EJCRIM
European Journal
of Case Reports
in Internal Medicine

A SPECTACULAR EFFECT OF TOCILIZUMAB IN TAKAYASU ARTERITIS

Fatma Saïd[1,2], Ines Naceur[1,2], Tayssir Ben Achour[1,2], Maysam Jridi[1,2], Monia Smiti[1,2]

[1] Internal Medicine, University Hospital La Rabta, Tunis, Tunisia
[2] Faculty of Medicine of Tunis, University Tunis El Manar, Tunis, Tunisia

Corresponding author's e-mail: saidzribifatma@yahoo.fr

Received: 03/09/2024
Accepted: 14/10/2024
Published: 07/11/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: We obtained written consent from patient.
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How to cite this article: Saïd F, Naceur I, Achour TB, Jridi M, Smiti M. A spectacular effect of tocilizumab in Takayasu arteritis. *EJCRIM* 2024;**11**:doi:10.12890/2024_004868

ABSTRACT

Background: Anti-interleukin-6 receptors (anti-IL-6R) have been a promising new therapeutic alternative in the treatment of Takayasu arteritis.

Case description: We report the case of a 34-year-old patient with Takayasu arteritis diagnosed in 2017. While she was on corticosteroid and methotrexate, the patient presented twice with clinical and radiological signs of activity, requiring an increase of corticosteroid dose and an increase in the methotrexate dose to 20 mg/week. Anti-IL-6R infusions were indicated. At the end of the fifth infusion, the patient was totally asymptomatic: she no longer experienced episodes of syncope or amnesia.

Conclusion: Our case perfectly illustrates the effectiveness of anti-IL-6R in the treatment of Takayasu arteritis, especially in its refractory form.

KEYWORDS

Takayasu arteritis, tocilizumab, anti-IL6 refractory form

LEARNING POINTS

- Takayasu arteritis may have a significant functional impact that affects quality of life.
- Tocilizumab is a very interesting therapeutic alternative in the refractory form of Takayasu arteritis.

INTRODUCTION

A vasculitis known as Takayasu arteritis (TAK) affects large arteries, especially the aorta and its major branches; it usually affects younger women. Although rare, the disease is associated with significant vascular complications, affecting both functional and vital prognosis[1]. The medical care centred on corticosteroid and immunosuppressive therapy, as well as endovascular treatment, has significantly improved the prognosis[2]. Certain forms are still refractory, though. Whether it is anti-receptor of interleukin 6 (anti-IL-6R), or anti-tumour necrosis factor (anti-TNF) agents, biotherapy continues to be an intriguing therapeutic option, particularly in refractory disease. According to the American College of Rheumatology (ACR) in 2021, these biological therapies can be utilised for refractory forms[3]. We describe the case of a patient who had significant supra-aortic trunk stenosis and a

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resistant form of TAK. The patient responded well to anti-IL-6R medication.

CASE DESCRIPTION

A 34-year-old woman was diagnosed with TAK in 2017 in the presence of bilateral carotid bruits, absent blood pressure in the upper two limbs, radial pulse abolition, upper limb claudication and a lower limb systolic blood pressure between 160 and 200 mmHg. The ultrasonography of the supra-aortic trunks revealed a diffuse and significant hypoechoic parietal thickening, particularly in the subclavian (sub-occlusive stenosis at its origin) and common carotid arteries (50% right and 80% left stenosis). A stenosis of little more than 40% thickened the inner carotid wall. No abnormalities were found on the lower limb ultrasonography. The computed tomography (CT) angiography revealed a parietal thickening of the right renal artery with sub-occlusive stenosis of the subclavian artery, as well as severe stenosis exceeding 90% in certain areas, and tight common carotid stenosis reaching 90% on the left and 85% on the right.

The patient received IV pulses of 1 g of methylprednisolone per day for three days. After that, she had oral corticosteroid therapy at a dose of 1 mg/kg/day of prednisone, along with an initial dose of 10 mg/week of methotrexate and hypertension medication (a calcium inhibitor and a central antihypertensive).

The upper limb claudication improved, the blood pressure rate returned to normal, and the CT angiography found a renal artery re-permeabilization. Methotrexate (10 mg/week) and prednisone (10 mg/day) were used as maintenance therapy. The patient did not exhibit any symptoms until June 2020. After a three-month break from methotrexate due to stomach intolerance, the patient complained of a deteriorating claudication of both upper limbs and the lower left limb, associated with periods of transitory amnesia, a sensation of heaviness in the left side of the body and syncope that occurred after exertion. The physical examination found abolition of the left posterior tibial, pedal, radial and humeral pulses. The humeral and right radial pulses were not strong. The angiotomography showed a left common carotid artery stenosis estimated at 70%, at 35 mm from its origin that extended by 15 mm, a right common carotid artery occlusive stenosis at 54 mm from its origin that extended to 33 mm, and a right subclavian artery occlusion. They were all caused by a circumferential and regular parietal thickening. It was advised to provide intravenous pulses of methylprednisolone along with oral corticosteroid therapy at a dose of 1 mg/kg/day and to increase the dose of methotrexate to 15 mg/week. Revascularisation of the left common carotid artery was accomplished using a dilated probe by transluminal angioplasty and a post-dilated stent for residual stenosis. The absence of syncope was a defining feature of the clinical course. The patient was treated with 7.5 mg/day of prednisone and 15 mg/week of methotrexate. She remained stable until December 2021, when she presented with a heavy sensation on the left side of her body and bilateral tenderness of the carotid arteries, while her speech problems spontaneously resolved. The patient complained of daily episodes of syncope and fainting that interfered with her daily activities, and she needed the assistance of a third party at the slightest exertion. She could not stand or walk. There were both transient and persistent episodes of memory loss. The CT angiography found a significant parietal infiltration surrounding the stent area at the primitive left carotid with a 90% stenosis of the vertebral artery in its pre-transversal portion. The brachiocephalic trunk, the right common carotid artery and the proximal portion of both vertebral arteries all showed significant inflammatory thickening. Once more, the patient received treatment with IV methylprednisolone (1 g/day for three days), followed by oral route prednisone (1 mg/kg/day) and methotrexate (20 mg/week). The almost complete stenosis of the right carotid artery precluded the consideration of revascularisation surgery.

In this refractory variant, tocilizumab treatment was advised after methotrexate withdrawal. After two months of treatment, fainting and syncope disappeared. The patient regained her normal daily activities and autonomy. After six months of treatment, she was able to reintegrate into society (for example, she returned to her job, had a normal social life, was able to provide parenting duties and her memory loss disappeared). Five months later, in April 2022, a CT scan found stabilised lesions devoid of any signs of activity. After a 32-month interval, there was no record of new symptoms. In August 2024, while the patient was on 7.5 mg/day of prednisone, the thoracic aorta and the supra-aortic trunks inflammatory artery involvement was stable as shown by the CT angiography. Besides this, the narrowing and stenosis of the right vertebral artery had vanished, and the stent placed in the left common carotid artery was completely permeable.

DISCUSSION

We describe the observation of a patient with a resistant form of TAK who had a significant improvement following tocilizumab treatment. The patient experienced cerebral hypoperfusion as a result of newly formed vascular lesions, including extremely tight artery stenosis, despite receiving well-managed corticosteroid and methotrexate treatment. Following tocilizumab treatment with radiological proof of stability, the hypoperfusion symptoms vanished. Given that the pathophysiology of TAK is thought to involve interleukin 6, the effectiveness of the anti-IL-6R appears reasonable[2]. This pro-inflammatory cytokine stimulates endothelial fibrosis and inflammation simultaneously. By using the transcription activators (JAK-STAT) of the signalling pathways and the signal transducers of Janus kinase, it encourages fibroblast activation and collagen deposition[4]. These developments in the understanding of pathophysiology were not accompanied by data from evidence-based medicine supporting tocilizumab's effectiveness in TAK. This monoclonal antibody would not achieve the main goal of a randomised clinical trial, which

was to shorten the length of illness remission, but it would decrease the frequency of relapses, reduce corticosteroid doses and improve quality of life[5]. Tocilizumab has been demonstrated to be a corticosteroid-sparing agent, with a promising clinical response and mitigation of iatrogenesis in patients with refractory TAK in a more recent meta-analysis[6]. The expert group that created the ACR 2021 recommendations had favoured the use of anti-TNF, despite the lack of a randomised controlled trial comparing it to tocilizumab[3]. Numerous investigations on anti-TNF agents showed that most patients only saw a partial clinical response[7,8]. Nevertheless, according to a recent meta-analysis contrasting anti-TNF with anti-IL-6R, the two biological treatments were equivalent in terms of iatrogenic effects, angiographic stabilisation and clinical response[9].

CONCLUSION

The clinical effectiveness of anti-IL-6R during TAK appears promising based on our experience, other observations documented in the literature and the outcomes of the most recent clinical trials. The therapeutic management guidelines for TAK need to be revised. Despite the radiological stabilisation, our observation is noteworthy for the quick and significant improvement in clinical symptoms and quality of life.

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