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Letter to the Editor (Case report)

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Successful treatment with the IL12/IL23 antagonist ustekinumab in a patient with refractory Takayasu arteritis

Key message

- The IL12/IL23 antibody ustekinumab might be safe and effective in the treatment of refractory Takayasu arteritis.

Dear Editor, Takayasu arthritis is a systemic vasculitis affecting the large arteries [1], typically in young women. The first-line approach is the use of high-dose CSs, which can be combined with DMARDs, such as MTX, if needed. Other immunosuppressants, including biological agents targeting TNF-α or the IL6 receptor are used to treat patients with refractory Takayasu arthritis [2]. Given that there are still refractory patients, there is a need for new therapeutic options. In a genome-wide association study, an association between the onset of Takayasu arthritis and *IL12B*, in addition to the HLA-B gene region was found. *IL12B* encodes the IL12p40 subunit, which is a component of IL12 and IL23, and patients with Takayasu arthritis show elevated levels of serum IL12 [3].

We present the case of a 20-year-old woman who emigrated to Germany from Afghanistan in the 2016, in whom refractory Takayasu arthritis was treated successfully with ustekinumab after the failure of multiple immunosuppressive and biologic approaches. At the age of 16, in October 2016, she was diagnosed with Takayasu arthritis according to ACR classification criteria of Takayasu arthritis based on age <40 years, claudication of the extremities, a difference in blood pressure of >10 mmHg between the arms, and documented inflammation of the carotid arteries and the subclavian arteries seen in MRI [4]. The patient tested positive for HLA-B52.

After an initial treatment course with high-dose CSs in combination with MTX without sufficient response, treatment with infliximab was initiated in December 2016. In March 2017, the MRI showed a mixed response, with rising parameters of inflammation; therefore, therapy was switched to tocilizumab. Unfortunately, the patient flared again only 2 months after initiation of tocilizumab. A therapeutic course with i.v. CYC from July to November 2017 failed. From December 2017 to July 2018, treatment with adalimumab in combination with LEF led to a stable disease course. In August 2018, therapy again had to be switched to i.v. tocilizumab owing to new disease activity. In March 2019, after five administrations of tocilizumab, the patient still complained about thoracic pain, carotidynia and headaches, and MRI showed persistent inflammation of all affected arteries. As a salvage therapy, the patient received two doses of rituximab without achieving any clinical improvement and with persistent elevation of all inflammatory parameters. LEF therapy had to be terminated owing to progressive peripheral neuropathy. In addition to all the immunosuppressive agents throughout the treatment course, the patient received several courses of high-dose i.v. CSs and also low-dose prednisolone at a dose never <10 mg/day.

In October 2019, the patient received the first s.c. dose of 90 mg ustekinumab, followed by a second dose of 90 mg at 4 weeks and third dose of 90 mg 16 weeks later (Fig. 1A). This therapy was well tolerated, and the patient reported an improvement of carotidynia and thoracic pain by January 2020 that resulted in a reduction of the ITAS2010-Score from six points (active disease) to zero points. Simultaneous to the clinical improvement, the parameters of inflammation normalized and the MRI showed a marked reduction in vessel inflammation (Fig. 1B), which was never achieved before. From September 2019, the patient did not receive any additional high-dose i.v. CS courses, and we were able to reduce the oral CS dose to 6 mg/day.

This case demonstrates that ustekinumab might be safe and effective in the treatment of refractory Takayasu arteritis. Our case supports the findings of three recently reported cases from Japan, in which ustekinumab was used successfully in refractory Takayasu arthritis disease. In contrast to our patient, those patients did not receive as many prior immunosuppressive therapies, and one had co-existent ulcerative colitis [5, 6].

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Data availability statement

Data available on request.

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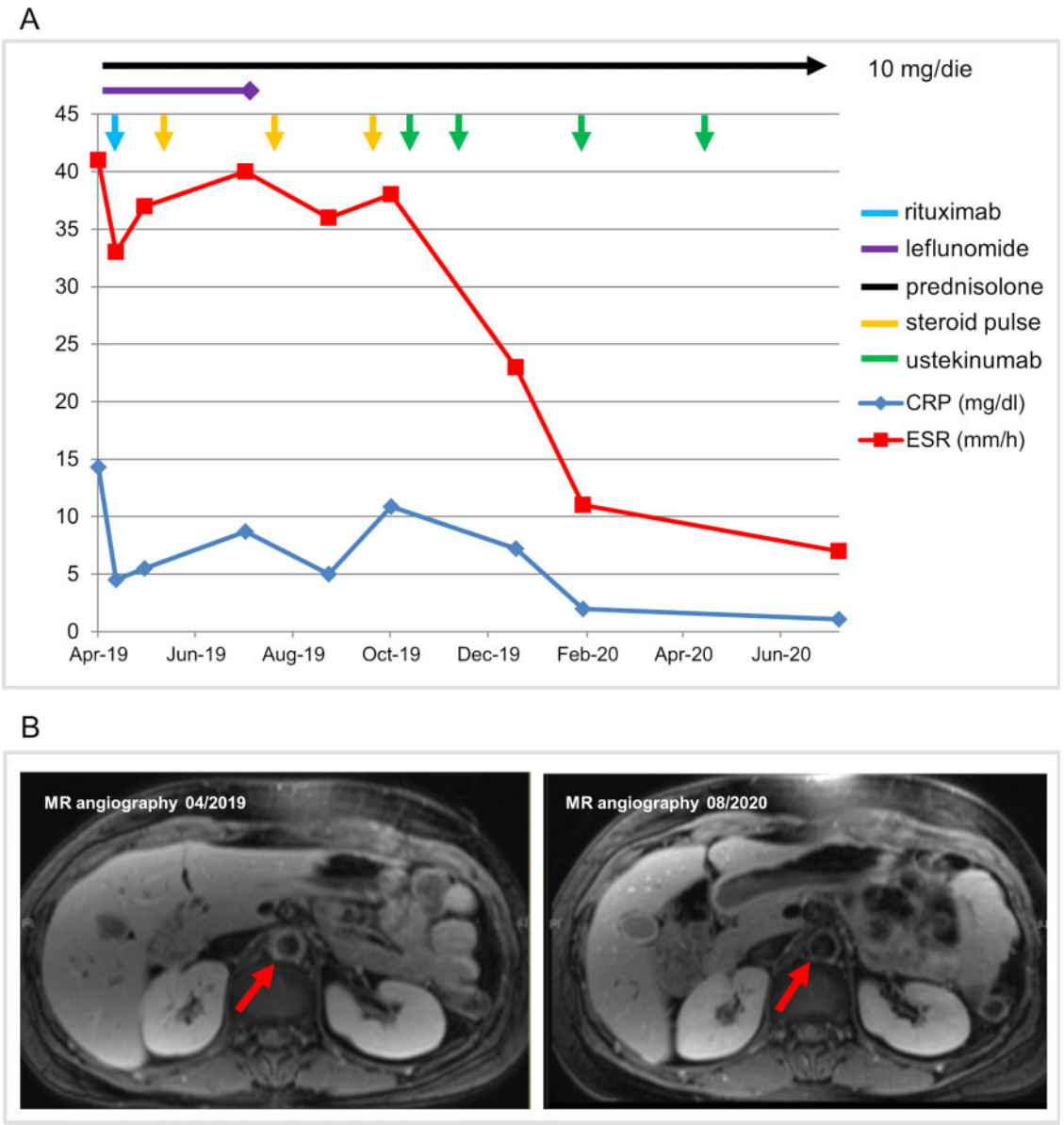
Fig. 1 Laboratory and imaging response to therapy with ustekinumab



(**A**) Treatment course of the patient from April 2019 to October 2020: prednisolone 10 mg/day (black arrow) was used. LEF (purple line) was discontinued owing to side-effects. Rituximab (light blue arrow) 1000 mg was used as salvage therapy. CS pulse courses (orange arrow) were administered as 500 mg methylprednisolone i.v. over 3 days. Ustekinumab (green arrow) was administered s.c. at a dose of 90 mg. Inflammation was monitored using CRP (blue line) and ESR (red line). (**B**) MRI, showing a marked reduction in inflammation of the abdominal aorta (red arrow).

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