

First case of demyelinating polyneuropathy probably related to treatment with golimumab

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Abstract

Treatment with anti-tumor necrosis factor alpha (anti-TNF α) drugs may lead to demyelinating polyneuropathies. Here, we present the case of a patient with rheumatic disease who developed sensory polyneuropathy probably related to anti-TNF α drugs. The patient was diagnosed with undifferentiated arthritis during treatment with weekly injection of golimumab. She presented a progressive picture of paresthesia of all four limbs, with distal and symmetrical predominance, associated with mild dysarthria and universal areflexia, except for the Achilles reflex. Hyperproteinorrachia was observed in a cerebrospinal fluid study, and demyelinating polyneuropathy with a sensory predominance appeared in an electroneurography/electromyography test. Full recovery was achieved, and 6 months later, the symptoms reappeared. The patient was discharged with a diagnosis of acute demyelinating polyneuropathy with sensory predominance and probable Guillain-Barré syndrome. In the absence of any other explanation, the symptoms of paresthesia were related to the administration of golimumab. After the drug was discontinued, the patient did not present the symptoms again.

Keywords: Polyneuropathies, golimumab, arthritis

Introduction

Among the adverse neurological effects of anti-tumor necrosis factor alpha (anti-TNF α) drugs, we can find the development of demyelinating diseases, including polyneuropathies (1).

We present the case of a patient with a history of undifferentiated arthritis who developed two episodes of sensory demyelinating polyneuropathy. Golimumab might have been involved in the etiopathogenesis of these episodes.

Case Presentation

The patient is a 58-year-old woman with a history of dyslipidemia, hypothyroidism (with good control for years over the blood levels of thyroid hormones and with excellent tolerance to medication), chronic migraine treated with injections of botulinum toxin, and since 2010, undifferentiated arthritis with overlapping clinical characteristics such as rheumatoid arthritis, spondyloarthritis, and sacroiliitis. Surgical operations included left ovarian cystectomy at the age of 25 years. The usual treatments included esomeprazole 40 mg (1-0-0), levothyroxine 50 μ g (1-0-0), desvenlafaxine 50 mg (1-0-0), methotrexate (6 tablets on Tuesdays), indometacin 25 mg (1-1-1), folate 5 mg (1 tablet on Wednesdays, Thursdays, and Fridays each), calcifediol (1 blister per month), and golimumab (1 injection per month started on November 26, 2015). The patient is allergic to celecoxib. She is an ex-smoker with a pack-year index of 10. She normally leads an active and independent life.

On March 21, 2016, the patient started experiencing paresthesia on the palms of both hands, and over the following days, it progressively spread to the soles of the feet, forearms, and legs in a symmetrical pattern. The fluctuating paresthesia also affected her thighs and arms. Together with these symptoms, the patient reported a more "nasal" voice. There were no other focal neurologic signs. Three weeks earlier, the patient had developed an upper respiratory tract infection that was treated with azithromycin. The last dose of golimumab (50 mg subcutaneously) had been administered 1 month prior to the onset of symptoms.

After 1 week of no improvement in the symptoms, the patient was admitted as an emergency. Neurological examination revealed mild dysarthria; universal areflexia except for the left brachioradialis reflex and the Achilles reflex, which were in all cases +/++++; and tacto-algesic hypoaesthesia of hands and feet with



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symmetrical and bilateral involvement. The vital constants and general examination were normal. She was hospitalized for further study and monitoring.

During hospitalization, the following complementary tests were performed: blood test (including blood levels of thyroid hormones, autoimmunity, and serology), urine, lumbar puncture (biochemistry, serology, and cultures), and neurophysiological study. The only pathological data found in the tests were hyperproteinorrhachia (240 mg/dL) and increased latency of the sensory potential in both median nerves and superficial peroneal and sural nerves. Given the lack of motor symptoms, the patient was not treated with intravenous immunoglobulins. The patient progressively improved, and the paresthesia areas retreated to hands and feet and dysarthria disappeared; however, the areflexia persisted.

The patient was discharged 8 days later with a diagnosis of acute demyelinating polyneuropathy with sensory predominance and probable Guillain-Barré syndrome due to areflexia, hyperproteinorrhachia, and the clinical picture of the infection that occurred 3 weeks earlier.

The dose of golimumab for the month of March was not administered because the patient was hospitalized. The dose for the month of April was not administered because the patient was traveling outside Spain; hence, the drug was administered again in May. She showed a favorable evolution over the next months until, on 13th September of the same year, she presented a clinical picture with similar characteristics but with lower intensity and no dysarthria (the last dose of golimumab was administered on August 19; hence, dysarthria reappeared again about 1 month from golimumab administration until the appearance of the symptoms). She was assessed as an emergency by the Neurology Department and was discharged on the same day. On an outpatient basis, some of the clinical tests were repeated, including blood analysis (thyroid hormones and autoimmunity, which were normal) and neurophysiological study, again appreciating increased latency of the sensory potential in both median nerves and superficial peroneal and sural nerves associated, in this occasion, with a slight decrease in nerve conduction velocity. In an ambulatory follow-up examination conducted some days later in the Unit of Cephalgia,

a possible connection was established between the symptoms and the administration of the anti-TNF α drug because in this case, there was no previous infectious episode, and a month had elapsed since the last golimumab injection. After this episode and by mutual agreement with the Department of Rheumatology, the drug was discontinued, and the patient has not presented similar manifestations since then.

Discussion

There are several published cases about patients treated with anti-TNF α drugs who later develop polyneuropathy symptoms. In most of these cases, there is a motor or sensorimotor involvement, and the drugs that mainly participate are adalimumab, etanercept, and infliximab (2-7).

We believe that the case of our patient is relevant because the drug associated with the clinical manifestations is golimumab, which appeared more recently than the ones mentioned above and, therefore, has been reported in fewer cases. The fact that the complementary tests performed for the etiological diagnosis were negative and that the symptoms have not appeared again after the drug was discontinued made us think that golimumab has played an essential role in the origin of the polyneuropathy. At the time of the first symptomatic presentation, the patient had a history of a respiratory infection, and the neurophysiological study was not very typical of the Guillain-Barré syndrome. However, at the second instance, there was no infectious antecedent, and in the new test that was performed, the velocity nerve conduction was slightly decreased, which was more associated with the disease.

Another reason that led us to publish this case is the particular characteristic of the symptoms, which were predominantly sensory. In literature, patients affected by motor polyneuropathy, with some components of sensory manifestations have been reported, although there are also cases in which the first episodes are sensory, and subsequently, after a repeated administration of the drug, the classical variant of the Guillain-Barré syndrome appears (3, 4, 7).

To date, the reason for the demyelinating effect of anti-TNF α drugs remains unclear. In contrast, there is a hypothesis that claims that they

facilitate infectious processes, and alternatively, there are complex mechanisms concerning the receptors and the apoptosis of T cells, which would ultimately lead to a decrease in TNF α in the nerve roots and endings, thereby promoting the action of T cells against myelin (5, 6).

In conclusion, due to the progressive appearance of new anti-TNF α drugs and their growing use in different pathologies, we must consider the possibility of similar adverse reactions. As some authors have suggested, we believe that it would be adequate to carry out a periodic assessment of the presence of signs and symptoms of a demyelinating disease, both at a central and a peripheral level, in patients who receive this type of drugs (6).

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