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Clinical research paper

Atopic myelitis with focal amyotrophy: A possible link to Hopkins syndrome

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Abstract

Among 22 consecutive patients with myelitis, of unknown etiology, and atopic diathesis (atopic myelitis) who from April 2002 to March 2006 had been studied in our clinic, 5 (23%) showed focal amyotrophy in one or two limbs. These 5 patients were subjected to combined clinical, electrophysiological, neuroimaging and immunological studies. Ages were 18 to 58-years-old (average 39). Four showed amyotrophy of unilateral or bilateral upper limbs while one showed amyotrophy in both thighs. All patients showed on-going denervation potentials in the affected muscles, while motor conduction study including F wave was normal except for in one patient who showed prolonged F wave latency in one nerve. Two had localized high signal intensity lesions involving anterior horns on spinal cord MRI and three showed abnormalities suggesting pyramidal tract involvement on motor evoked potentials. All had a present and/or past history of atopic disorders and specific IgE against common environmental allergens, such as mite antigens and cedar pollens, and four showed mild eosinophilia, all of which were compatible with atopic myelitis. When clinical and laboratory findings were compared between atopic myelitis with ($n=5$) or without focal amyotrophy ($n=17$), the former showed a significantly higher frequency of present and past history of asthma (80% vs. 24%, $p=0.0393$) and tended to have higher EDSS scores (3.8 ± 1.6 vs. 3.1 ± 1.4). Two patients showed mild to moderate improvements after immunotherapies such as methylprednisolone pulse therapy or plasma exchange, while two recovered with low dose corticosteroids and one without treatment had a gradually progressive course.

Although atopic myelitis preferentially involves the posterior column of the cervical spinal cord, it is possible that anterior horn cells are affected in some cases of atopic myelitis, especially in patients with asthma. This suggests a possible link between atopic myelitis and Hopkins syndrome (asthmatic amyotrophy).

Keywords: Myelitis; Atopy; Muscle atrophy; Anterior horn; IgE

1. Introduction

Atopic myelitis (AM) is a myelitis of unknown cause that occurs in patients with longstanding atopic disorders, such as atopic dermatitis and airway allergy [1,2]. The disease preferentially affects the posterior column of the cervical spinal cord, thus predominantly presenting paresthesia/dysestheisa in the distal parts of four limbs [1–3]. The condition has been reported in Japan [4] and recently also in Europe [5].

On the other hand, Hopkins syndrome, asthmatic amyotrophy, is a rare disease involving anterior horn cells following an acute asthma attack [6]. This condition usually affects children with atopic asthma. Typically, from several days to a few weeks after an acute asthma attack, affected children show acute onset of flaccid paralysis of one or two limbs, later resulting in severe muscle atrophy of the affected limb [7]. There is a poor response to corticosteroids in most cases, which usually show no recurrence [8]. We previously

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reported the occurrence of asthmatic amyotrophy in adults [9]. Interestingly, one of our patients showed two attacks affecting different limbs following separate asthma attacks and had involvement of the pyramidal and sensory tracts in addition to anterior horn cell damage. Such a case, having transitional features between asthmatic amyotrophy and AM, suggests a possible link between the two conditions.

Here we describe young to middle-aged adult patients with AM showing focal amyotrophy and characterize their features, which further support such a link.

2. Subjects and methods

2.1. Subjects

Twenty-two consecutive patients with myelitis and atopic diathesis, who had been referred to our Department of Neurology, Kyushu University Hospital, and who were comprehensively studied from April 2002 to March 2006, were enrolled in the present study. All met the proposed criteria for AM [1–4], i.e., myelitis of an unknown cause with either (1) hyperIgEaemia and allergen-specific IgE positivity against common allergens, such as *Dermatophagoides pteronyssinus* (*D. pteronyssinus*), *Dermatophagoides farinae* (*D. farinae*), and cedar pollen, or (2) coexistent atopic diseases. Subjects were 9 men and 13 women, mean age at onset was 37.7±12.4 years, mean age at examination was 39.7± 12.5 years and disease duration was 22±38 months before admission (3 days to 15 years). Mode of onset and clinical course were acute monophasic in 5, acute relapsing or fluctuating in 7, subacute in 3 and chronic in 6.

Their clinically estimated main lesions were cervical cord in 18, thoracic cord in 3 and lumbar cord in 1. Disability was evaluated according to the Kurtzke's expanded disability status scale (EDSS) scores [10] and the mean±SD was 3.3± 1.3. Twenty-one had coexistent atopic disorders, i.e., allergic rhinitis in 14, atopic dermatitis in 3, bronchial asthma in 3, food allergy in 3 and allergic conjunctivitis in 2, while only 1 patient had no coexistent atopic disorder but did have a past history of asthma. HyperIgEaemia was present in 14 (63.6%) and all had allergen-specific IgE. Cerebrospinal fluid (CSF) cell counts were normal in all and protein increase (higher than 40 mg/dl) was present in 4/21 (19.0%).

2.2. Assay for total and allergen-specific IgE

Total serum IgE and allergen-specific IgE were measured by an enzyme-linked immunosorbent assay (ELISA), as described previously [9]. The allergens studied were two mite antigens (*D. farinae* and *D. pteronyssinus*), cedar pollen, Candida, egg white, milk, wheat, rice, soybean, mold, anisakis and animal skins.

2.3. Magnetic resonance imaging

All MR studies were performed using 1.5T units, Magnetom Vision and Symphony (Siemens Medical Systems, Erlangen, Germany) [11]. The typical imaging parameters of the spinal cord were as follows: sagittal T2-weighted turbo spin-echo imaging using TR/TE range= 2500–2800/90–116 MS, flip angle=180°, number of excitations=3–4; sagittal T1-weighted spin-echo imaging using TR/TE range=400–440/11–12 MS. flip angle range=90–170°, number of excitations=2–3; axial T2-weighted turbo spin-echo imaging TR/TE range=3200–5360/99–116 MS, flip angle=180°, number of excitations=3–4; axial T1-weighted spin-echo imaging using TR/TE range=400–440/12 MS, flip angle range=90–170°, number of excitations=2. For sagittal imaging, a matrix of 256×256 or 512×512, a slice thickness of 4 mm and a slice gap of 0.4 mm were used, and for axial imaging, a matrix of 256×256 or 512×512, a slice thickness of 5 mm, and a slice gap range of 1.5–5 mm were used. Gadopentetate dimeglumine at 0.1 mmol/kg body weight was administered intravenously for contrast-enhanced studies. The typical imaging parameters of muscles were as follows: sagittal and axial T2-weighted turbo spin-echo imaging using TR/TE range=3120–3880/90–94 MS, flip angle=150°, number of excitations=1–2; precontrast and postcontrast sagittal and axial T1-weighted spin-echo imaging using TR/TE range=400–694/7.7–11 MS, flip angle range=75–90°, number of excitations=1–2. For sagittal and axial imaging, a matrix of 256×256, a slice thickness of 5 mm and a slice gap of 6.5–15 mm were used. Fat saturation pulse was used for T2-weighted turbo spine-echo imaging and postcontrast T1-weighted spine-echo imaging. Gadopentetate dimeglumine at 0.1 mmol/kg of body weight was administered for postcontrast imaging.

2.4. Evoked potentials

Motor evoked potentials (MEPs) with transcranial magnetic stimulation were recorded as previously described [12]. Upper limb MEPs were recorded from the abductor pollicis brevis muscle. To stimulate the hand motor area, the center of the eight-shaped coil was placed over a point 2 cm anterior to either C3 or C4 (International 10-20 System). To stimulate the cervical root, the center of the coil was placed on the posterior neck over the 7th cervical spinous process. Lower limb MEPs were recorded from the abductor hallucis muscle. To stimulate the leg motor area, the coil was positioned over the vertex. Magnetic stimulation to the lumbar root was performed by placing the center of the coil over the 4th lumbar spinous process. Somatosensory evoked potentials (SEPs) were analyzed following electric stimulation of the median nerve. The peak amplitudes of the far-field P14 and the cortical N20 were measured. The latency of each peak was also measured. When MEPs were either unevoked by scalp simulation but were normally elicited by cervical or lumbar stimulation, or when central conduction time was abnormally prolonged, the pyramidal tract was considered to be involved, as described previously [12]. Normal range of MEP latency was set as the mean±3SD msec by the study of more than 40 healthy subjects [12].