Severe Neuropathy and Tetraparesis Induced by Adalimumab

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Abstract

We report a case of severe axonal and demyelinating peripheral polyneuropathy with consecutive tetraparesis following the second application of adalimumab in a 55-year-old man with rheumatoid arthritis. The treatment provided 40 mg of adalimumab s.c. every 2 weeks. Modest muscle pain and weakness followed the first dose, but the second dose resulted in progressive tetraparesis and complete immobility. Electroneurography revealed almost complete denervation of all muscles of the upper extremities, and no motor response at the lower extremities. The finding was suggestive of severe subchronic axonal and demyelinating peripheral polyneuropathy induced by adalimumab. A comprehensive medical work out excluded the possibility of other etiology. At discharge, methylprednisolone was continued for the next 3 months. Nine months of physical rehabilitation and supportive treatment resulted in a modest recovery. Anti-TNF-α agents may induce vasculitis neuropathy at any time during treatment which must be distinguished from the neuropathy of the underlying disease. Appropriate therapy should be initiated immediately and continued long enough.

Keywords: Anti-TNF-α neuropathy; Adalimumab neuropathy; Anti-TNF-α vasculitis

Introduction

Elevated levels of proinflammatory cytokine tumor necrosis factor alpha (TNF-α) were detected in patients with various immune diseases [1]. TNF-α inhibition represents a significant advance in the treatment of rheumatoid arthritis, and is useful in the treatment of ankylosing spondylitis, psoriatic arthritis, Crohn’s disease and ulcerative colitis [2]. Adalimumab is a human recombinant IgG1 anti-TNF monoclonal antibody that binds specifically to soluble and membrane-bound TNF-α and inhibits its interaction with the p55 and p75 cell surface TNF receptors [3]. Serious neurologic side effects suggestive of demyelination have been reported in patients receiving adalimumab or other anti-TNF agents [4, 5]. We describe an early and severe axonal and demyelinating peripheral polyneuropathy with consecutive tetraparesis following the second application of adalimumab in a patient with rheumatoid arthritis.
of circulating factors such as immunoglobulins, cytokines, and the blood-nerve barrier that results in increased vascular permeability and a breakdown of the development of inflammatory demyelination [7]. It exerts its effects by these T cells or macrophages and acts at several stages in the activation, circulation, and autoreactive T cells [6]. TNF-α is released into the circulation and at the site of inflammation to activate the development of inflammatory demyelination.

Discussion

An important step in the pathogenesis of inflammatory demyelination is the invasion of the peripheral nervous system by activated, circulating, autoreactive T cells [6]. TNF-α is released by these T cells or macrophages and acts at several stages in the development of inflammatory demyelination [7]. It exerts cytotoxic damage to vascular endothelium and a breakdown of the blood-nerve barrier that results in increased vascular permeability, which facilitates access to the nerve microenvironment of circulating factors such as immunoglobulins, cytokines, and complement [7, 8]. TNF-α may cause selective cytotoxic damage to Schwann cells and myelin sheaths [9], and may also represent a major noxious molecule by which macrophages damage peripheral nerve in Guillain-Barre syndrome [7].

The exacerbation of rheumatoid vasculitis, associated polymyositis, neurotoxic effect of adalimumab induced vasculitis or a combination of these factors were considered on differential diagnosis. The rheumatoid factor was highly increased, 1,518 IU/mL (normal ≤ 14) as were circulating immune complexes IgG 1,020 mg/L (normal ≤ 130) and IgM 1,415 mg/L (normal ≤ 100). For suspicion of adalimumab induced vasculitis, methylprednisolone was started at a dose of 1 mg/kg/b.w. Only 24 hours later, the patient became afebrile, and inflammatory parameters soon returned to normal.

Polyneuropathy was excluded by ENG, serologic test, and muscle biopsy. Anti-dsDNA, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibody, anti-myeloperoxidase antibodies, autoantibodies to proteinase 3, anti-cyclic citrullinated peptide antibody, anti Jo1, lupus anticoagulant, anti-cardiolipin antibodies, tests for cytomegalovirus, toxoplasmosis, HIV infection, antistreptolysin O, antistaphylolysin, thyroid hormones, and tumor markers were within the normal range. At discharge, methylprednisolone was continued for the next 3 months. Continuous physical therapy and symptomatic treatment were recommended.

Nine months later, neurologic examination indicated modest recovery of proximal segments and residual paresis of the fists and feet associated with significant muscular hypotrophy. ENG still showed severe distal polyneuropathy accompanied by the signs of complete denervation and satisfactory recovery of proximal segments comparing with previous finding.

Conflict of Interests

All authors deny any conflict of interests related to this manuscript.

References

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