Journal of Neuroimmunology 264 (2013) 130–133

Contents lists available at ScienceDirect

Journal of Neuroimmunology

journal homepage: www.elsevier.com/locate/jneuroim

Short communication

Muscle-specific kinase antibody positive myaesthenia gravis and multiple sclerosis co-presentation: A case report and literature review

Jessica Sylvester [a,*], Grant Purdie [b], Mark Slee [c], James X. Gray [d], Simon Burnet [e], Simon Koblar [f]

[a] Neurology Department (Clinical Administration 3E), Royal North Shore Hospital, Reserve Rd, St Leonards, NSW 2065, Australia
[b] Neurology Department, Queen Elizabeth Hospital, Woodville Rd, Woodville, SA 5011, Australia
[c] Neurology Department, Flinders Medical Centre, Flinders Drive, Bedford Park, SA 5042, Australia
[d] Haematology Department, Queen Elizabeth Hospital, Woodville Rd, Woodville, SA 5011, Australia
[e] Rheumatology Department, Queen Elizabeth Hospital, Woodville Rd, Woodville, SA 5011, Australia
[f] School of Medicine, University of Adelaide, North Terrace, Adelaide, SA 5000, Australia

ARTICLE INFO

Article history:
Received 19 June 2013
Received in revised form 20 August 2013
Accepted 26 August 2013

Keywords:
Myaesthenia gravis
Multiple sclerosis
Muscle-specific kinase antibody
Demyelination

ABSTRACT

We present the first case of simultaneous muscle-specific kinase antibody positive myaesthenia gravis and relapsing–remitting multiple sclerosis to be reported in the English literature along with the inherent diagnostic and treatment challenges. There may be an association between myaesthenia and central nervous system demyelination. We identified 72 previously published cases of myaesthenia with central nervous system demyelination. Of 19 cases of myaesthenia with relapsing–remitting multiple sclerosis, nine (47%) were acetylcholine receptor antibody negative, but there were no previously published cases with muscle-specific kinase antibody. Further research is required to clarify this association and optimal treatment in such cases.

© 2013 Elsevier B.V. All rights reserved.

1. Case summary

A 48-year-old Caucasian male manager presented in November 2009 with left hemiparaesthesia lasting ten hours. A provisional diagnosis of transient ischaemic attack was made following standard cerebrovascular investigation.

In November 2010, he presented with lethargy, intermittent diplopia, phonophobia, episodic slurred speech, unsteadiness of gait, short-term memory loss, and impaired concentration. He reported two episodes of transient neurological symptoms lasting more than 24 h in the five months prior—an episode of blurring of the right visual field and an episode of mild right hemiparesis. His neurological examination was normal. Magnetic resonance imaging (MRI) of the brain revealed 8 small cortical foci of non-specific hyperintense T2 signal.

In March 2011, he was admitted to the hospital with severe fatigue, diplopia, dysphonia, dysphagia, unsteadiness of gait and involuntary upper limb jerks. His symptoms were more prominent in the evening. Examination revealed myoclonic jerks of the upper limbs, fatigable bilateral ptosis and dysphonia. His upper and lower limb power was normal and not fatigable. There were no pyramidal, cerebellar or sensory abnormalities. His weakness progressed to a diurnal pattern of marked neck extensor and proximal lower limb weakness. There was no metabolic or endocrine disturbance on routine laboratory testing. The patient was on regular low-dose aspirin and a statin, and other medication.

Brain MRI demonstrated new multifocal T2 hyperintense lesions in a periventricular distribution (Fig. 1). Cerebrospinal fluid (CSF) analysis was positive for unmatched oligoclonal bands. CSF cell count and biochemistry were normal. Visual evoked responses were abnormally prolonged in the right eye. Anti-acetylcholine receptor binding antibody (AChR Ab) was negative. There was no thymic mass on computed-tomography (CT) of his chest. Autoimmune and metabolic screening was normal. Anti-muscle-specific kinase binding antibody (MuSK Ab) was requested but there was a technical delay in the result being reported.

A clinical diagnosis of seronegative myaesthenia gravis (MG) and concurrent relapsing–remitting multiple sclerosis (RRMS) was proposed. Treatment was commenced with pyridostigmine and oral prednisolone (1 mg/kg per day). Although, pyridostigmine was not tolerated due to diarrhoea, he nonetheless improved and after 6 weeks steroid treatment was reduced by 0.125 mg/kg every month and ceased after 8 months.

In May 2011, his diplopia recurred with signs consistent with bilateral internuclear ophthalmoplegia. Interferon-beta 1a therapy was commenced (44 micrograms three times per week by subcutaneous injection). Brain MRI with gadolinium did not reveal any new or enhancing T2 lesions. During the following three months his symptoms progressed with limb weakness, dysarthria, gastro-oesophageal reflux, exertional dyspnoea and upper limb myoclonic jerks. These symptoms

* Corresponding author. Tel.: +61 2 9463 1835; fax: +61 2 9463 1058.
E-mail address: jsyl2313@uni.sydney.edu.au (J. Sylvester).

0165-5728/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jneuroim.2013.08.016

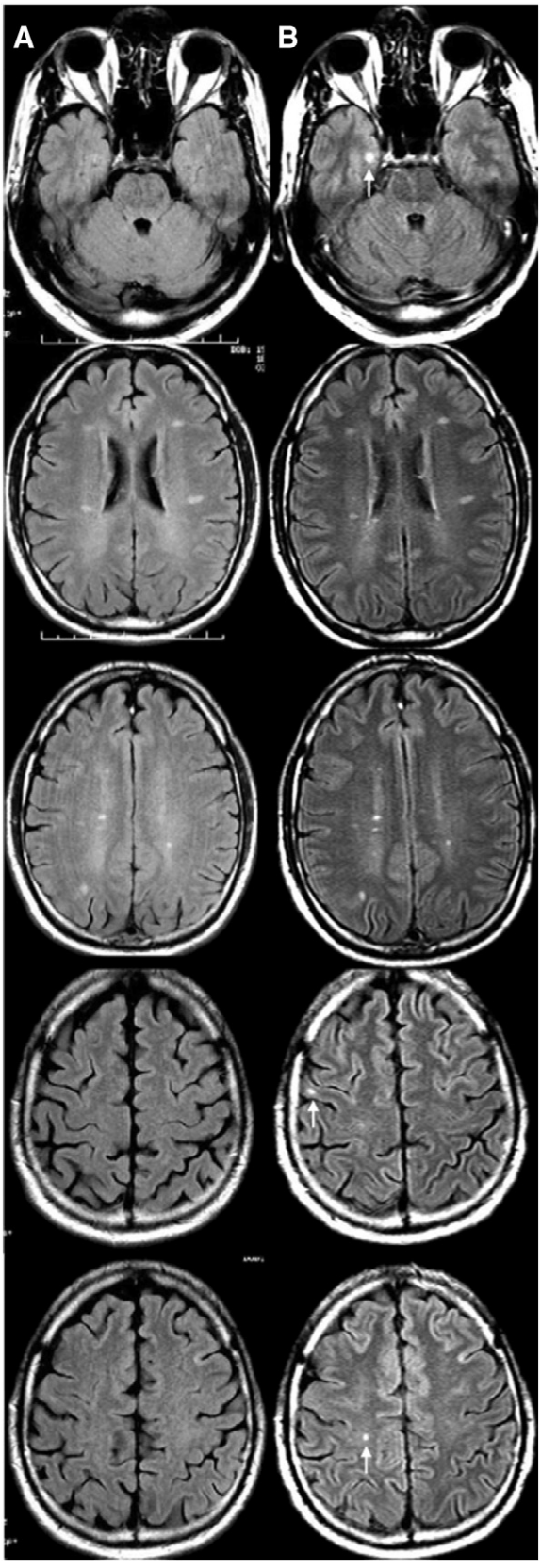

Fig. 1. MRI of the brain (A) Axial FLAIR sequences from November 2010 showing 8 small hyperintense foci and (B) Axial FLAIR sequences from March 2011 showing interval development of new hyperintense lesions *(marked with white arrows)*.

resolved within a week of high dose oral prednisolone (1.5 mg/kg per day) but recurred when the dose was reduced. Azathioprine was introduced but was not tolerated and failed to replace steroid treatment. At this time, positive MuSK binding Ab (titre 0.78 nmol/L) from March 2011 was reported and the diagnosis of MuSK MG (MMG) was confirmed.

In October 2011, interferon-beta therapy was stopped and he commenced rituximab (375 mg per m^2 weekly for four weeks then monthly for five months). Oral steroid treatment was weaned. After completing rituximab he developed a seronegative inflammatory polyarthropathy requiring oral methotrexate therapy. Laboratory investigations were negative for rheumatoid factor, anti-nuclear antibodies, extractable nuclear antigens (SS-A, SS-B, RNP, SM, Scl-70, Jo-1, PCNA, ribosomal P, PM-Scl), anti-neutrophil cytoplasmic antibodies, lupus anticoagulant, cyclic citrullinated peptide antibodies, and antiphospholipid antibodies. C related peptide (CRP) was 4.0 mg/L (normal < 3.0 mg/L). Creatine kinase, C3 and C4 complement were all within normal limits.

By October 2012, he had no detectable anti-MuSK Ab. Lymphocyte studies found no detectable B cell population.

At three years since his original presentation he has been free of symptoms of MMG for 12 months and there have been no further symptoms suggestive of demyelination.

2. Discussion

2.1. Muscle-specific kinase antibody positive myaesthenia gravis

MuSK is an agrin-dependent protein on the muscle surface that plays a key role in clustering AChR at the end plate zone of the neuromuscular junction. Antibodies to MuSK are found in 40 to 70% of patients with AChR Ab negative MG. MMG is more common in women and presents in younger patients than AChR Ab positive MG (Pasnoor et al., 2010).

Clinical features of MMG and AChR Ab positive MG are similar, although isolated ocular myaesthenia is rare in MMG. Neck, shoulder girdle and respiratory muscle weakness are prominent in MMG, and these patients are more prone to the adverse effects of acetylcholine esterase inhibitors (Guptill and Sanders, 2010).

MuSK has been shown to be expressed in neuronal and non-neuronal central nervous system (CNS) tissues in rats, including hippocampal expression. There are reports of CNS symptoms in humans with MMG, including seizures and cognitive impairment (Garcia-Osta et al., 2006; Bhagavati et al., 2007; Lanfranconi et al., 2011). This patient experienced myoclonic upper limb jerks and cognitive difficulties that resolved when his myaesthenia was treated. There was no medication or metabolic disturbance, such as renal, hepatic or thyroid dysfunction, to which this was attributable.

Pseudo-internuclear ophthalmoplegia has been well described in ocular MG and this was a confounding sign in this case in view of the concurrent presentation of RRMS (Ito et al., 1997). MRI scans of the midbrain did not show demyelination at times of ocular presentation and clinically we favour the opinion that this was due to his MMG rather than RRMS.

2.2. MG and associated CNS demyelination

We propose that this case presented concurrently with MMG and RRMS. There were typical MRI lesions suggestive of MS and evidence of dissemination in time with new T2 lesions on follow-up MRI. This, along with his episodic neurological symptoms, fulfilled the revised 2010 McDonald criteria for a diagnosis of RRMS (Polman et al., 2011). Although his initial symptoms in November 2010, attributed to a transient ischaemic attack, did not persist for more than 24 h, in retrospect the authors feel it is more probable that this was a first episode of demyelination. A prolonged visual evoked response and CSF oligoclonal bands support the diagnosis of multiple sclerosis.

Download English Version:

https://daneshyari.com/en/article/6020608

Download Persian Version:

https://daneshyari.com/article/6020608

Daneshyari.com