

Autoimmune Disorder of the Central and Peripheral Nervous Systems: Report of a Case With Very Long Follow-Up

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Received 2015 February 25; Accepted 2015 July 4.

Abstract

Introduction: Autoimmune diseases usually affect central or peripheral nervous system and can affect both only in rare cases.

Case Presentation: A 55-year-old female was referred with symptoms of multiple mononeuritis associated with central signs and she had a dramatic improvement with steroid therapy. An attempt to stop steroid therapy after four years resulted in an almost immediate reappearance of symptoms. Despite some episodes of paresthesias or weakness in the lower limbs, steroid therapy at full dosage prolonged until the age of 76 years allowing an almost normal life. At the age of 86 years, the patient has been relatively well.

Conclusions: Overlap syndrome of some autoimmune diseases is discussed; need for a very prolonged therapy, non-response to intravenous immunoglobulin and relatively good prognosis are stressed.

Keywords: Autoimmune Disease, Central Nervous System, Multiple Sclerosis, Peripheral Nervous System, Guillain Barre Syndrome

1. Introduction

Autoimmune diseases usually affect central or peripheral nervous system. However, several studies have shown that diseases with predominantly central involvement, such as multiple sclerosis, frequently affect peripheral nervous system. Conversely, diseases with predominantly peripheral involvement, such as the Guillain-Barre' syndrome (GBS), may also affect the central nervous system. Usually these are subclinical damages detectable through instrumental examinations; however, in rare cases, damages can become of clinical importance.

2. Case Presentation

A 55-year-old female, in August 1982, was referred with weakness in the right lower limb. Within few weeks, she developed paresthesias in the territory of the left ulnar nerve and in the lateral aspect of the left thigh; also, numbness in the right hand, instability in walking, diplopia and burning tongue. Familial history was negative for neurological diseases; the only remarkable personal history was borderline arterial hypertension; no recent symptoms of upper respiratory tract infections, flu-like illness or diarrhea were noted. The patient was hospitalized three months after the symptoms onset. Neurological examination showed diplopia in the left lateral gaze, lack of strength in the left upper limb, especially distally with atrophy of the thenar and ipothernar muscles and ipotrophy of the left quadriceps muscle. There was hy-

poesthesia in the territory of the left ulnar nerve, in the anterolateral aspect of the thigh and the left hemithorax. The stiloradial, bicipital and ankle jerks were absent bilaterally; the left and right patellar and the left tricipital jerks were brisk and Babinski's-sign was present on the right. Gait was ataxic and the blood pressure was 180/100 mmHg. Blood tests including electrophoresis, Widal's and Wright's tests, tuberculin test and thyroid function had normal findings; chest X-ray, myelography and CT-scan of the brain had normal findings as well. Cerebrospinal fluid (CSF) analysis showed lymphocytes 33, protein 110 mg (normal range 25 - 45 mg), IgG 7.2 mg (normal range 0.8 - 3.8 mg), albumin 32.4 (normal range 12 - 29 mg), IgG/albumin ratio 22.4% (normal range 10% - 22%) and the Link index 0.55 (normal range 0.50 - 0.80). An electromyographic examination showed chronic neuropathic changes in the right and left interosseus muscles, in the left deltoid muscle and the right quadriceps femoris muscle. The motor conduction velocity (MCV) of the left ulnar nerve was 20 m/second with polyphasic potentials. Stimulating the facial nerve yielded a response with latency of 5.8 milliseconds from the frontal muscle and with latency of 4.6 milliseconds from the orbicularis oculi muscle. Biopsy of the left quadriceps muscle showed mild atrophy due to neurogenic damage or inactivity. Therapy with 1 mg/kg prednisone quickly resulted in dramatic improvement of symptoms. After discharge and despite steroid therapy, the patient continued to have

episodes of paresthesias and/or weakness in the territory of one or more nerves; these events were not disabling and symptoms receded when the prednisone dosage increased over a short time. An attempt to stop prednisone after a prolonged period of wellbeing was made in 1986 when the patient aged 59 years, resulting in an almost immediate reappearance of symptoms, which subsequently receded when the therapy was resumed. With the exception of some episodes of paresthesias or modest weakness in the lower limbs, the patient's conditions remained generally good allowing an almost normal life until June 1998. After a prolonged period of immobility because of femur fracture following a car accident, the patient re-experienced paresthesias and weakness in the lower limbs. Neurological examination showed hyposthenia prevailing in the left lower limb with distal hypotrophy and hypopallesthesia, left Babinski's-sign, urge incontinence and waddling gait. Brain and cervical spine MRIs yielded normal findings as well as blood tests. CSF analysis showed protein of 104 mg, IgG 6.34 mg, Pandy's reaction was negative and there were no oligoclonal bands. electromyography (EMG) showed axonal neuropathy in the left Superficial peroneal nerve (SPE); somatosensory evoked potentials (SEP) from the upper limbs were normal, whereas no response could be recorded from the lower limbs. The P100 wave of the visual evoked potentials (VEP) was prolonged. A therapeutic attempt with immunoglobulins intravenously was ineffective. In December 1998, a neurological examination showed weaknesses of the orbicular muscles of the eyelids, cheeks bilaterally, left hand fifth finger's abductor and lower limbs and hypotrophy of the proximal muscles. The patient could stand despite a waddling gait. In CSF analysis, protein was 95 mg, cells 2, VDRL and Pandy's reaction negative, IgG 5.43 mg, the Link index 0.55 and absent oligoclonal bands. MRI of the brain had normal findings. Distal latency of the left and right SPE were respectively 4.4 milliseconds and 4.5 milliseconds with MCV of 51 m/second and 50 m/second, amplitudes were 0.30 mV and 0.40 mV, respectively; latency of distal response of the ulnar nerve was 2.6 milliseconds on the left and 3.1 milliseconds on the right with an amplitude of 2.10 mV and 5 mV, respectively; latency of distal response of the sural nerve was 1.7 milliseconds on the left and 2.5 milliseconds on the right with an amplitude of 10 mV and 13 mV, respectively. SEP and motor evoked potentials (MEP) of the lower limbs had normal findings; whereas, VEP was of low amplitude. A new biopsy of the right quadriceps femoris muscle showed non-specific myopathy likely due to chronic steroid therapy. A few months of steroid therapy at full dosage determined remarkable improvements and allowed a life completely independent, consequently prednisone was slowly reduced to 10 mg/die. In 2003 (age 76 years), the patient stopped using steroid, but adrenal insufficiency symptoms appeared and necessitated resumption of steroid therapy. The last EMG in 2012 (age 85 years) showed latency of distal potential

of the nerve SPE as 2.30 milliseconds on the left and 2.40 milliseconds on the right with amplitudes of 2.3 mV and 1.1 mV, respectively; latency of distal potential of the nerve SPI were 5.45 milliseconds on the left and 4.45 milliseconds on the right with amplitudes of 2.95 mV and 1.7 mV, respectively; latency of distal potential of the sural nerve were 2.30 milliseconds on the left and 2.40 milliseconds on the right with amplitudes of 4.30 mV and 8.5 mV, respectively. Neurological examination in September 2013 (age 86 years) showed atrophy of the interosseous muscles of the hands bilaterally and proximal lower limbs weakness with atrophy of the left buttock. Proximal motility in the upper limbs was limited because of bilateral periarthritis. The patient walked autonomously at home, whereas in the last two years a walker was needed for outside walking.

3. Discussion

The disease started as a multiple mononeuritis associated with central signs and over the years developed into an axonal neuropathy associated with relapses characterized by signs of CNS involvement. The literature discusses a number of PNS diseases such as chronic idiopathic demyelinating polyneuropathy (CIDP) and GBS, which may involve CNS as well (1); conversely, some diseases of CNS including multiple sclerosis are known to show signs of peripheral involvement (2), albeit rarely and typically resulting in subclinical involvement, usually detectable only through instrumental examinations and in extremely rare cases, simultaneous involvement of CNS and PNS has shown clinical relevance. The overlap between GBS, the Fisher's syndrome and the Bickerstaff's brainstem encephalitis should be considered as some authors (3) proposed the term "anti-GQ1b IgG antibody syndrome" including ataxic GBS, ophthalmoparesis without acute ataxia, isolated internal ophthalmoplegia, acute oropharyngeal palsy and pharyngeal-cervical-brachial weakness. The common element in the above cases is presence of anti-GQ1b antibodies cross-reacting with GT1a expressed in oculomotor nerves, in motor nerves of the limbs and in muscle spindles. Patients with a clinically relevant involvement of both CNS and PNS were reviewed by Kamm and Zettl (4): 37 cases, of which 32 adults with onset age of 10 to 65 years and 5 children with onset age of 22 months to 9 years were assessed. In 26 cases, initial symptoms were related to CNS involvement and in 7 cases involvement of PNS; whereas, in 3 cases central and peripheral signs appeared at the same time and in 1 case reliable data was missing. In our patient, central and peripheral signs likely appeared simultaneously. Although clinical signs were related to PNS involvement already in the first hospitalization, some reflexes were brisk and the Babinski's-sign could be observed. The possibility that central signs were due to arterial hypertension was excluded since in multiple occasions CT scans or MRIs showed no vascular damage. However in CSF in

the first examination, a mild pleiocytosis and elevated protein levels were found, in the following examinations only elevated protein levels remained and oligoclonal bands were never found. These data are similar to those found in GBS syndrome where pleiocytosis is found in a minority of patients, while increased proteins are more common (5). Unfortunately, anti-GQ1b antibodies have never been assayed. The patient had no response to intravenous immunoglobulins, whereas she had a good response to steroids; the therapy needed to be continued for many years because an attempt to discontinue it after four years caused an immediate recurrence of symptoms. A very long follow-up of over thirty years allowed us to exclude diseases such as sarcoidosis or malignancy and evaluate the effectiveness of steroid therapy, which allowed the patient to live an active life despite some relapses. CIDP can also manifest as multiple mononeuritis demyelinating or axonal and often associated with increased CSF protein, but without CNS damage. It remains the question how to classify these diseases. An axonal GBS was described in a patient with multiple sclerosis and it seems unlikely to be a casual association; it is more likely a primary immunologic reaction against the myelin or

the axons. Autoantibodies to gangliosides GM1 and GD1 are associated with motor axonal neuropathy and its subtypes, whereas autoantibodies to GQ1b are associated with Miller-Fisher's syndrome and its subtypes. In some cases, antibodies develop against two different gangliosides, thus explaining coexistence of damage to CNS and PNS (6).

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