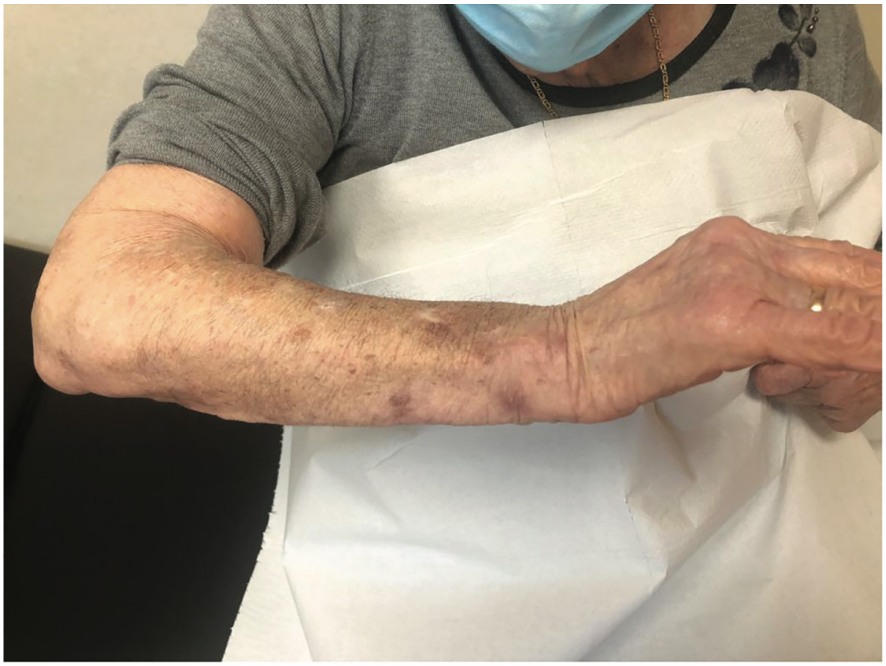

Fig. 2. After treatment.

cutaneous vessels, and temporal artery biopsy frequently supporting the diagnosis. Systemic glucocorticoids led to resolution of the nodular lesions in all reported cases, although the rarity of this presentation and limited follow-up preclude definitive conclusions regarding prognosis.

Multiple cytokines implicated in GCA pathogenesis signal through the JAK-STAT pathway, providing a biological rationale for Janus kinase inhibition. Clinical interest is supported by an open-label study of baricitinib in relapsing GCA (9) and, more recently, a phase 3 trial of upadacitinib (10). While our observation is hypothesis-generating, it suggests that JAK inhibition may represent a therapeutic option in carefully selected patients with relapsing disease when IL-6 blockade is discontinued or not feasible, including those with rare extracranial nodular manifestations.

Written informed consent for publication was obtained.

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