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Clinical and laboratory characteristics of atopic myelitis: Korean experience

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ABSTRACT

HyperIgEemia and atopy have recently been reported to be related to various neurological diseases such as Hirayama disease and idiopathic myelitis. The aims of this study are to determine frequency of atopy or hyperIgEemia in idiopathic myelitis and to characterize the clinical and laboratory profiles of atopic myelitis (AM). From January 2006 to August 2008, 29 consecutive patients with idiopathic myelitis were recruited. We compared demographic data, laboratory results and radiologic findings between patients with atopic diathesis and those without. Allergic or atopic history was found in only 4 patients (13%), but hyperIgEemia and mite antigen-specific IgE were observed in 17 (58%) and 19 (65%) of idiopathic myelitis patients, respectively. Patients with AM ($n = 14$, 48%) showed the following distinctive features: (1) younger age at onset, (2) non-acute onset and long duration of symptoms at admission, (3) predominant sensory symptoms with mild weakness, (4) low EDSS score, (5) low frequency of abnormal SEP findings, and (6) increased eosinophils in peripheral blood. Common MR findings of AM included eccentric lesions occupying more than two-thirds of spinal cord with focal peripheral enhancement on axial image. These lesions were usually extended over more than 3 to 5 vertebral segments with cord swelling. HyperIgEemia and mite antigen-specific IgE are fairly common in idiopathic myelitis patients. The AM patients show relatively homogenous clinicolaboratory and radiological features. It is noteworthy that none of these patients showed brain abnormalities suggestive of multiple sclerosis or neuromyelitis optica (NMO).

1. Introduction

Atopy refers to enhanced IgE response to common antigens. Recently, various neurological diseases including Hopkins' syndrome [1], Hirayama disease [2,3] and idiopathic myelitis [4–7] have been found to be related to atopy such as atopic dermatitis, allergic rhinitis, or bronchial asthma. Kira et al. were first to describe 4 patients with atopic dermatitis suffering from myelitis during the exacerbation of atopic symptoms [4]. More recently, they found a substantial portion of idiopathic myelitis to be associated with hyperIgEemia as well as atopic disease [5–7]. Of interest, patients with hyperIgEemia and mite specific antibody (IgE) in the absence of known history of atopy share common clinicolaboratory features with those with known atopy [6]: young age of onset, slow progressive course and predominant sensory symptoms with mild motor weakness, and few CSF abnormalities. These findings were recently confirmed by a Japanese nation-wide survey [7]. Based on these distinct clinicolaboratory features, the term “atopic myelitis (AM)” has been proposed.

Most AM patients have been investigated in Japan, with very few cases of AM being reported in western countries [8,9]. It has been unclear whether AM was as frequent in other Asian countries as in the case of Hirayama disease and whether it was a distinct entity, different from other idiopathic myelitis disorders, multiple sclerosis or neuromyelitis optica (NMO).

2. Methods

2.1. Patients

From January 2006 to August 2008, patients with idiopathic myelitis were recruited from the prospectively enrolled Ajou Myelitis Registry. Inclusion criteria were as follows: 1) acute or non-acute myelitis confirmed by clinical findings and spine MRI 2) no previous history of other neurological diseases or symptoms. Patients with a clinical course of more than one month were included given that long duration had been frequently seen in atopic myelitis [6,7]. Exclusion criteria were as follows: 1) compressive lesion 2) collagen-vascular diseases 3) parainfectious myelitis (clinical infection with fever within one month of the onset of clinical symptoms and CSF pleocytosis (>50 mg/dl) and 4) history of previous radiation of the spinal cord.

AM is defined as idiopathic myelitis with either: 1) atopic diseases such as bronchial asthma, atopic dermatitis, and allergic rhinitis, or 2) hyperIgEemia and specific IgE to mite antigen (*Dermatophagoides*

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pteronyssinus, D1 and *fabrinae*, D2), as proposed by Kira et al. [5]. Thirty-nine age and sex-matched subjects without a history of any atopic diseases were recruited as a control.

2.2. Clinical assessment

The mode of onset was defined as either acute (a maximal deficit within two weeks) or non-acute. The disability was evaluated according to Kurtzke's expanded disability status scale (EDSS) [10]. Steroid response was considered effective if improvement of more than 1 point in EDSS score was achieved.

2.3. Measurement of total and specific IgE

The level of total IgE and two common mite antigens, *D. pteronyssinus* (D1) and *fabrinae* (D2)-specific IgE were measured using the CAP system (Pharmacia) according to the manufacturer's instructions. The upper normal limit of the serum total IgE and the mite antigen-specific IgE level were 250 IU/ml and 0.35 IU/ml, respectively.

2.4. Measurement of NMO-IgG

Testing for NMO-IgG was performed by indirect immunofluorescence on a substrate of mouse cerebellum and midbrain, as previously described [11]. Readers were blind to all clinical information.

2.5. MRI

Spine MRIs were performed on all patients using the 1.5 T GE system after intravenous injection of contrast material. The MR imaging protocol for spine included the collection of T1- and T2-weighted images as well as gadolinium-enhanced T1-weighted images in the axial and sagittal planes. The MR images were reviewed for the following characteristics: cord swelling on T1-weighted sagittal images, segmental body length of the high signal on T2-weighted sagittal images, cross-sectional location, size and pattern of the high signal on T2-weighted images, and the location, extent, and pattern of contrast enhancement on T1-weighted axial and sagittal images. Lesions spanning three or more vertebral segments in length were regarded as longitudinally extensive spinal cord lesions (LESCL) [12]. Central linear high signal intensity seen above or below the diffuse lesion on T2WI was not considered as a true lesion. Brain MRI was obtained in all of 29 patients with myelitis. Brain lesions were classified as suggestive or atypical for multiple sclerosis, according to Barkhof's criteria [13].

2.6. Statistical analysis

A Mann Whitney-*U* test was used for comparison of continuous variables (the level of total IgE and mite antigen-specific IgE) and a Chi-square or Fisher's exact test was applied to compare frequency data. Statistical significance was set at $p<0.05$.

3. Results

During the study period, 32 patients with non-compressive myelopathy were identified. After excluding 3 cases (SLE 1, spinal cord infarction 1, parainfectious myelitis 1), 29 patients (19 men, 10 women; mean age at onset, 45.5 years) were diagnosed with idiopathic myelitis.

Of them, four patients had known atopic disease (2 allergic rhinitis, 2 bronchial asthma). All 4 of these patients had both hyperIgEemia and mite antigen-specific antibodies; however, none of them experienced an exacerbation of atopic symptoms during the course of myelitis. Another 10 patients showed both hyperIgEemia and mite specific antibody but without a known history of atopic disease. Thus, these 14 patients were considered as AM whereas the remaining 15 patients as non-AM.

3.1. Comparison of total IgE and mite specific IgE between myelitis patients and normal control

The level of total serum IgE and two mite antigen-specific IgE in patients with myelitis and in normal control are shown in Fig. 1. HyperIgEemia was more frequent in patients with myelitis (58%) than in normal control (20%, $p=0.005$) (Table 1). The level of total IgE was significantly higher in the myelitis group (median 324 IU/ml, range 18–2345 IU/ml) than in the control group (median 62 IU/ml, range 8–472 IU/ml) ($p<0.005$) (Fig. 1A).

Both D1 and D2 mite antigen-specific IgE were detected in about two-thirds of myelitis cases and in about one-fifth of control subjects ($p=0.05$ and $p=0.001$, respectively) (Table 1). In addition, myelitis patients showed significantly higher median level of *D. pteronyssinus*

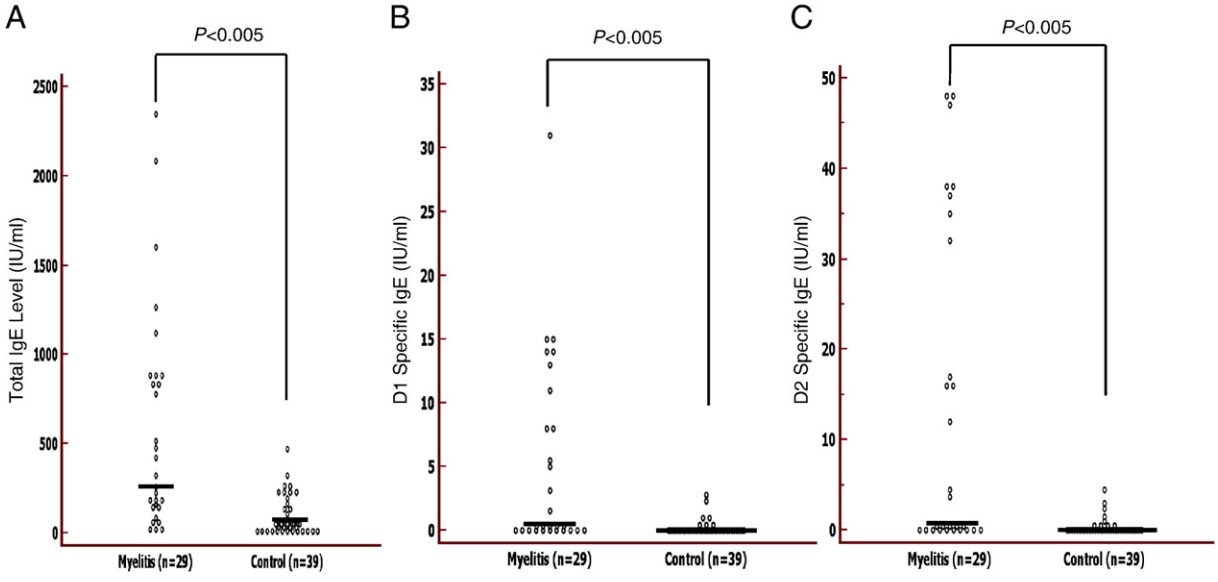

Fig. 1. Distribution of the level of total IgE (A) as well as *Dermatophagoides pteronyssinus* (D1) and *fabrinae* (D2)-specific IgE (B, C) in myelitis patients and normal control. NC = Normal control. The upper normal limit of serum total IgE and the mite antigen-specific IgE level are 250 IU/ml and 0.35 IU/ml, respectively. Horizontal bars indicate median values.