A 19-year-old man was admitted in our tertiary care center in August 2014 for a 10-kg weight loss in a few months (48 kg, 1.80 m, and body mass index, 14.8 kg/m²), claudication in the lower limbs after a 500-m distance and a postprandial abdominal pain associated with mild renal insufficiency and proteinuria with no hypertension (100/80 mm Hg). The patient had no medical history and was an active smoker (tobacco and cannabis, estimated consumption: 2 pack-years). Laboratory parameters were elevated (blood leukocyte count (13×10⁹/L), C-reactive protein level (55 mg/L), creatinine (14 mg/L), and B-natriuretic peptide (4246 pg/mL). No thrombophilia, autoimmune disorders, or viral infections were identified. The patient underwent a B-mode Doppler ultrasound that showed multiple proximal arterial occlusions and stenoses of large vessels confirmed by a computed tomographic angiography: occlusions of bilateral subclavian arteries, superior and inferior mesenteric arteries, and right renal artery with kidney atrophy were found (Figure 1A). Furthermore, significant stenoses of celiac artery, left renal artery (Figure 1B), right internal iliac artery, and bilateral superficial femoral arteries were identified. A discrete circumferential thickening of the abdominal aorta was suggestive of aortitis. Cervical magnetic resonance angiography showed a complete occlusion of both subclavian and vertebral arteries (Figure 2). Transthoracic echocardiography revealed a severe left ventricular (LV) systolic dysfunction (LV ejection fraction was 27%), with elevated LV filling pressure (E/e' = 16) and no right ventricular dysfunction (Movies I and II in the Data Supplement). Takayasu arteritis was diagnosed according to Ishikawa–Sharma and the American College of Rheumatology criteria. An anti-coagulant treatment using low molecular-weight heparin was initiated together with intravenous steroids, aspirin, and β-blockers. Few days later, a positron emission tomographic (PET) scan revealed an hypermetabolism located in the ascending thoracic aorta and the proximal portion of the aortic arch and the right external iliac artery (Figure 3A and 3B). A cardiovascular magnetic resonance imaging showed a left ventricular dilation with hypokinesia and severe LV ejection fraction impairment of 18% associated with a concentric remodeling (mass/end-diastolic volume close to 1; Figure 4A; Movie III in the Data Supplement), without any argument for an acute myocarditis or myocardial infarction. Given the severity of arterial lesions and clinical symptoms, a short-term surgical treatment was planned after the initiation of intravenous tocilizumab (8 mg/kg). A dramatic improvement of cardiac function (LV ejection fraction, 35%; laboratory parameters on Figure 5) occurred in 10 days. However, the patient presented an acute mesenteric ischemia requiring an urgent aortomesenteric and aortohepatic bypass using the great saphenous vein and a prosthetic enlargement patch on the left renal artery. Histological examination of the excised aorta showed a thickening of the aortic wall with an intima fibrosis and incipient on the media, a mild lymphocytic inflammation without granuloma or giant cell, and no damage of the vasa vasorum (Figure 6A and 6B). Monthly tocilizumab pulses were continued until 18 months of follow-up, and glucocorticoids tapering began 1 month after surgery. No active vasculitis was identified by PET scan after 3 months of treatment (Figure 3C and 3D). The patient recovered a nearly normal heart function (Figure 4B; Movies IV through VI in the Data Supplement). Eighteen months later, Takayasu disease was inactive and most clinical manifestations had disappeared.

Thus, the present case reports the efficacy and organ response to the anti-interleukin-6 receptor antibody (tocilizumab) associated with steroids as a first-line therapy in a patient with severe Takayasu disease before surgery. In this setting, most commonly used agents include corticosteroids and methotrexate, azathioprine, or mycophenolate mofetil. In patients who remain resistant or intolerant to these agents, biological drugs including tumor necrosis factor inhibitors...
(infliximab) and tocilizumab are promising.1 In the presence of a life-threatening arterial stenosis or occlusion, the mainstay of treatment is urgent revascularization of affected organs using surgical bypass, which is associated with lower morbidity–mortality than endovascular intervention.2 Of note, as a general rule, both endovascular intervention and surgical procedures should be avoided during the active phase of the disease to decrease the risk of vascular complications (eg, restenosis).2 In our case, the patient was categorized in grade V of disease severity.3 Therefore, a quick improvement was needed before revascularization to minimize postoperative complications. Indeed, tocilizumab was effective on both clinical laboratory and imaging parameters. Furthermore, reviews confirmed that tocilizumab may be an effective steroid-sparing option for rapid control of refractory disease activity in patients with Takayasu arteritis.1,4 Finally, it has been shown that tocilizumab is efficient and well tolerated in patients with refractory Takayasu arteritis; based on our observation, it may be now an alternative for first-line therapy in selected cases.

Disclosures
None.

References

Keywords: biological therapy ■ surgery ■ Takayasu arteritis ■ tocilizumab ■ tomography, emission-computed ■ vasculitis ■ ventricular dysfunction, left

Figure 1. Abdominal computed tomographic angiography 3-dimensional volume rendering reconstructions showing the stenosis of the celiac artery (B, blue arrow); a proximal occlusion of the superior mesenteric artery (A and B, cross) and the right renal artery (A, white arrow) along with parenchymal atrophy, a thrombosis of the inferior mesenteric artery and a stenosis with prestenotic dilation of the left renal artery at the distal part of its truncular segment (A and B, green arrow).
Figure 2. Neck magnetic resonance angiography showing a complete occlusion of subclavian arteries (white arrow) and V1–V2 segments of vertebral arteries (A) with a late gadolinium enhancement of the V4 segments suggestive of vasculitis (B, green arrow).

Figure 3. A positron emission tomographic scan performed during the acute phase demonstrating an fluorodeoxyglucose uptake of the periaortic fat (A and B) of the aortic wall and the right external iliac artery (E and G arrow) in sagittal section. Decreasing fluorodeoxyglucose uptake after 3 tocilizumab and steroids pulses (C, D, F, and H). SUV indicates standard uptake value.
Figure 4. Cardiovascular magnetic resonance imaging. Midventricle short-axis slice at end diastole demonstrating a symmetric hypertrophic and dilated left ventricle (LV) at the initial presentation (A), with an improvement at 6 months of follow-up (B) with septal thickness decreasing from 10.5 to 8 mm, LV mass from 139 to 91 g/m², and LV end-diastolic diameter from 64 to 60 mm. In the meantime, LV ejection fraction increased from 18% to 42% (Data Supplement).

Figure 5. B-natriuretic peptide (BNP) and C-reactive protein level (CRP) at baseline and post therapy.
Figure 6. Microscopic section of the excised aorta showing mild lymphocytic inflammation. **A**, Hematoxylin and eosin aortic sections with fibrosis of the intima (magnitude ×5, black arrow) and the media (cross). **B**, Hematoxylin and eosin inflammatory cell infiltrates of the media (magnitude ×100, white arrow).
Dramatic Response to Tocilizumab Before Emergency Surgery in Severe Active Takayasu Disease
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Movie Legends

Movie I and II:

Transthoracic echocardiography; short-axis view (Movie 1); apical view (Movie 2); revealed an hypertrophic cardiomyopathy with elevated LV filling pressure (E/e’ = 16), severe systolic dysfunction (LVEF = 27%), no right ventricular dysfunction.

Movie III. Cardiovascular magnetic resonance imaging. Mid ventricle short axis slice at end-diastole demonstrating a symmetric hypertrophic and dilated left ventricle (septal thickness measured at 10.5 mm, left ventricle end-diastolic diameter measured at 64 mm, LVEF = 18%)

Movie IV. Cardiovascular magnetic resonance imaging six month after Tocilizumab showing an improvement with septal thickness decreasing from 10.5 to 8 mm and left ventricle end-diastolic diameter from 64 to 60 mm. In the meantime, LVEF increased from 18% at 42%

Movie V and VI: Transthoracic echocardiography eighteen month after Tocilizumab; short-axis view (Movie 5); apical view (Movie 6); Left ventricular systolic function recovery and complete reverse remodeling (LVEF = 55%) and normal diastolic function (E/e’ = 7)