New-onset aortitis manifesting as relapsing giant cell arteritis successfully managed with tocilizumab monotherapy.

A comment on: Optimisation of tocilizumab therapy in giant cell arteritis. A multicentre real-life study of 471 patients. by Calderon-Goercke *et al*.

Sirs,

We read with interest the article by Calderon-Goercke *et al*. describing their experience with tocilizumab optimisation in patients with giant cell arteritis (GCA) (1). The findings from this study are noteworthy showing ongoing clinical effectiveness combined with improved safety through reduction in severe infections among patients undergoing dose optimisation (1). Optimal dose and duration of tocilizumab therapy in patients with GCA is largely unknown given the clinical trial data is limited to 12 months (2, 3). Discontinuation of tocilizumab after 12 months among patients in clinical remission off glucocorticoids has been associated with rates of relapse in >50% (4, 5). The findings from Calderon-Goercke *et al*. demonstrate the capacity for providers to consider reduction in tocilizumab dose or frequency while maintaining clinical benefit. However, an area that remains unknown and was not explored in the study by Calderon-Goercke *et al*., is whether patients with GCA on tocilizumab have a lower risk of subsequent relapse following tocilizumab discontinuation if they have either been treated for >12 months or have undergone dose optimisation prior to cessation of therapy. Herein we share an illustrative case from our institution highlighting relapse after dose optimisation followed by tocilizumab discontinuation.

A 74-year-old male presented locally in January 2018 with a four-month history of bilateral stiffness in hips and shoulders, initially treated with non-steroidal anti-inflammatories. Two months later, symptoms progressed to include bilateral temporal artery tenderness and jaw claudication. C-Reactive protein (CRP) was 47 mg/L and erythrocyte sedimentation rate (ESR) was 48 mm/hr. Unilateral left temporal artery biopsy confirmed presence of GCA. Oral prednisone 60 mg/day was initiated. Given baseline evidence of osteoporosis, weekly tocilizumab 162 mg/0.9ml by subcutaneous injection was started at diagnosis. Baseline chest magnetic resonance imaging with angiography (MRI/MRA) was negative for presence of large-vessel involvement (Fig. 1A). Clinical remission was achieved and prednisone was discontinued after 6 months. After 12 consecutive months of weekly subcutaneous tocilizumab, he was dose-optimised to every other week for an additional 12 months followed by further injection interval prolongation of 2 additional days (*i.e*. 16, 18, etc.) between each injection until achieving a dosing cycle of 28 days before tocilizumab discontinuation in October 2020 (29-month total duration). One year after stopping tocilizumab he reported mild hip stiffness but no other associated symptoms. CRP had risen to 43.4 mg/L and ESR 41 mm/hr. Repeat MRI/MRA chest was performed and disclosed new diffuse, circumferential enhancing mural wall thickening of the entire thoracoabdominal aorta (Fig. 1B). Weekly subcutaneous tocilizumab monotherapy was re-initiated without glucocorticoids. Five months after treatment initiation the patient remained in clinical remission with normal inflammatory markers and repeat MRI/MRA demonstrated near resolution of the aortitis (Fig. 1C).

This case highlights several important concepts. First, extended duration treatment with 12-month standard dosing followed by >12-month dose optimisation did not prevent subsequent relapse following tocilizumab discontinuation. Second, while the majority of patients with GCA discontinuing tocilizumab relapse within subsequent 6–8 months, long-term surveillance for relapse is necessary and advocated due to possibility of later stage recurrence. Third, new-onset large-vessel involvement can develop as a feature of GCA relapse and should be considered in patients with inflammatory marker elevation even if symptoms are mild or absent. Fourth, tocilizumab monotherapy may be considered in certain patients with relapse following tocilizumab discontinuation.

Neither clinical trial nor real-world experience data evaluating tocilizumab in GCA have identified established features predictive of long-term remission following tocilizumab discontinuation after ≥12 months of treatment (4-8). Given more than half of patients relapse following tocilizumab cessation, future studies are needed to identify which subset of patients are most suitable for tocilizumab continuance, optimisation, or stoppage.

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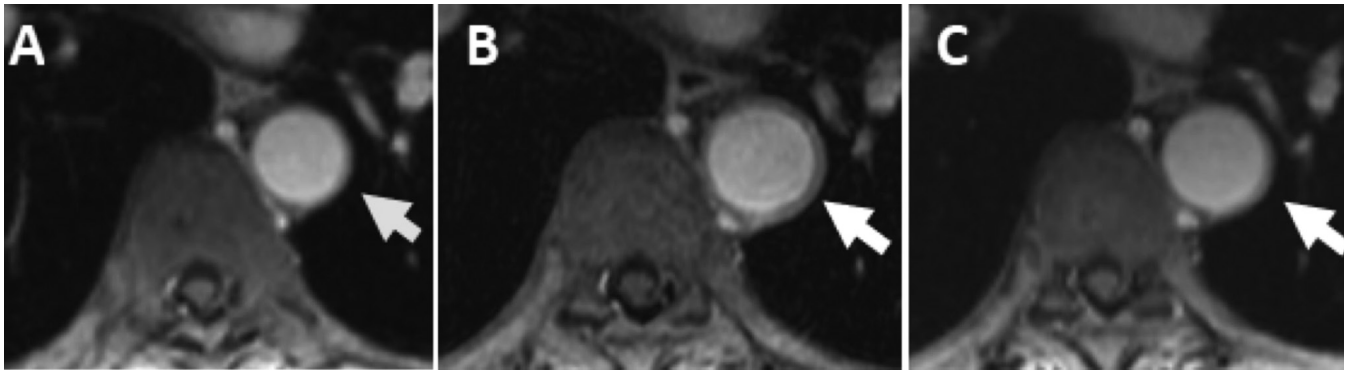

Fig.1. Radiographic improvement of new-onset large-vessel vasculitis following reinstitution of tocilizumab monotherapy.
MRI/MRA of the descending thoracic aorta (post-contrast DIXON technique, water only images) demonstrating normal wall thickness (arrow) at initial GCA diagnosis (**A**). Repeat MRI/MRA one year after tocilizumab discontinuation with circumferential, enhancing wall thickening of the descending thoracic aortic wall (arrow) (**B**). Near resolution of aortic wall thickening (arrow) following tocilizumab re-initiation as monotherapy (arrow) (**C**).

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