Acute myelitis after asthma attacks with onset after puberty

Izumi Horiuchi, Kenji Yamasaki, Manabu Osoegawa, Yasumasa Ohyagi, Akio Okayama, Tomomi Kurokawa, Takeshi Yamada, Jun-ichi Kira

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 another 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 widespread involvement of the spinal cord and a more varied course.

Keywords: myelitis; asthma; atopy; mite; Hopkins’ syndrome

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...
left leg 6 days after an acute asthma attack. A
general physical examination showed no ab-
normality. 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 ampi-
tude of 0.1 mV. No F waves were evoked in
either nerves. The sensory nerve conduction
velocity (SCV) of the left sural nerve was nor-
mal. Needle EMG showed fibrillation poten-
tials in the left L4–5 myotomes and right L2–4
myotomes, and giant motor unit potentials
(MUPs) and polyphasic MUPs and a reduc-
tion 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 lumbar root stimulation recorded
from the left abductor hallucis muscles were
not elicited. The total white blood count was
4440/mm^3, with 43.0% neutrophils, 8.0% eosin-
ophils, 44.0% lymphocytes, 4.0% monocytes,
and 1.0% basophils. The antiviral antibodies in
the paired serum samples showed no signifi-
cant 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, pro-
genesis, 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 lumbar spinal cord. Methylpred-
nisolone pulse treatment (1g×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 abnor-
malities. 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 myo-
tomes, 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
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/mm^3, with 51.5% neutrophils, 6.5%
eosinophils, 35.5% lymphocytes, 5.7% mono-
cytes, 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 lumbar spinal cord. Methyl-
prednisolone 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 cortico-
steroid therapy, she experienced another
asthma attack, and 9 days later she developed
left arm weakness with mild hyperreflexia.
Total white blood count was 13040/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/µl, 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. 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 (Allastat, Sankojunyaku, Tokyo). 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. 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. 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 nerves or the spinal root has occasionally been reported in Hopkins' syndrome, and
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.13 However, no increase in antipoliovirus 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.13 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 dysesthesia 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.
Acute myelitis after asthma attacks with onset after puberty

Izumi Horiuchi, Kenji Yamasaki, Manabu Osoegawa, Yasumasa Ohyagi, Akio Okayama, Tomomi Kurokawa, Takeshi Yamada and Jun-ichi Kira

J Neurol Neurosurg Psychiatry 2000 68: 665-668
doi: 10.1136/jnnp.68.5.665

Updated information and services can be found at:
http://jnnp.bmj.com/content/68/5/665

These include:

References
This article cites 16 articles, 7 of which you can access for free at:
http://jnnp.bmj.com/content/68/5/665#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Immunology (including allergy) (1943)
- Infection (neurology) (494)
- Spinal cord (542)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/