

***Tropheryma Whipplei* infection mimicking giant cell arteritis flare in a patient treated with interleukin-6 receptor blocker tocilizumab**

Sir,
Whipple disease (WD) is a very rare infection that can mimic rheumatic disease flare. We report the case of patient who developed WD after treatment with interleukin-6 (IL-6) receptor blocker for giant cell arteritis (GCA).
A 50-year-old-patient was referred for headache, abdominal pain and increased C reactive protein (CRP) level. He had medical history of disc herniation. He had no smoking or drinking habits and worked as a fish-farmer. The history began with sudden right temporal headache without fever. Patient also had left flank pain. Laboratory exams were normal, except CRP level at 79 mg/L. Abdominal computed tomography (CT) showed diffuse wall thickening of aorta descending below the level of renal arteries; fluorodeoxyglucosed-positron emission tomography (FDG-PET) confirmed diffuse radiotracer uptake at all segments of the aorta; but also in common carotid and both subclavian arteries (Fig. 1). Physicians concluded GCA with aortic involvement and patient received glucocorticoids regimen at 1mg/kg/day permitting clinical and biological improvement.

Because of glucocorticoids dependence (30 mg/day) at four months, patient received methotrexate (15 mg/week) in addition to steroids. Two months after methotrexate treatment, patient described headache and arthralgia of the shoulder and hips. He also had increased of CRP level (23 mg/L) with steroids regimen tapered to less than 15 mg/day. ¹⁸F-FDG-PET showed persistent radiotracer uptake of aortic wall (Fig. 1). Patient received tocilizumab (IL-6 receptor-blocker) 0.7 mg/kg/month for refractory GCA permitting clinical and biological remission with discontinuation of steroids and methotrexate.
At the 6th infusion, patient suffered from abdominal pain, diarrhea, peripheral arthralgia and had an increased CRP level (20 mg/L). Body CT-scan and FDG-PET showed intense radiotracer uptake of bowel loops (Fig. 1) without vessels involvement. Patient also complained of memory loss and mood disorder. Neurological examination was normal and cerebral magnetic resonance imaging showed no abnormality. Patient refused lumbar puncture. Screening for infectious agents (HIV, HBV, HCV, blood cultures, *Treponema Pallidum*) were negative and digestive endoscopy showed non-specific oedema of caecum. Due to abdominal pain, arthritis and neurological symptoms without evidence of GCA flare, WD was suspected. Polymerase chain reaction (PCR) was positive for *Tropheryma Whipplei* in saliva and stool. Periodic acid-

Schiff stain (PAS) was negative on duodenal biopsy tissues. The patient received hydroxychloroquine and doxycycline with clinical and biological improvement at 12 months; and to date, patient had no relapse of GCA without steroids or immunosuppressive agents.
We report the first case of WD in a patient treated with tocilizumab. WD is a systemic disorder caused by gram-positive bacteria, *Tropheryma Whipplei*. WD has a heterogeneous presentation (fever, abdominal pain, arthritis, endocarditis, dementia) associated with increased CRP level (1, 2). *Tropheryma Whipplei* is an environmental bacteria (present in contaminated soil) hosting in the digestive system and is rarely responsible for chronic systemic infection (3). During the course of WD, digestive symptoms are present in almost 90% of patients (4). Immunosuppression enhances the proliferation of *T. Whipplei*, which is responsible for exacerbated gastrointestinal symptoms and complicates the course of the disease (5). Diagnosis is based on clinical presentation and PAS positive staining of duodenal biopsy. However, PAS has a poor sensitivity and specificity and PCR can be useful to assess the diagnosis in cases where PAS biopsy is negative (6, 7). Treatment is based on combination therapy with hydroxychloroquine and doxycycline (1). Regarding GCA, therapeutic approaches include glucocorticoids, immunosuppressive agents (methotrexate) and biologic agents (IL-6 receptor blockers)

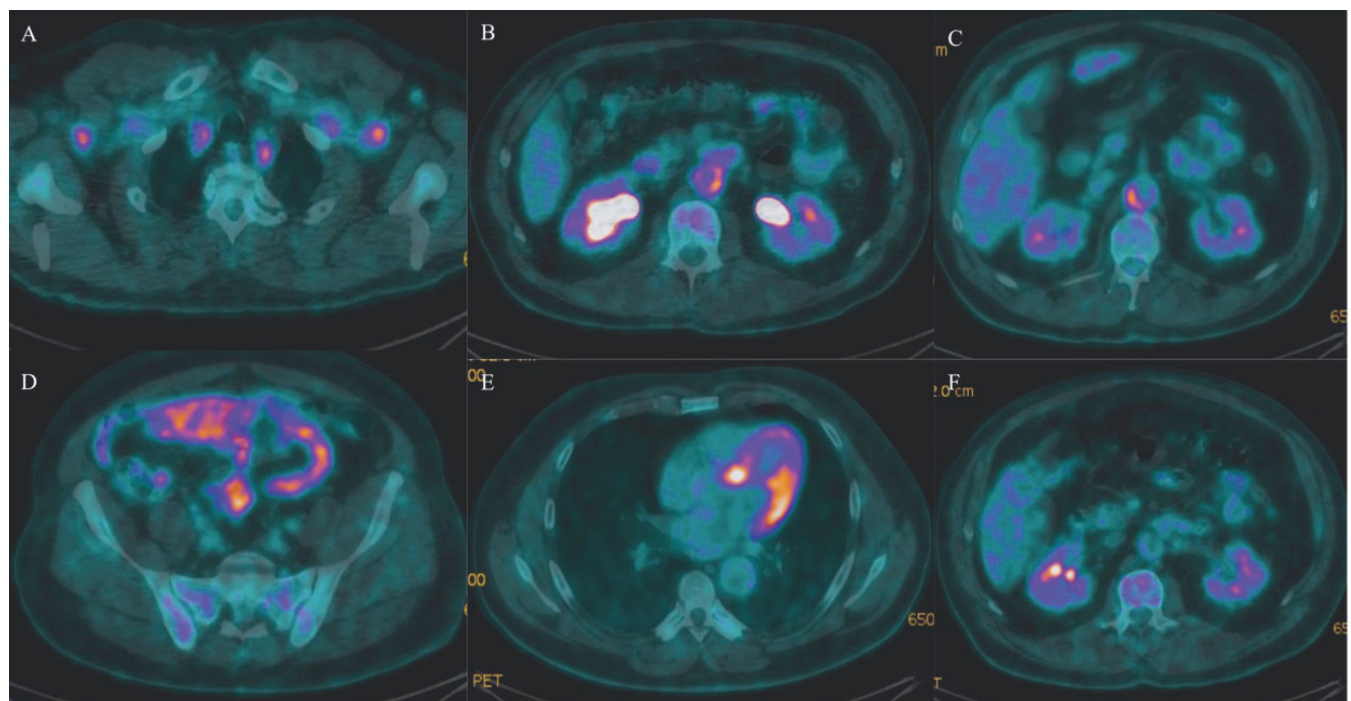


Fig. 1. Imaging of patient showing evidence for giant cell arteritis and digestive *Tropheryma Whipplei* involvement. A: Axial fused (¹⁸F) fluorodeoxyglucosed (FDG)-positron emission tomography demonstrates radiotracer uptake in common carotid artery and both subclavicular arteries at GCA diagnosis; B: Axial fused (¹⁸F) fluorodeoxyglucosed (FDG)-positron emission tomography demonstrates radiotracer uptake in abdominal aorta at GCA diagnosis; C: Axial fused (¹⁸F) fluorodeoxyglucosed (FDG)-positron emission tomography demonstrates radiotracer uptake of aorta before tocilizumab infusion; D: Axial fused (¹⁸F) fluorodeoxyglucosed (FDG)-positron emission tomography demonstrates radiotracer uptake of bowels loop at Whipple disease diagnosis; E-F: Axial fused (¹⁸F) fluorodeoxyglucosed (FDG)-positron emission tomography demonstrates the absence of radiotracer uptake of aorta at Whipple disease diagnosis after tocilizumab infusion.

Letters to the Editors

in refractory patients (8) providing efficacious results. Under inhibited inflammatory response, infectious agents can proliferate and mimic disease flares. In the present case, digestive symptoms consistent with WD began after six tocilizumab infusions.

Few cases of WD have been reported inpatient with biologic agents (mostly TNF-alpha blockers) (9) but at our knowledge, no patient developed WD after tocilizumab infusion.

To conclude, Whipple disease must be investigated in patients treated with biologic agents presenting digestive symptoms and arthralgia concomitant with increased CRP level.

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