Comment on: 'Successful remission with tofacitinib in a patient with refractory Takayasu arteritis complicated by ulcerative colitis' by Kuwabara *et al*

We read with great interest the case report by Kuwabara *et al*.[1] With this comment, we want to share the case of a 38-year-old male patient with a long history of radiographic axial spondyloarthritis (r-axSpA)—with HLA-B27 positivity, peripheral joint involvement and skin psoriasis—complicated by Takayasu arteritis (TAK), showing a favourable response to a combination therapy of Tofacitinib (TOF) and methotrexate (MTX) with the readers of the *'Annals of the Rheumatic Diseases'*.

The r-axSpA was well-controlled under tumour necrosis factor alpha inhibiton with infliximab and MTX between 2013 and 2017 (figure 1). At the beginning of 2017, he presented a worsening of his disease with peripheral arthritis/enthesitis in addition to fatigue and myalgia of the neck and shoulder region. Therefore, in 2017/2018, the treatment was changed to golimumab, and then—due to persistent symptoms—to etanercept, secukinumab and certolizumab pegol and additionally MTX was switched to sulfasalazine (SSZ). All treatment courses failed to achieve an adequate disease control (figure 1). Additionally, the patient self-administered oral prednisolone (PSL) (between 50 and 15 mg daily) during that period.

In December 2018, certolizumab pegol and SSZ were discontinued because of persistent symptoms described above, in addition to progressive weight loss as well as C reactive protein (CRP) elevation (51.3 mg/L) and treatment with TOF (5 mg two times per day) was initiated (figure 1). A week later, the patient presented with tongue swelling, muffled speech and headache. The clinical examination revealed a hypoglossal paresis. An urgent CT angiography (CT-A) showed an aneurysm of 1.7 cm of the left external carotid artery (figure 2A) and a thickening of the wall of the carotid arteries. The aneurysm was resected and TOF therapy was stopped as a precaution measure due to a temporal relationship with the acute vascular event. On the next day, the patient experienced symptoms of dysesthesia and pain in the ulnar nerve region. Ultrasound revealed an extension of the right subclavian artery, which CT-A proved to be a new pseudoaneurysm of 2.7 cm (figure 2B). This aneurysm was also resected, and a vascular prosthesis was incorporated (figure 2C).

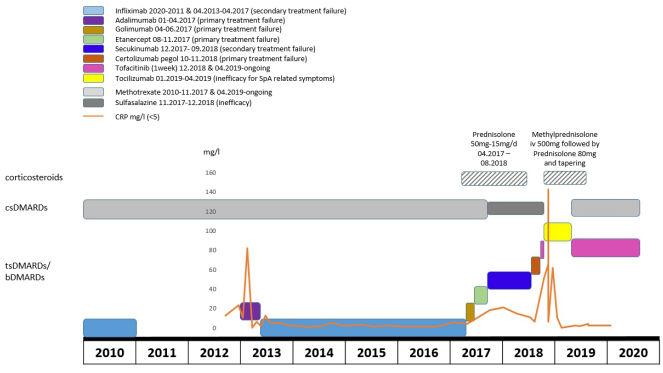

Figure 1 Treatment and CRP courses overview of the different treatment strategies and the CRP course over time. bDMARDs, biological disease modifying antirheumatic drugs; CRP, C reactive protein; csDMADRs, conventional synthetic disease modifying antirheumatic drugs; tsDMARDs, targeted synthetic disease modifying antirheumatic drugs.

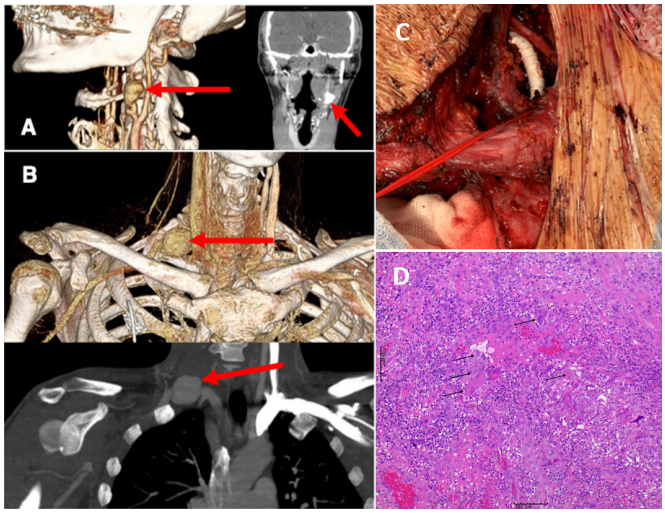

Figure 2 CTangiography, intraoperative and histological images. (A) 3D-Volume Rendering Technique (VRT) and coronal reconstructions of the neck. 1.7 cm diameter pseudoaneurysm of the left external carotid artery (red arrows). (B) 3D-VRT and coronal reconstructions of the upper thoracic aperture. 2.7 cm diameter pseudoaneurysm of the right subclavian artery (red arrows). (C) Aneurysmatectomy, replacement of the artery with subclavio-subclavian bypass using 6 mm polytetrafluorethylen (PTFE) graft. (D) Higher magnification of arterial wall reveals lymphozytes, plasma cells, macrophages and several giant cells (marked with black arrows) partially rimming necrosis.

The histopathological analysis of the aneurysm of the external carotid artery showed a lympho-histiocytic vessel wall infiltration with the presence of giant cells (figure 2D) compatible with TAK. Therefore, we started treatment with systemic corticosteroids (methylprednisolone 500 mg intravenously) and tocilizumab 8 mg/kg body weight intravenously every 4 weeks together with a tapering scheme of oral PSL starting from 80 mg daily (figure 1). However, the patient experienced a flare of his SpA-symptoms. Therefore, we switched the treatment back to TOF 5 mg two times per day together with MTX 15 mg weekly. This combination led to a rapid improvement of SpA symptoms with no new vascular episodes. The follow-up CT-A 6 months after reinitiation of the JAK-inhibition showed no further symptom progression and the CRP remained normal; PSL was tapered and subsequently stopped, while the combination therapy of TOF and MTX was continued and the patient is now in sustained clinical and laboratory remission for 12 months (figure 1).

Several cohort studies have recently reported that SpA features are common in TAK patients, and suggested potential shared genetic or immunopathogenic mechanisms.[2 3] For that reason, we believe it is utterly important to find therapeutic regimens showing efficacy for both diseases. Our case underlines the potential efficacy of JAK inhibition (in combination with MTX) in the treatment of TAK[4]; this idea is supported by the data published by Regnier *et al* in this journal presenting in vitro data as well as a case series of three TAK patients receiving baricitinib and ruxolitinib treatment,[5] and corroborates the promising data on TOF treatment in aknylosing spondylitis[6] illustrating potential future treatment options for both diseases.

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