Upadacitinib in resistant Takayasu's arteritis with coexisting ulcerative colitis

Sir,

Takayasu's arteritis (TAK) and ulcerative colitis (UC) rarely coexist (prevalence ~6.4%) and their concurrent management poses significant challenges when conventional biologics fail (1, 2). We report a case of refractory TA-UC treated with upadacitinib, a selective Janus kinase (JAK) inhibitor targeting the JAK1 enzyme-, which achieved complete UC remission but failed to prevent vascular progression.

A 17-year-old female patient with a diagnosis of juvenile onset UC presented with polyarthritis and a CRP level of 126 mg/L while on adalimumab (3 months). Vascular bruits, pulselessness, and hypertension with a discrepancy between the upper extremities on physical examination were compatible with a new diagnosis of TAK. CT angiography revealed wall thickening in the bilateral common carotid, vertebral, subclavian, axillary, brachial, renal, and superior mesenteric arteries, although this was not accompanied by postprandial ischemic symptoms. After receiving methylprednisolone (3 g) and six courses of cyclophosphamide, adalimumab was increased to a weekly dose. One year later, UC was active and there was new involvement of the celiac and mesenteric arteries, leading to a switch from adalimumab to infliximab. Six months later, the patient experienced a relapse of UC and transient unilateral visual loss accompanied by an increased CRP level (74 mg/L). Methylprednisolone was reintroduced, and infliximab was intensified to 10 mg/kg every four weeks. In the fifth month of therapy, serum CRP levels rose again (157 mg/L) with low serum infliximab levels, prompting escalation to 20 mg/kg every two weeks. Despite this intensified regimen, UC remained active with diffuse ulcerations on colonoscopy. Additionally, she experienced a TAK relapse following elective pilonidal sinus surgery. Due to the refractory course of both TAK and UC, alternatives to infliximab were reassessed but all were in vain. UC remained active with diarrhoea up to nine times daily, accompanied by 10% weight loss and CRP levels exceeding 300 mg/L. Baseline PET-CT in May 2024 demonstrated active UC and minimally active arterial involvement (Fig. 1), while CT showed critical stenosis of the celiac trunk and superior mesenteric artery, along with diffuse concentric wall thickening of the abdominal aorta and a short segment of the inferior mesenteric artery. At this stage, upadacitinib 30 mg/day was initiated. Within a week, clinical and laboratory remission was achieved, with CRP decreasing 300 to 0 mg/L, resolution of diarrhoea, and weight gain. Follow-up PET-CT showed complete disappearance of intestinal uptake while only minimal metabolic activity along the aortic arch (Fig. 1). Despite sustained clinical and biochemical UC control at one-year follow-up in February 2025, arterial imaging revealed progressive wall thickening and new stenotic lesions (Fig. 2). It must be noted that despite extensive arterial involvement, no abdominal or extremity pain was noted.

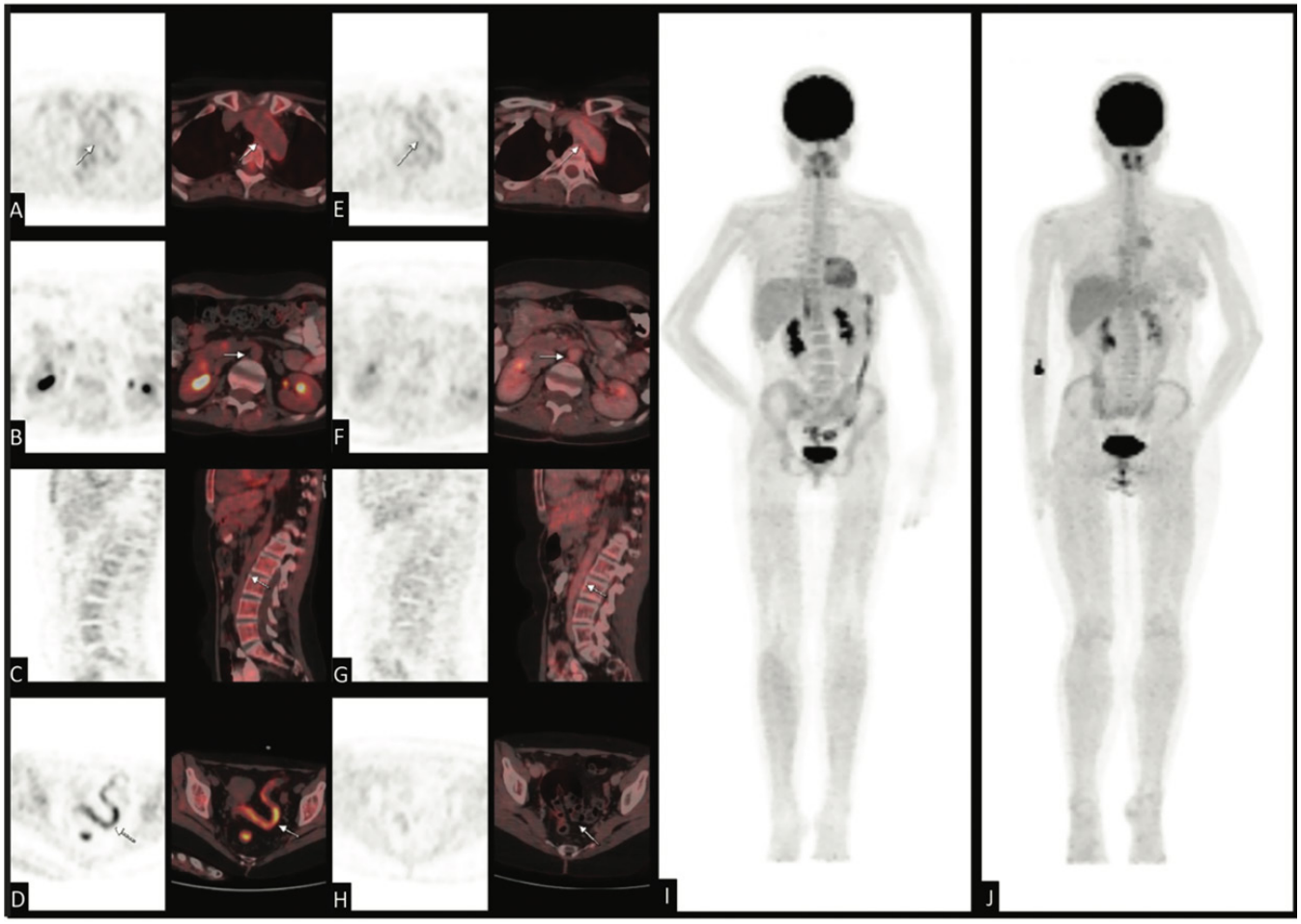

Fig. 1. Comparative 18F-FDG PET and fused PET/CT images obtained at baseline (May 2024; left: A-D, I) and follow-up (May 2025; right: E-H, J). **A, E** (axial plane, aortic arch): white arrows show persistent mild mural uptake on the arcus aorta, unchanged at follow-up. **B, F** (axial plane, abdominal aorta): white arrows point no abnormal FDG uptake. **C, G** (sagittal plane, abdominal aorta): again, no abnormal uptake. **D, H** (axial pelvis): arrows mark the large intestine; prominent FDG activity visible at baseline which has fully resolved on follow-up. **I** (May 2024) and **J** (May 2025) illustrate whole-body maximum intensity projection images: focal FDG activity in the descending colon is evident in I but absent in J.

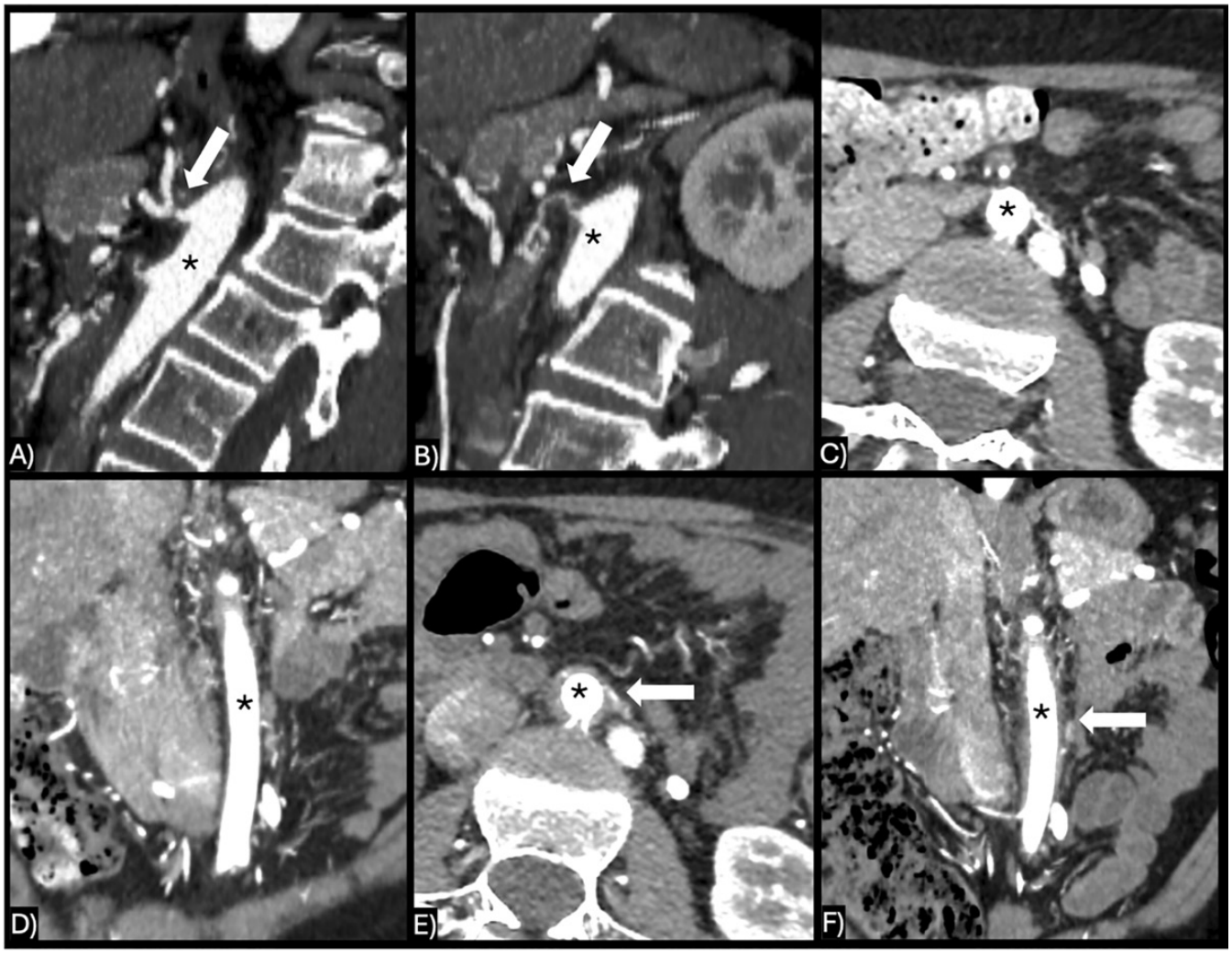

Fig. 2. Sagittal oblique reconstructed CT angiography images in February 2024 reveal stenoses in (**A**) superior mesenteric arteries (arrow) and (**B**) celiac (arrow) just distal to their origin from the aorta (asterisk). Axial (**C**) and coronal-oblique reformatted (**D**) CT angiography images show no wall thickening of the abdominal aorta (asterisk). Despite sustained clinical and biochemical control of ulcerative colitis at one-year follow-up in February 2025, axial (**E**) and coronal-oblique reformatted (**F**) CT angiography images demonstrate progressive, diffuse wall thickening (white arrow) of the abdominal aorta (asterisk).

While the effective use of tofacitinib, a JAK1/JAK3 inhibitor, in coexisting UC and TAK have been documented (3-5), our patient, to our knowledge, represents the first use of upadacitinib in such a condition. Our observation of a complete intestinal response contrasting with vascular progression suggests a possible divergence between inflammatory pathways of UC and TAK despite their clinical association (1, 2). In fact, upadacitinib seems to be a mechanistically rational approach to treating TAK by targeting the dysregulated JAK-STAT signalling pathway central to disease pathogenesis (6). The drug blocks multiple inflammatory cytokines, including IL-6, interferon-γ, type I interferons, and IL-12/23, providing broader immunomodulation than single-target biologics like tocilizumab or TNF inhibitors (6-8). Our case on the other hand, showed that while intestinal inflammation appears sensitive to JAK1 inhibition, suggesting predominant JAK-STAT dependence, vascular pathology presumably involves JAK-independent mechanisms, including direct medial smooth muscle proliferation, adventitial fibrosis, and extracellular matrix remodelling that escape cytokine-targeted therapy (9, 10). TAK seems to have a complex pathogenesis, and cytokine-targeted therapy alone may not be sufficient to achieve remission. In conclusion, our observation suggests that intestinal and vascular inflammation may respond differently in TAK-IBD overlap; selective JAK inhibitors merit careful, controlled evaluation in large-vessel vasculitis.

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