



Case Report

Immune-Mediated Mechanisms in the Pathogenesis of Hopkins Syndrome

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ARTICLE INFORMATION

Article history:

Received 30 March 2012

Accepted 1 August 2012

ABSTRACT

Hopkins syndrome occurs after an acute asthma attack. An immune-mediated mechanism has been suggested. Immunoglobulin or methylprednisone pulse therapies comprise the most useful treatment. We describe a 3-year-old girl who developed severe weakness in her left arm, 7 days after an acute asthma attack. A complete blood count with autoimmune biomarkers, immunoglobulin profile, and virology study and magnetic resonance of the brain, spine, and brachial plexus produced normal results. In the cerebrospinal fluid, T lymphocytes comprised the predominant leukocyte population, and oligoclonal bands were positive. An electromyogram revealed a partial axonal lesion (normal motor nerve conduction velocity with low amplitude) of the axillary, musculocutaneous, and interosseous nerves of the left arm, with normal sensory nerve conduction and partial denervation. We began therapy with intravenous immunoglobulin for 5 consecutive days, repeated every 4 weeks for 2 months. Afterward, our patient recovered. This report contributes to understanding the role of immune-mediated mechanisms in the pathogenesis of this disease, and the importance of immunotherapy in its treatment.

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Introduction

Poliomyelitis-like illness associated with asthma or asthmatic amyotrophy, or Hopkins syndrome, was first described by Hopkins in 1974. He described 10 children who developed a poliomyelitis-like illness 4–7 days after an acute asthma attack, during the recovery phase. The illness was characterized by a phase of fast evolution over a period of several days of severe and extensive lower motor neuron paralysis, affecting only one limb in most cases [1,2]. The patients subsequently developed marked amyotrophy of the affected limb, and remained severely handicapped [3].

The etiology of this illness affecting spinal anterior horn cells has not been fully elucidated, although a viral infection in an immunologically compromised person was reported previously in the literature [1–5]. In this study, we report on

the clinical profile and possible mechanisms of the pathogenesis of Hopkins syndrome, and its treatment.

Case Report

The patient was a 3-year-old girl who had manifested bronchial asthma for 5 months. She was receiving inhalation therapy with budesonide and montelukast, and occasionally salbutamol. She developed severe weakness in her left arm 7 days after an acute asthma attack.

In terms of previous medical history, the girl was the product of an uncomplicated pregnancy. No previous developmental concerns were evident, and she was performing well at her daycare center. She was current with all immunizations, including polio.

A general physical examination produced normal results. Her cranial nerves and the results of a neurologic examination of her lower limbs were normal. She could not move her left arm, but the mobility in her left hand was normal. Tone was decreased, with weakness of the elbow flexor and extensor muscles and shoulder abduction. Sensations of touch and pain and sphincter function were normal. The deep tendon reflexes were absent in her left limb.

A complete blood count with an autoimmune biomarkers study (anticardiolipin, antiphospholipin, anticytoplasmic, anti-DNA, antinuclear factor, and rheumatoid factor) and an immunoglobulin profile

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(including immunoglobulin E) produced negative results. A lumbar puncture demonstrated a leukocyte count of $4/\text{mm}^3$, glucose at 52 mg/dL (normal values, 50–80 mg/dL), protein at 20 mg/dL (normal values, 15–90 mg/dL), and lactic acid at 15.57 mg/dL (normal values, 6–20 mg/dL). Her cerebrospinal fluid was analyzed by flow cytometry. The predominant leukocyte population comprised T lymphocytes ($1.15 \text{ cells}/\mu\text{L}$; 72%), with a CD4/CD8 ratio of 0.76. This value represented an increase in the ratio of cytotoxic T lymphocytes in the cerebrospinal fluid, compared with her peripheral blood (with a CD4/CD8 ratio of 2.87). Oligoclonal bands were positive. The virology study of her serum and cerebrospinal fluid (including echovirus, enterovirus, coxsackievirus, and poliovirus) and magnetic resonance imaging of the brain, spine and brachial plexus produced normal results. An electromyogram revealed a partial axonal lesion (normal motor nerve conduction velocity with low amplitude) of the axillary, musculocutaneous, and interosseous nerves of the left arm. It exhibited normal sensory nerve conduction and partial denervation in the biceps, triceps, and pronator, with positive sharp waves and fibrillation potentials. It was a preganglionic lesion at the cervical 6 and cervical 7 level.

We reviewed the literature and decided to begin therapy with intravenous immunoglobulin at 2 g/kg for 5 consecutive days. We repeated this treatment every 4 weeks for 2 months. After treatment, the arm of our patient regained complete tone, strength, and mobility.

Discussion

We treated a patient who manifested a rare disease involving the anterior horn cell after an acute asthma attack, similar to an infection by poliomyelitis. Our differential diagnosis included segmental or atopic myelitis, Guillain-Barré syndrome, brachial plexus injury, and painful brachial neuropathy. However, the lack of sensory changes, normal bladder and bowel signs, the asymmetric presentation, a normal level of immunoglobulin E, the cerebrospinal fluid protein count without pleocytosis, and the lack of pain or history of trauma or pain militated against these diagnoses [1,4,6].

The pathogenesis of Hopkins syndrome remains unclear, and different possibilities have been suggested. In their review [1], Yeung et al. summarized the theories of Hopkins syndrome as a viral infection that triggers an asthmatic attack and invades the anterior horn cells with or without a reduced immunologic response [1,2], or of Hopkins syndrome as an allergic mechanism attributable to cross-reactivity between an allergen and the peripheral nervous system. Atopic disorders with specific actions of immunoglobulin E against common environmental allergens such as mite antigen result in an atopic myelitic picture. This picture would suggest a link between these atopic disorders and Hopkins syndrome [4,5,7]. In our case, no virus or other microorganisms were detected, and the level of serum immunoglobulin E was normal. The cerebrospinal fluid findings without pleocytosis were similar to those previously reported in the literature [5], but we detected oligoclonal bands and a relative increase of cytotoxic CD8 T lymphocytes, compared with the peripheral blood. To the best of our knowledge, this case report is the only one in which the oligoclonal bands and CD8 T lymphocytes were positive, and both indicate a central nervous

system inflammation or immune mechanism with intrathecal immunoglobulin synthesis, which may explain the role of immune-mediated mechanisms in the pathogenesis of Hopkins syndrome.

According to the results of electrophysiologic studies, our patient seemed to present a subtle involvement of the peripheral nerves. Such an involvement with either the peripheral nerves or the spinal root has occasionally been reported in Hopkins syndrome [5].

Various treatments have been included in the management of this syndrome, including oral prednisone [8], methylprednisone [1,4,5] and intravenous immunoglobulin [1,4,9]. After two cycles of treatment with immunoglobulin, our patient's arm was normal.

Hopkins syndrome is known for unfavorable outcomes with persistent weakness, muscle wasting, and disability [2]. Therefore, the correct treatment is very important. Our point of view, based on the literature [1,3,9], holds that immunoglobulin or pulse therapy with methylprednisone comprise the most useful treatments. Plasmapheresis has not proved relevant in Hopkins syndrome, but may be important in severe cases. Despite correct treatment, relapses were also reported in the literature [4,10].

With this case, we offer a contribution to understanding the etiology and treatment of Hopkins syndrome, but more collaborative studies are required.

References

- [1] Yeung SC, Antonio G, Ip KS. Flaccid paralysis of the limbs after an asthmatic attack. *Pediatr Neurol* 2010;42:133–6.
- [2] Manson JI, Thong YH. Immunological abnormalities in the syndrome of poliomyelitis-like illness associated with acute bronchial asthma (Hopkins syndrome). *Arch Dis Child* 1980;55:26–32.
- [3] Shahar EM, Hwang PA, Niesen CE, Murphy EG. Poliomyelitis-like paralysis during recovery from acute bronchial asthma: Possible etiology and risk factors. *Pediatrics* 1991;88:276–9.
- [4] Pavone P, Longo MR, Scalia F, Polosa R, Kira J, Falsaperla R. Recurrent Hopkins syndrome: A case report and review of the literature. *J Neurol Sci* 2010;297:89–91.
- [5] Horiuchi I, Yamasaki K, Osogawa M, et al. Acute myelitis after asthma attacks with onset after puberty. *J Neurol Neurosurg Psychiatry* 2000;68:665–8.
- [6] Summer AJ. Idiopathic brachial neuritis. *Neurosurgery* 2009;65:150–2.
- [7] Okayama A, Hara H, Shigeto H, Yamada T, Kira J. A case of Hopkins syndrome with onset at puberty. *Rinsho Shinkeigaku* 1999;39:452–5.
- [8] Nakano Y, Kohira R, Yamazaki H, Fujita T, Okubo O, Harada K. Hopkins syndrome: Oral prednisolone was effective for the paralysis. *No To Hattatsu* 2001;33:69–73.
- [9] Cohen HA, Ashkenasi A, Ring H, et al. Poliomyelitis-like syndrome following asthmatic attack (Hopkins' syndrome) recovery associated with i.v. gamma globulin treatment. *Infection* 1998;26:247–9.
- [10] Nora DB, Gomes I, El Ammar G, Nunes ML. Hopkins' syndrome in the differential diagnosis of flaccid paralysis in children: Clinical and neurophysiological features: Case report. *Arq Neuropsiquiatr* 2003;61:494–8.