

Undifferentiated spondyloarthritis with late onset large-vessel vasculitis and upadacitinib induced remission

Sirs,

Spondyloarthritis with concomitant large-vessel vasculitis (LVV) extending beyond the aortic root, generally seen in HLA-B27 negative patients, is a rare but increasingly recognised extraarticular manifestation (1, 2). Spondyloarthritis generally precedes the onset of LVV and has been associated with Takayasu's arteritis (TAK), giant cell arteritis (GCA), and Behçet's disease (1-4). Identifying therapies to treat spondyloarthritis-LVV overlap can be difficult.

We describe a 59-year-old female who developed upper extremity heaviness, claudication, weakened grip with overhead activity, asymmetric polyarthralgia, infrequent occipital headaches and blurred vision. She had a longstanding history of HLA-B27 negative undifferentiated spondyloarthritis well-controlled on sulfasalazine and certolizumab. Exam noted decreased radial pulses and upper extremity blood pressure discrepancy. Laboratory workup noted CRP of 8.7 (<5mg/L), LDL 74mg/dL, normal haemoglobin, platelets, erythrocyte sedimentation rate (ESR) and expanded immune serologies. Computed tomographic angiography (CTA) revealed circumferential wall thickening of the brachial, axillary, subclavian arteries, brachiocephalic artery, and thoracic aorta, high-grade stenoses of the brachial arteries and ostial stenosis of the left vertebral artery (Fig. 1A-B). Combined positron emission tomography with CT (PET-CT) noted mild-moderate hypermetabolism of the axillary, subclavian arteries and thoracoabdominal aorta (Fig. 1C). She was initiated on upadacitinib 15 mg/day and prednisone 40 mg/day with a 2.5mg/week taper until reaching 10 mg/day. At ten month follow up on upadacitinib and 3mg/day prednisone, symptoms had resolved, labs showed ESR 2 (2-22mm/h), CRP <3mg/L. PET-CT demonstrated significant improvement with mild residual arterial hypermetabolism (Fig. 1D). Randomised controlled trials (RCTs) demonstrated substantial efficacy of TNF-alpha inhibitors (TNFai) for spondylarthritis. Less definitive evidence exists for their use in LVV. While observational studies demonstrated efficacy of TNFai in inducing remission for treatment-refractory TAK, glucocorticoid-independence was infrequent, and relapse was common (5). RCTs evaluating TNFai in GCA failed to demonstrate benefit and primarily included patients with cranial-ischaemic GCA. Although RCTs demonstrated efficacy of tocilizumab for large-vessel GCA and observational data suggests tocilizumab and TNFai are similarly efficacious for TAK, tocilizumab is not approved for spondyloarthritis (5).

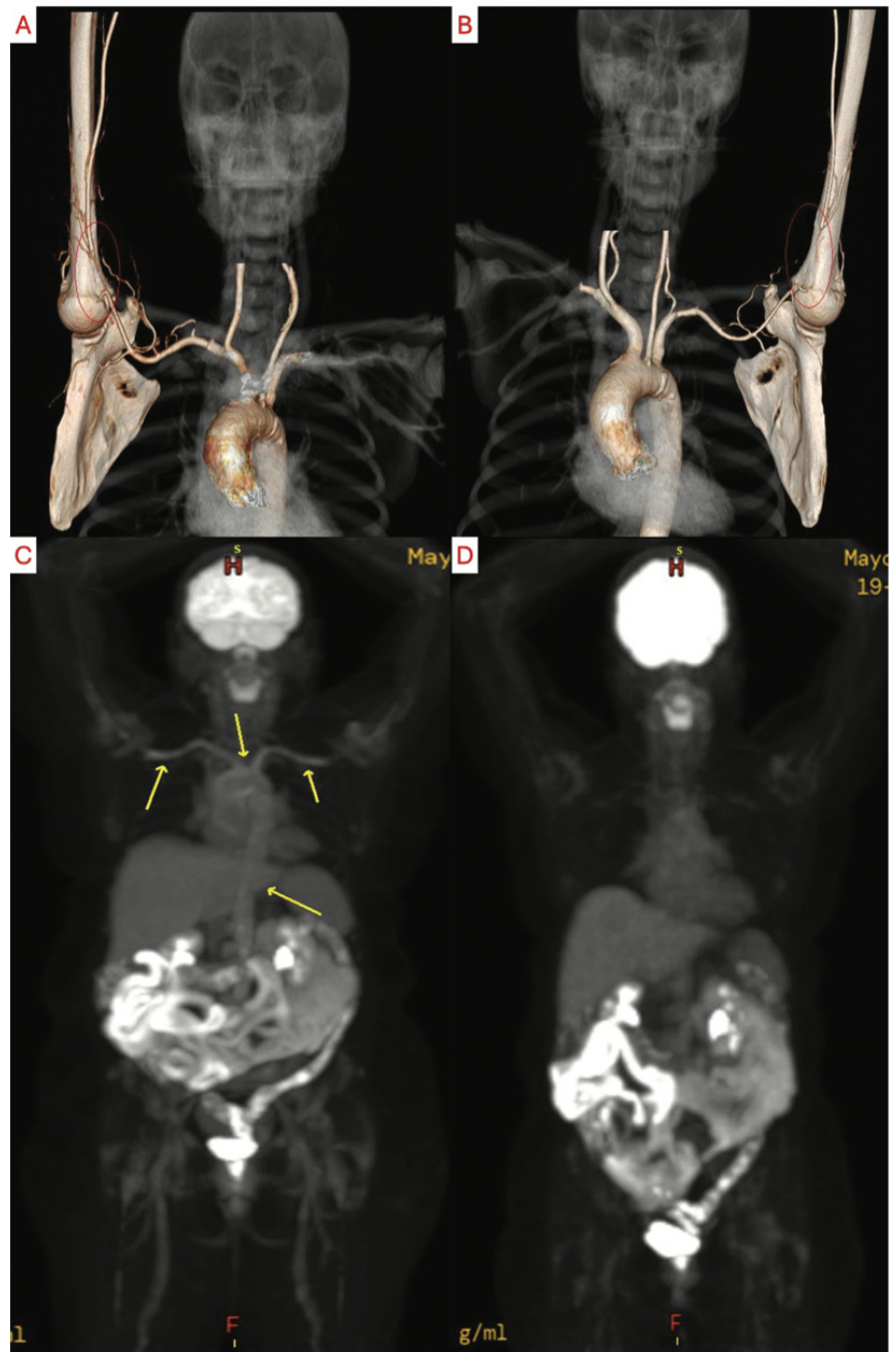


Fig. 1. Three-dimensional reconstruction of computed tomographic angiography demonstrating high-grade stenosis of the right brachial (A) and left brachial (B) arteries. Initial combined positron emission tomography with CT (PET-CT) demonstrating mild-moderately increased hypermetabolism of the bilateral brachial and subclavian arteries, brachiocephalic artery, and thoracoabdominal aorta (C). Repeat PET-CT after ten months of upadacitinib therapy demonstrating significant interval improvement of the arterial hypermetabolism (D).

Based on multiple RCTs, upadacitinib is approved for radiographic and non-radiographic spondylitis. While primarily based on case reports and observational data, the use of JAK inhibitors (JAKi) for LVV is a promising area of investigation. Upadacitinib in combination with methotrexate and infliximab induced clinical remission in a patient with biologic-refractory TAK (6). In a retrospective analysis of relapsed-GCA with a significant proportion of biologic-

refractory patients with LVV, JAKi resulted in complete remission for 46% of patients (7). Upadacitinib had the lowest rate of persistent disease and relapse with no serious adverse events (7). In the SELECT-GCA RCT, upadacitinib 15mg daily was superior to placebo in inducing remission for both new-onset and relapsed-GCA (8). Similar cases of spondyloarthritis-LVV overlap have been reported. An 83-year-old man with ankylosing spondylitis developed

late onset, biopsy-proven GCA (4). However, his primary manifestations were cranial-ischaemic GCA managed effectively with prolonged glucocorticoid taper (4). In small retrospective studies, TAK has emerged in patients with spondyloarthritis despite active treatment with TNF α , suggesting a distinct pathophysiology in overlap patients (9, 10). One such case documents emergence of TAK in a patient with axial spondyloarthritis on adalimumab. Notably, discontinuation of adalimumab and transition to methotrexate was sufficient for disease control (10). Finally, upadacitinib induced remission in a patient with ankylosing spondylitis and Behçet's disease manifesting primarily as hearing loss, hypopyon, oral and genital ulcerations (3).

In conclusion, providers should be aware of the increasingly recognised phenomenon of spondyloarthritis-LVV overlap, as finding therapies that adequately treat both entities can be difficult. Prior similar overlap cases rarely document the use of upadacitinib. This case adds to the developing literature demonstrating potential of upadacitinib in patients with spondyloarthritis-LVV overlap and highlights the need for further evaluation of JAKi in various large-vessel vasculitides.

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