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ANCA-related vasculitic neuropathy mimicking Motor Neuron Disease

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Abstract

Several conditions have been reported to mimic motor neuron disease (MND) and misdiagnosis remains a common clinical problem. Peripheral neuropathy is a classic feature of many vasculitic syndromes and in some patients it may be the only manifestation of vasculitis. We report a case of ANCA-related vasculitic neuropathy where the clinical presentation was suggestive of MND. A 42-year-old woman was admitted to our centre to confirm a diagnosis of MND made elsewhere. Clinical examination revealed postural tremor at the right hand, mild tongue atrophy with diffuse fasciculations and brisk tendon reflexes without other muscular weakness or atrophies. Electromyography demonstrated denervation in tongue and in the first dorsal interosseous of right hand ; motor evoked potentials disclosed normal central motor conduction time. Laboratory studies revealed only a mild increase of p-ANCA. A muscle biopsy showed a small inflammatory infiltrate around a vessel. The patient started high dosage of oral steroids. After one year of follow-up the patient suspended oral steroids, postural tremor of the right hand disappeared and tongue fasciculations were reduced. Vasculitis may mimic a MND, particularly in the absence of sensory involvement. Caution should be exercised in the clinical diagnosis of MND. Muscle biopsy is indicated in patient with atypical MND especially in those with an exclusive involvement of lower motor neuron.

Key words : Amyotrophic lateral sclerosis ; vasculitis ; infiltrates.

Introduction

Amyotrophic Lateral Sclerosis (ALS) is the most common and best recognized form of Motor Neuron Disease (MND). It is characterized by relentless degeneration of both upper and lower motor neurons leading to progressive muscular paralysis, with death usually occurring 1-5 years after the onset (Bonduelle, 1975). The clinical picture of ALS is usually stereotypical, resulting from a combination of signs secondary to dysfunction of both upper and lower motor neurons. Based on the clinical pattern in the initial phases of illness different variants have been described, including spinal, bulbar and pseudoneuritic forms, flail arm syndrome and Mill's hemiparetic type. Bulbar-onset of the disease is a common finding, particularly with advancing age. Criteria for diagnosis are based on the original El Escorial or revised Airlie House criteria (Brooks, 1994). Conditions such as multifocal motor neuropathy, Kennedy disease and inflammatory myopathies could all be misdiagnosed as ALS.

Vasculitis is a disorder in which blood vessel walls are infiltrated and destroyed by inflammatory cells, with secondary ischemic damage in the affected tissues (Fauci, 2001). An involvement of peripheral nerves and muscles may occur in association with various diseases including systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, infection, malignant neoplasia, and cryoglobulinemia. In addition to vasculitic neuropathies in the setting of these conditions, primary systemic vasculitis, including microscopic polyangiitis (MPA), Churg-Strauss syndrome, and Wegener's granulomatosis, are known to involve selectively the peripheral nervous system (Bouche *et al.*, 1986). Finally, vasculitis confined to the peripheral nervous system without systemic manifestations has been reported (Dyck *et al.*, 1986).

We describe an atypical case of ANCA-related vasculitis in which the initial clinical presentation was suggestive of ALS.

Case report

A 42-year-old woman was admitted to our centre that is the referral centre for ALS of Lazio Region to confirm a diagnosis of MND. She reported since one year tremor at the right hand and generalized weariness. Previous clinical history revealed only chronic gastritis and bilateral renal stones. A clinical diagnosis of MND was made elsewhere considering the presence at clinical visit of tongue fasciculations with brisk reflexes at all four limbs and denervation in tongue, first digital interosseous and tibialis anterior. Our examination confirmed mild tongue atrophy with weakness and diffuse fasciculations, brisk tendon reflexes and postural tremor at the right hand without other muscular weakness or atrophies. The patient underwent extensive laboratory tests, cranial and spinal cord

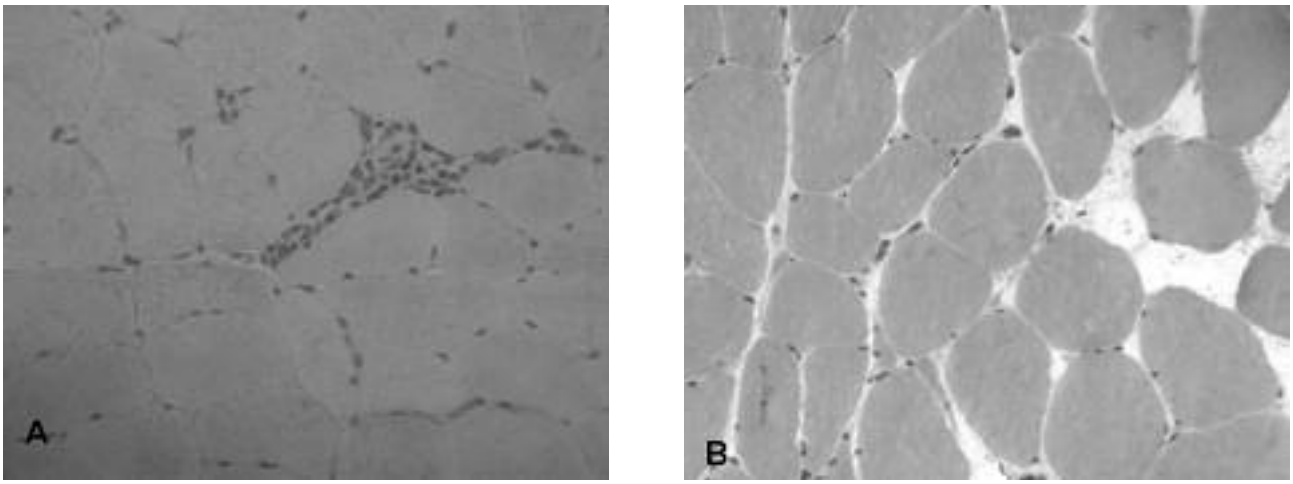

FIG. 1. — Muscle biopsy of left deltoid (PAS and H&E stain). Small perivascular inflammatory infiltrate with complete obliteration of vessel lumen (A) and scattered angulated fibers (B).

MRI, electromyographic examination, nerve conduction study, motor evoked potentials examination and functional respiratory tests. Laboratory studies including blood cell count, electrolyte level, erythrocyte sedimentation rate, C-reactive protein, creatine kinase level, immunofixation electrophoresis, FT3, FT4, TSH, hepatic enzymes, creatinine, urinalysis, antinuclear antibody (ANA), anti-DNA antibody, antineutrophil cytoplasmatic antibodies (ANCA), depressed C3 and C4 and dosage of anti-GM1, anti-GM2, anti-GD1, revealed only a mild increase of p-ANCA (MPO) with value of 76.00 UI/ml (normal range < 25). Analysis of cerebrospinal fluid was performed and was normal. Serologic tests for HBV, HCV and HIV were negative. Cranial and spinal MRI detected no abnormalites. Forced vital capacity as percent predicted was 100%. Motor and sensory nerve conduction study were normal. Electromyography demonstrated denervation in tongue and in the first dorsal interosseous of right hand. Motor evoked potentials disclosed normal central motor conduction time. Genetic test for Kennedy disease didn't show any amplification of polyglutamine repeat in the Androgen Receptor gene.

We performed a muscle biopsy that showed the presence of a perivascular inflammatory infiltrate together with some small endomysial infiltrates and scattered angulated fibers (Fig. 1A-B). We tried to characterize this inflammatory infiltrate with immunohistochemistry using antibody against human B cells (CD20), helper/inducer T cells (CD4), suppressor/cytotoxic T cells (CD8) and macrophages (CD68) but we couldn't find it in a section different from the one we show. This indeed suggested us the presence of an inflammatory process involving only focally scattered vessels.

All these findings were suggestive of ANCA-related vasculitis. The patient started high dosage oral steroids (prednisone 75 mg/daily). After six months of follow-up electrophysiological examination were repeated ; motor evoked potentials were still normal while electromyography showed denervation only in the tongue. Considering that the disease didn't show any progression the patient started to reduce the steroids. After one year of follow-up the patient suspended oral steroid, postural tremor of right hand disappeared and tongue fasciculations were reduced.

Discussion

Peripheral nervous system involvement is a common complication of systemic vasculitis and has been well documented. Although mononeuritis multiplex is thought to be the most frequent neuropathic manifestation of systemic and nonsystemic vasculitis, symmetrical polyneuropathy and asymmetrical sensory or motor neuropathy have also been reported in a considerable number of patients (Collins *et al.*, 2003).

We described a case of ANCA-related vasculitis in which cardinal feature was bilateral involvement of hypoglossal. Systemic signs or symptoms of sensory involvement were not present. Considering the absence of sensory impairment and the presence of clinical and electrophysiological findings of lower motor neuron involvement with brisk tendon reflexes at all four limbs a diagnosis of MND was made elsewhere. However, some elements that could suggest an alternative diagnosis like the absence of electrophysiological involvement of upper motor neuron prompted us to perform a muscle biopsy. The presence of a perivascular inflammatory infiltrate together with some small endomysial infiltrates and scattered angulated fibers (Fig. 1A-B) and the increased value of p-ANCA suggested the diagnosis of MPA. Although the patient didn't show any sign or symptom of other organ involvement, especially kidney that is frequently affected in this

primary systemic vasculitis, diagnostic criteria established for MPA were satisfied. These criteria include ANCA positivity or histology confirmation or both (Jennette *et al.*, 1994). Histological confirmation requires a necrotizing crescentic glomerulonephritis on renal biopsy if kidney is affected or necrotizing vasculitis of microscopic vessels (small arteries, arterioles, capillaries or venules) on biopsies from other sites.

The absence of disease progression after one year follow-up and the clinical improvement with steroids confirmed this diagnosis and excluded the presence of a MND.

Vasculitis like MPA may mimic MND, particularly in the absence of sensory involvement. Caution should be exercised in the clinical diagnosis of MND. Muscle biopsy is indicated in patients with atypical MND especially in those with an exclusive involvement of lower motor neuron.

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