CASE REPORT

Infliximab induced chronic inflammatory demyelinating polyneuropathy: a case report

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Abstract

Background: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare immune-mediated disease of the peripheral nervous system characterized by motor weakness, sensory symptoms, areflexia, and specific electrophysiological findings. Rarely, Anti-Tumor Necrosis Factor-alpha (anti-TNFa) agents, which are used as a treatment for immune-mediated diseases, can cause neurological adverse effects on the central nervous system, as well as peripheral nervous system demyelination.

Case report: We describe the case of a 63-year-old woman with ankylosing spondylitis who developed chronic inflammatory demyelinating polyneuropathy after infliximab initiation. Considering the absence of other trigger agents from her medical history and the symptom onset, we assume that the development of CIDP is secondary to the anti-TNFa treatment.

Conclusion: Although demyelinating neurological complications of anti-TNF are rare, pharmacovigilance is required. HIPPOKRATIA 2019, 23(4): 179-180.

Keywords: anti-TNFa; infliximab; CIDP.

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Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare acquired immune-mediated disease of the peripheral nervous system (PNS), with a prevalence range between 0.8 to 8.9 per 100,000 population[1]. It is characterized by motor dysfunction of all limbs, sensory disorders, and areflexia[2]. CIDP may progress or relapse over a period of time[2]. Immunomodulating drugs such as oral corticosteroids, intravenous immunoglobulin G (IVIG), and plasma exchange are widely used for CIDP treatment; however, a disease-specific agent is not yet available[3]. It is thought to have multiple triggers, without a distinct causal factor.

Anti-Tumor Necrosis Factor-a (anti-TNFa) agents are an established treatment for various immune-mediated diseases. Although neurological complications of anti-TNFa are rare (<1 %), demyelination of both the central nervous system (CNS) and the peripheral nervous system have been lately described[4,5].

We describe a patient with ankylosing spondylitis (AS) who developed CIDP after the initiation of an anti-TNF agent.

Case report

A 63-year-old woman with AS was referred by her rheumatologist to our department due to paresthesias and muscle weakness. Personal medical history was significant for AS, thrombocytosis of unknown etiology, and a cardiac pacemaker due to persistent sinus bradycardia. No history of smoking, alcohol abuse, toxin exposure, recent infection, or vaccination was reported. Her family history was unremarkable for any demyelinating disease.

The patient received two sequential injections of a 5 mg infliximab with two weeks interval in between, for an AS relapse. Twenty four days after the first dose, she reported paresthesias of both feet, with gradual deterioration. On neurological assessment, we identified a proximal lower limb muscle weakness and paresthesias to the level of both knees, along with absences on the deep tendon reflexes on the lower limbs. Nerve conduction studies (NCS) were consistent with acute inflammatory demyelinating polyneuropathy (AIDP). Due to extensive degenerative bone lesions of the spine, computed tomography (CT)-guided lumbar puncture was performed, which was indicative of albuminocytologic dissociation. The laboratory testing revealed elevated anti-ganglioside GM1 titers[6].

At this point, infliximab was discontinued, and IVIG therapy was initiated. The patient received a dosage of 0.4 g/kg/d for five days, with a significant improvement of muscle strength and paresthesias.

Four months later, the patient experienced a clinical relapse of her neurological symptoms. The neurological assessment revealed a proximal weakness of the upper and lower extremities, right foot drop, steppage gait, numbness with stockings and gloves pattern, impaired light touch, and loss of vibration of lower limbs. New NCS revealed a reduction of motor conduction velocity

in bilateral peroneal and tibial nerves, a prolongation of F waves in the majority of nerves tested, and a motor distal and sensory nerve latency ≥50 % in all nerves tested. The patient fulfilled the clinical and electrodiagnostic criteria for CIDP[2], and according to the above, we revised our initial diagnosis of AIDP to CIDP. Thereafter, the patient was treated with 1 g/kg IVIG for two days every three weeks, remaining relatively stable.

Discussion

In the reported case, considering the absence of former infection or vaccination and the fact that the symptoms appeared and deteriorated after the initiation of infliximab, we assumed that the development of CIDP was secondary to anti- TNFa treatment.

According to the diagnostic criteria[2], CIDP should be considered in patients with progressive, recurrent symmetrical, or asymmetrical polyradiculoneuropathy of all limbs, with or without positive sensory symptoms and areflexia developing over at least two months.

The recommended treatment is IVIG or corticosteroids, and if they are ineffective, plasma exchange should also be considered. The recommended use of IVIG includes a loading dose of 0.4 g/kg/d over 2-5 consecutive days, and the maintenance dose is 1 g/kg over 1-2 days every three weeks[2].

Monoclonal antibodies are newly introduced and widely used pharmacological agents.

They have been occasionally connected with rare and potentially life-threatening adverse events[4]. Various anti-TNFa agents (infliximab, adalimumab, etanercept, golimumab, certolizumab pegol) have been correlated with demyelinating diseases of the nervous system[7,8]. Multiple studies indicate a possible role of anti-TNFa in the pathogenesis and evolution of CNS demyelinating diseases, but this connection is less clear for demyelinating diseases of PNS. Only a few cases of AIDP, CIDP, and motor neuropathy with conduction block have been described in literature[6,9-13]. However, the exact mechanism is unknown. Several hypotheses have been suggested to explain this adverse event: i) immunosuppression with a consequent susceptibility to infections, ii) autoimmunity, both cellular (elevated autoreactive peripheral T-cells) and humoral (high titers of anti-myelin and anti-Schwann-cell autoantibodies), and iii) imbalance of TNFa or its receptors[3,9,14].

We extended the previously reported anti-TNFa related CNS demyelination criteria to our case, which led us to the attribution of CIDP to infliximab and possibly the chronic use of anti-TNFa agents. Specifically, these are the following: i) obvious chronological concordance, ii) the lack of any other trigger event, iii) the stabilization and improvement of symptoms observed when treatment was ceased, iv) the pharmacodynamic pattern, v) previous reports of other cases of neurological disorders induced by TNF-alpha antagonist drugs[8,3].

Although demyelinating neurological complications of anti-TNF are rare, early discontinuation of the drug and initiation of immunomodulating treatment stop or improve symptoms. We must emphasize the role of pharmacovigilance and guide our patients treated with anti-TNFa agents to identify and report new neurological symptoms early.

Conflict of interest

Authors declare no conflict of interest.

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