Guillain-Barré syndrome in a patient on adalimumab for the treatment of psoriasis*

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Abstract: The use of TNF-α inhibitors for the treatment of moderate to severe psoriasis and psoriatic arthritis is increasingly more frequent. The authors report a case of Guillain-Barré syndrome as a late manifestation of the treatment with adalimumab. Although unusual, this is relevant for professionals who prescribe biologic drugs. We also stress the importance of investigating the past and family medical history regarding demyelinating diseases before starting treatment.
Keywords: Arthritis, psoriatic; Demyelinating diseases; Psoriasis; Guillain-Barre syndrome

INTRODUCTION

The treatment of moderate to severe psoriasis with biologics must be carried out in patients that are intolerant to traditional treatments or in whom these treatments failed.[1,2] Two classes of biologic drugs are highlighted: anti-TNF-α (tumor necrosis factor alpha inhibitors), such as etanercept, adalimumab and infliximab; and interleukin 12 and 23 (ustekinumab) and 17A (secukinumab) inhibitors. Studies demonstrated that these drugs are effective to provide remission and control of symptoms in moderate to severe psoriasis.[3] Among the main side effects related to them, infections, neoplasias and demyelinating diseases are of note.[4]

The objective of this article is to document a case of development of Guillain-Barré syndrome (GBS) during treatment with adalimumab for psoriasis and psoriatic arthritis and review the current literature.

CASE REPORT

A 45-year-old male patient had severe psoriasis for 10 years. We initially opted to treat with methotrexate (MTX), with improvement of skin lesions on the body but little improvement of lesions on the scalp. MTX was discontinued and we prescribed acitretin with phototherapy. Since there was no clinical improvement and the patient still complained of intense pruritus and axial and peripheral arthritis, adalimumab was started, with improvement of the joints and skin.

One year later, he presented to the emergency department complaining of acute pain in the lower limbs, difficulty walking and diarrhea, being treated with systemic steroids and opioids. He progressed to acute flaccid paralysis and respiratory insufficiency. Lumbar puncture and electroneuromyography were performed, and Guillain-Barré syndrome was diagnosed. Adalimumab was discontinued, and intravenous immunoglobulin and physical therapy were immediately started. The patient improved from the neurologic involvement but the flaccid paralysis in the lower limb remained.

DISCUSSION

GBS is an acute, autoimmune and demyelinating polyradiculoneuropathy, frequently severe and fulminant. It is characterized by areflexic motor paralysis of rapid onset, with

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Table 1: Cases under treatment with anti-TNF-α that developed Guillain-Barré syndrome*

	Infliximab	Etanercept	Adalimumab	Total
Reported cases	11	5	7	23
Rheumatoid arthritis	6	5	5	16
Psoriatic arthritis	2		1	3
Crohn's disease	2		1	3
Ulcerative colitis + spondyloarthropathy	1			1
Previous infections	RI: 3 FE: 2 V: 1	RI: 1 F: 1	RI: 1 FE: 1 F: 1 GE: 1 CJI: 1	RI: 5 FE: 3 F: 2 GE: 1 V: 1 CJI: 1

CJI: C. jejuni infection; FE: fever; F: flu; GE: gastroenteritis; RI: respiratory infection; V: flu vaccination. *Alvarez-Lario *et al*.[8]

or without sensory changes. The common pattern is ascending paralysis, that can be first noticed as heavy legs. Weakness appears within hours to days and, in the majority of cases, is accompanied by dysesthesia such as tingling sensation in the limbs. Motor sequelae persist in 5% to 10% of patients.[5-7]

About two-thirds of GBS cases occur one to three weeks after an acute infectious process, being *Campylobacter jejuni* the microorganism most commonly involved.[6,8] GBS also occurs with higher frequency in immunosuppressed patients, such as those with lymphoma, acquired immunodeficiency syndrome, systemic lupus erythematosus and Sjögren syndrome.[6]

As stated by Alvarez-Lario *et al*., there are few reports of demyelinating diseases linked to TNF-α inhibitors use: less than 30 cases were published according to PubMed's database. The search was conducted in December 2012, when 23 case reports of demyelinating diseases related to the use of anti-TNF-α were found. Eleven of those were related to infliximab; five to etanercept; and seven to adalimumab. The underlying disease was rheumatoid arthritis in 16 cases, Crohn's disease in 3 cases, psoriatic arthritis in 3 cases and ulcerative colitis associated to spondyloarthropathy in only 1 case. There was no report in a patient undergoing treatment for psoriasis. Previous infection was seen in 56.5% of cases, including respiratory infection in 5 cases, fever in 3 and flu symptoms in 2; flu vaccination, gastroenteritis and *C. jejuni* infection were related to 1 case each (Table 1).[8]

Anti-TNF-α agents can cross the blood-brain barrier, increasing its concentration in the compartment of the peripheral nervous system, reducing TNF-α concentration and prolonging the response of myelin-specific T-cells, triggering or worsening the demyelinating process.[9,10]

It is believed that anti-TNF-α could activate a latent infection, which could trigger an autoimmune process. This could deregulate TNF-α intrinsic balance and its receptors in the peripheral nervous system, creating a different gradient on each side of the blood-brain barrier, leading to an upregulation and resulting in inflammation and demyelination.[5,10]

Even though the patient was being treated with a TNF-α inhibitor, the development of GBS only occurred 12 months after the beginning of therapy. It is possible to state that the action of anti-TNF-α biologics in the onset of GBS is indirect. For example, the use of biologics increases the incidence and severity of infections and reduces the production of defense complexes; an infection in a patient with an altered immune system, producing less defense cytokines is the optimal environment for the development of GBS. The lack of complete improvement after discontinuing the medication makes the assessment of the relationship between adalimumab and the neurologic involvement difficult.

The occurrence of GBS and other demyelinating diseases during treatment with anti-TNF-α drugs is known. The causal relationship in this case cannot be established, but it is crucial to inquire about personal or family history of demyelinating diseases prior to biologic therapy. In this case, the patient had no previous infectious process, neither had improvement after cessation of therapy. Therefore, it was not possible to evaluate if the occurrence of GBS was only casual or a consequence of anti-TNF-α use.❑

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