SHORT REPORT

Acute myelitis after asthma attacks with onset after puberty

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Abstract

A poliomyelitis-like illness after asthma attacks has been found and is called asthmatic amyotrophy (Hopkins' syndrome). All of the previously reported cases were under 13 years of age. Three patients are described who developed acute myelitis after asthma attacks at 15, 22, and 73 years of age. All of them showed acute flaccid monoparesis, and needle EMG disclosed denervation potentials in the relevant muscles. In addition, in the two adult patients the sensory or pyramidal tracts were involved, and evoked potential studies confirmed an involvement of the pyramidal tracts in one of them. This 22 year old patient showed a second episode of monoparesis in the other limb after another asthma attack. All three patients had no significant changes in their antiviral antibody titres, whereas every patient had hyperIgEaemia and allergen specific IgE. These findings suggest that asthmatic amyotrophy can develop after puberty and that patients who develop this disease in adulthood seem to show both a wide-spread involvement of the spinal cord and a more varied course.

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A poliomyelitis-like illness presenting as flaccid paralysis in one or more limbs after asthma attacks is known as Hopkins' syndrome.¹ Although either a viral infection²⁻⁵ or multifactorial immune suppression during an acute attack of bronchial asthma⁶ has been proposed to be the mechanism of this syndrome, the precise mechanism still remains to be elucidated. All previously reported patients were children younger than 13 years of age.¹⁻¹³ We recently saw three patients who showed acute flaccid paralysis after asthma attacks after puberty. We report the clinical pictures and the results of allergen specific IgE assays of these patients.

Patients and methods

PATIENTS

The clinical findings of the patients are summarised in the table.

Patient 1

The patient was a 15 year old boy who had had bronchial asthma since he was 6 years old. He sometimes received inhalation therapy (β agonists). He developed severe weakness in his

Table 1 Clinical data of patients with acute myelitis after asthma attacks

	Patient 1	Patient 2	Patient 3
Age at onset/sex	15/Male	22/Female	73/Female
Serum total IgE (U/ml)	1300	298	306
Eosinophil (%)	8%	6.5%	8.7%
Interval between asthma attack and onset of myelitis (days)	6	7 (1') and 9 (2')*	2
Symptoms and signs during illness:			
Motor weakness	+ (mono)	+ (mono)	+ (mono)
Muscle atrophy	+	+	+
Increased tendon reflex	-	+ (2')	+
Sensory signs	-	+	-
Sphincter disturbance	-	-	-
Clinically estimated main lesions	LS	LS (1'), C (2')	C
EDSS	3	3.5	3
Spinal cord MRI	-	+ (C, 2')	-
Needle EMG (myotomes)†	Neurogenic changes (lt L2-S1, rt L2-L4)	Neurogenic changes (rt L2-S2)	Neurogenic changes (rt C5-T1)
CSF:			
Pleocytosis (>5/ μ l)	7	1	1
Increased protein (>45 mg/dl)	54	52	40
Clinical course	Unimproved	Slightly improved	Unimproved

*Patient 2 had a second asthma attack during the corticosteroid therapy and 9 days later she developed another episode of monoparesis.

1'=the first episode; 2'=the second episode.

C=Cervical; T=thoracic; LS=lumbosacral; mono=monoparesis; EDSS=Kurtzke's expanded disability status scale.¹⁶

†Myotomes showing neurogenic changes on needle EMG; lt=left; rt=right.

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left leg 6 days after an acute asthma attack. A general physical examination showed no abnormality. A neurological examination showed severe muscle weakness and atrophy at the L5-S1 level and mild muscle weakness and atrophy at the L2-4 level in the left leg (fig 1). The tendon reflexes were normal in the arms and slightly brisk in both legs except for the absence of an Achilles tendon reflex on his left side. His sensation and sphincter function were normal. The motor nerve conduction velocity (MCV) data were as follows; 36 m/s for the left tibial nerve with an amplitude of 0.3 mV, and 35 m/s for a left peroneal nerve with an amplitude of 0.1 mV. No F waves were evoked in either nerves. The sensory nerve conduction velocity (SCV) of the left sural nerve was normal. Needle EMG showed fibrillation potentials in the left L4-5 myotomes and right L2-4 myotomes, and giant motor unit potentials (MUPs) and polyphasic MUPs and a reduction of motor units in the left L2-S1 myotomes and right L2-4 myotomes. The somatosensory evoked potentials (SEPs) in the legs were all normal. The motor evoked potentials (MEPs) with lumbosacral root stimulation recorded from the left abductor hallucis muscles were not elicited. The total white blood count was $4440/\text{mm}^3$, with 43.0% neutrophils, 8.0% eosinophils, 44.0% lymphocytes, 4.0% monocytes, and 1.0% basophils. The antiviral antibodies in the paired serum samples showed no significant changes in any viruses examined including echovirus, enterovirus, coxsackievirus, and poliovirus types 1, 2, and 3. The serum IgE was raised to 1300 U/ml (normal <250 U/ml). The CSF showed seven mononuclear cells/ μl , protein 54 mg/dl, glucose 56 mg/dl, an increased IgG index (0.677, normal <0.65), and negative oligoclonal IgG bands. Spinal cord MRI showed no abnormality in either the thoracic or the lumbosacral spinal cord. Methylprednisolone pulse treatment (1g $\times$ 3 days) followed by oral prednisolone (60 mg/day) with gradual tapering was not beneficial.

Patient 2

The patient was a 22 year old woman who noticed sensorimotor disturbances in her right leg 7 days after an acute asthma attack. She had had bronchial asthma since 10 years of age. She had been receiving inhalation therapy (β agonists) at the time of the asthma attacks. A general physical examination found no abnormalities. A neurological examination disclosed moderate muscle weakness and atrophy and superficial and deep sensory deficits at the L2-S2 level in the right leg. Her tendon reflexes were normal in both arms and the left leg but were slightly depressed in her right leg. The sphincters were normal. The MCV and the F wave of right tibial and peroneal nerves were normal. The SCV of the right sural nerve was also normal. Needle EMG showed fibrillation potentials in the right L4-S2 myotomes, and positive sharp waves in the right S1-2 myotomes, and a severe reduction in the motor units in the right L2-S2 myotomes. The SEPs and MEPs in both lower limbs were normal. The antiviral antibodies in the paired serum

Figure 1 Patient 1, showing muscle atrophy in the left leg.

samples showed no significant changes in any viruses examined including the echovirus, enterovirus, coxsackievirus, and poliovirus types 1, 2, and 3. The total white blood count was $5070/\text{mm}^3$, with 51.5% neutrophils, 6.5% eosinophils, 35.5% lymphocytes, 5.7% monocytes, and 0.8% basophils. The serum IgE was raised (298 U/ml). A CSF examination showed 1 mononuclear cell/ μl , protein 52 mg/dl, and glucose 56 mg/dl, an increased IgG index (0.92), and negative oligoclonal bands. Spinal cord MRI showed no abnormality in either the thoracic or lumbosacral spinal cord. Methylprednisolone pulse therapy was initiated on day 42 and followed by oral corticosteroids (50 mg/day) with gradual tapering. Corticosteroids alleviated her sensory impairment, but had no effect on muscle weakness. During corticosteroid therapy, she experienced another asthma attack, and 9 days later she developed left arm weakness with mild hyperreflexia. Total white blood count was $13040/\text{mm}^3$, with 73.5% neutrophils, 1.0% eosinophils, 20.5% lymphocytes, and 5.0% monocytes. Serum IgE was further increased (522 U/ml). Cervical MRI demonstrated a high signal intensity lesion at C2-7 level on T2 weighted images,

and the lesion was slightly enhanced by gadolinium DTPA (fig 2). Needle EMG showed no denervation potentials in her left arm muscles. Moderate weakness in her left arm and right lower leg remained despite corticosteroid therapy.

Patient 3

A 73 year old woman, who had had bronchial asthma since 53 years of age, developed weakness in her right arm 2 days after an acute asthma attack. She was treated by intravenous theophylline and oral prednisolone (10 mg/day). She had severe muscle weakness and atrophy at the C7-T1 level in the right arm. Her tendon reflexes were absent in the right arm, normal in the left upper arm, and brisk in both legs. Her sensation and sphincters were normal. The motor nerve conduction study of the right median and ulnar nerves showed a marked reduction in amplitude, and no action potential was evoked in the right radial nerve. Sensory nerve conduction studies of the right median and ulnar nerves were normal. Needle EMG showed giant MUPs in the right C5–8 myotomes, and a reduction in the number of motor units in the right C5–T1 myotomes. No denervation potentials were found in her right

leg muscles. The N9 to N13 interpeak latency on SEPs to median nerve stimulation was prolonged bilaterally (right N9–N13 interval=5.20 ms, left N9–N13 interval=4.64 ms, normal<4.58 ms). The MEPs of the right thenar muscles showed a marked reduction in amplitude and prolonged central conduction time (CCT=13.05 ms, normal<10.67 ms). Antiviral antibodies in her serum samples were negative for all examined viruses including poliovirus types 1, 2, and 3. Serum IgE was increased to 306 U/ml. Examination of CSF showed 1 mononuclear cell/ μ l, protein 40 mg/dl, glucose 55 mg/dl, and a normal IgG index (0.35). An MRI study showed cervical spondylosis at the level of C3–C6.

METHODS

Total IgE in the serum was measured by an enzyme linked immunosorbent assay (ELISA) as described previously.¹⁴ Two common mite antigens (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), *Chironomus plumosus*, orchard grass, Sweet vernal grass, dog epithelium, Timothy grass, wheat, cedar pollen, candida, egg white, milk, rice, and soybean were used as the antigens for ELISA (Ala-STAT, Sankojunyak, Tokyo).¹⁴ The cut off value for allergen specific IgE was 0.34 IU/ml.

Results

Allergen specific IgE was found in all three patients. The specific IgE antibodies against two mite antigens were present in patients 1 and 2 at high titres, whereas patient 3 had the specific IgE to cedar pollen. The titres of specific IgE antibodies in the positive allergens were as follows; *Dermatophagoides farinae* 93.22, *Dermatophagoides pteronyssinus* 88.47, *Chironomus plumosus* 13.4, orchard grass 7.84, Sweet vernal grass 3.19, dog epithelium 2.12, Timothy grass 0.55 and wheat 0.37 in patient 1, *Dermatophagoides farinae* 43.71, *Dermatophagoides pteronyssinus* 40.63 and cedar pollen 0.56 in patient 2, and cedar pollen 1.16 in patient 3.

Discussion

This is the first report describing the occurrence of asthmatic amyotrophy after puberty. All of our patients developed amyotrophy with a close temporal relation to an acute asthma attack. Asthmatic amyotrophy in childhood is called Hopkins' syndrome.¹ Our patient 1 fits well into this category. Two other patients in adulthood, however, did not, because they showed an involvement of either the posterior horns or the pyramidal tract as well as anterior horn cell involvement clinically and electrophysiologically. In addition, patient 2 also showed an additional episode of myelitis after another asthma attack, although no relapse has ever been reported in cases of Hopkins' syndrome.^{1–13} According to the results of electrophysiological studies, patient 1 seemed to have a subtle involvement of the peripheral nerves whereas patient 3 had an additional lesion between Erb's point and the spinal cord. Such an involvement with either the peripheral nerves² or the spinal root^{3,9} has occasionally been reported in Hopkins' syndrome, and

Figure 2 T2 weighted spinal cord MRI (TR 2898.1 ms/TE 90.0 ms) in patient 2 indicates a high signal intensity lesion (arrows) in the cervical cord.

therefore the electrophysiological findings suggesting peripheral nerve involvement could not rule out a diagnosis of Hopkins' syndrome in our patients. Our findings thus indicate that asthmatic amyotrophy could occur after puberty, and that patients who develop this disease in adulthood may show a more widespread involvement of the spinal cord than that seen in childhood.

It has been postulated that latently infected polioviruses within the anterior horn cells are activated under non-specific immunosuppressed conditions induced by bronchial asthma, thereby destroying the infected cells in Hopkins' syndrome.¹¹ However, no increase in antipoliiovirus antibodies has ever been found in this condition, including our patients. Moreover, the destruction of the posterior horn and pyramidal tract as well as the relapse after another asthma attack can hardly be explained by a poliovirus infection alone.

Because all of our patients had hyperIgEaemia and allergen-specific IgE, the bronchial asthma seen in both of our patients was most likely atopic. HyperIgEaemia and allergen specific IgE were also found in the reported cases of Hopkins' syndrome.¹² As a result, the preceding asthma in Hopkins' syndrome is also considered to be atopic. On the other hand, we recently reported the occurrence of myelitis associated with hyperIgEaemia and mite antigen specific IgE and named it atopic myelitis.^{14, 15} In this condition, atopic dermatitis in adulthood often precedes the development of myelitis. Such patients showed a preferential involvement of the cervical cord and presented with paraesthesia and dysaesthesia in the distal parts of all four limbs. Hopkins' syndrome and atopic myelitis differ from each other in the preceding atopic disorders, preferential age of onset, neurological manifestations, and preferential sites of spinal cord involvement. However, both conditions are similar regarding the most important point that myelitis develops in the presence of atopic disorders, which suggests a link between atopy and the development of spinal cord inflammation.

As our study is a small case series, we consider that a further large scale study is necessary to clarify the relation between asthma and myelitis. As the number of adult patients with atopic disorders is greatly increasing in many industrialised countries nowadays, it is important in clinical practice to be aware of the possibility of encountering myelitis associated with atopic disorders.

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