Recurrent Acute Cerebellar Ataxia of Childhood Following Nonspecific Respiratory Tract Infection

ANANNIT VISUDTIBHAN, M.D.*,
PONGSAKDI VISUDHIPHAN, M.D.*,
SURANG CHIEMCHANYA, M.D.*

Abstract

Acute cerebellar ataxia in childhood following viral infection is a self-limited disease. The disease with recurrent course has rarely been reported. At the Department of Pediatrics, Ramathibodi Hospital, three children with recurrent episodes of acute cerebellar ataxia following nonspecific viral infection were encountered. The age at onset of each patient was 2 years, 18 months and 2 years old. The clinical symptoms were similar and improved rapidly after glucocorticoid was given. All patients recovered without residual deficit. Six, 5 and 3 recurrent attacks of similar illness were noted in each patient respectively after the first episode. However, no further attack occurred after the age of 5 years and the age of last follow-up was 17, 16 and 14 years old respectively. The pathogenesis of the recurrent episodes is uncertain. The abnormal immunological response is postulated.

Acute cerebellar ataxia in childhood has multiple etiologies[1-3] and is usually associated with nonspecific viral infection[4-6]. Children with this condition often present with the history of a nonspecific infection 1 to 3 weeks prior to the development of profound truncal ataxia and signs suggesting a disorder predominantly of the cerebellum[4-6]. Some children also have minimal involvement of the cerebrum as well[5,6]. The condition is self- limited, with patients improving rapidly within a week, although complete recovery often takes 1-2 months. Nevertheless, significant residual neurological deficit may result[5-7].

A rare reported case of acute cerebellar ataxia associated with viral infection in childhood suffered a recurrent attack after recovery from the acute stage[6]. At the Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Bangkok, we have seen three children who, after the first episode of acute cerebellar ataxia following nonspecific respiratory tract infection, had multiple recurrent attacks. Each attack had a similar course

* Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

of illness and seemed to respond to glucocorticoid treatment. However, after the age of 5, there were no further attacks. These patients have been followed-up for more than 10 years. The clinical courses of these patients are briefly described.

CASE REPORT

Patient 1.

A 2-year old girl was admitted in October 1980 because of gait disturbance 2 weeks following a mild respiratory tract infection. On admission, she was afebrile and had normal vital signs. She walked with a wide base gait and only with support. She was noted to have truncal ataxia with intentional tremor of all limbs. Horizontal gaze nystagmus and hypoactive tendon reflexes were also noted. Cranial nerves, sensory function and motor strength were normal. Laboratory findings which included CBC, urinalysis, blood chemistry, chest X-rays, computerized tomography (CT) scan of the brain and electroencephalography (EEG) were all normal. Lumbar puncture revealed normal pressure and the cerebrospinal fluid (CSF) contained 10 lymphocytes/µl, protein 30 mg/dl and normal glucose level. IgG level in the CSF was not elevated. Cultures for bacteria and fungi were negative.

Prednisolone 2 mg/kg/day was given for one week. Rapid improvement of the cerebellar function was observed and the child almost completely recovered within 2 weeks. Examination one month later revealed no residual neurologic deficit. Following the first episode, she had six more similar attacks during a period of 3 years, at intervals ranging from 3 to 6 months. Each attack followed a non-specific infection, and seemed to respond to treatment with prednisolone. She also had two generalized seizures at the age of 7 years. Phenobarbital treatment was given and was discontinued 2 years later. From the age of 5 years until the last follow-up at 17 years, she has had no further attack of ataxia or seizure. Neurological examination was normal and magnetic resonance imaging (MRI) of the brain showed no abnormality.

Patient 2.

In April 1981, one week following a nonspecific viral infection of the respiratory tract, an 18-month old boy was admitted with ataxia. The mother's history of pregnancy and delivery was normal. The developmental milestones prior to this illness were also normal. There was no history of ataxia in the family.

On examination he was afebrile and could walk only with support. Truncal ataxia with intentional tremor of both arms was noted. The rest of the neurological examination was unremarkable. Laboratory examinations, which included CBC, urinalysis, blood electrolytes, liver function test, chest X-ray and CT scan of the brain, were all normal. Lumbar puncture revealed an opening pressure of 145 mmH_2O and the CSF contained 4 lymphocytes/µl. Glucose, protein and IgG levels in the CSF were normal.

Prednisolone (2 mg/kg/day) was then given for 5 days. Rapid improvement of ataxia was observed and all the symptoms gradually disappeared within 3 weeks. Between the ages of 1 1/2 and 4 years he had five more similar attacks, at intervals ranging from 2 to 6 months. Each attack seemed to respond to similar treatment. From the age of 4 years until October 1996 at the age of 16, no further attack of ataxia was observed. A neurological examination and MRI scan of the brain at the last follow-up were normal.

Patient 3.

A 2-year old girl was admitted in October 1983 because she was unable to walk without support a week following an upper respiratory tract infection. Her perinatal history and psychomotor development were normal. There was no family history of ataxia.

Physical examination revealed an afebrile girl with severe gait and truncal ataxia. The finger-to-nose test of both hands was impaired. Horizontal nystagmus was also noted. The fundi, cranial nerves, sensory function and motor power were all normal. The CBC, urinalysis, blood sugar, blood electrolytes, liver function test, chest X-ray, CT scan of the brain and CSF examination were also normal. Prednisolone at 2 mg/kg /day was then given for 5 days with marked improvement of ataxia. The patient recovered within 2 weeks. However, three more similar episodes of acute ataxia following nonspecific infection of the respiratory tract occurred within the next 2 years, at intervals ranging from 4 to 10 months. The symptoms gradually improved with prednisolone treatment and she became normal within 2-4 weeks. No further attack of ataxia occurred after 4 years of age and the last follow-up 10 years later revealed

normal neurological examination and MRI scan of the brain.

DISCUSSION

Acute cerebellar ataxia occuring in childhood has been accorded considerable interest by most pediatricians and pediatric neurologists[1-7]. A previously normal child suddenly developed ataxia, tremor and hypotonia, often with nystagmus and dysarthria. In some patients the subsequent manifestations of speech and intellectual impairment suggested subtle cerebral involvement[5-7].

In most reported cases, the onset of illness occurred before 3 years of age. Upper respiratory tract infection may preceed the onset of ataxia by 1-3 weeks. No patients were exposed to known contagious diseases and none had a history of head trauma. The cerebrospinal fluid examination was often normal and other laboratory data obtained at time of initial evaluation proved to be of no value[4-7].

Three of our patients developed the first attack of acute cerebellar ataxia before the age of 2. They had preceeding nonspecific infection of the respiratory tract within three weeks prior to the onset of ataxia. No known cause of ataxia and no family history of ataxia were noted. The clinical features and laboratory findings were quite similar to previous reports of this entity in the literature[4-7].

The relatively rapid recovery of the patients was possibly due to the beneficial effects of glucocorticoid treatment. However, they all subsequently had multiple recurrent attacks of similar illness. No further attacks were observed after the age of 5 years, the patients were followed-up through the age of 15 years.

Reported cases of recurrent acute cerebellar ataxia similar to these 3 patients are rare[6]. There is much speculation concerning possible etiologies of acute cerebellar ataxia. Demyelinating disease, toxin allergy, known and unknown viral infection have all been postulated. Demyelinating disease might be considered as a possible etiology in patients who showed some fluctuation of this ataxia in the early stage of their illness. However, the very early age of onset and the lack of new neurologic manifestations over the long follow-up period, including normal magnetic resonance imaging of the brain, argue against multiple sclerosis[8].

Intermittent cerebellar ataxia, which is a feature of several heritable metabolic diseases including Hartnup disease and pyruvate decarboxylase deficiency[1,9-12] and all dominant and recessive inherited familial intermittent ataxia have yet to be ruled out[14,15]. However, all of these diseases could be ruled out in our patients on clinical grounds and on the outcome of long term follow-up.

We are uncertain about the pathogenesis of recurrent acute cerebellar ataxia related to nonspecific infection of the respiratory tract in these patients. It is perhaps an inflammatory lesion primarily in the cerebellum of the hypersensitive host triggered by viral infection.

Normally the specific activation of the immune response begins in the circulatory and lymphoid tissue. The circulating T cells are in a state of self-tolerance. The infecting virus may share epitopes with host CNS antigens, resulting in an immune response against not only the infectious agents but also the host antigen, involving antigen-specific T cell activation[16]. The immunological process is then responsible for the central nervous system dysfunction. In addition, viruses may act as superantigens responsible for triggering recurrent attacks of ataxia similar to the postulation of the pathogenesis in many other neurological autoimmune diseases[17].

At present, we are following two more patients similar to the cases presented, but the duration of the follow-up is not yet long enough to exclude other possible causes of ataxia. The three reported patients may represent a unique entity of ataxia in childhood. The viral-induced immunologic change is probably the basic pathogenesis of this condition. Why they do not develop symptoms after 5 years of age, and whether they really do respond to treatment with glucocorticoid, are questions that need further study.

(Received for publication on June 2, 1998)

REFERENCES

1. Salam M. Metabolic ataxias. In: Viken PJ, Bruyn GW, eds. Handbook of clinical neurology. vol 21. Amsterdam: North-Holland, 1975: 573-85.
2. Gieron-Korthals MA, Westberry KR, Emmanuel PJ. Acute childhood ataxia: 10 year experience. J Child Neurol 1994; 9: 381-4.
3. Horowitz MB, Pang D, Hirsch W. Acute cerebellitis: case report and review. Pediatr Neurosurg 1991-2; 17: 142-5.
4. Cottom DG. Acute cerebellar ataxia. Arch Dis Child 1957; 32: 181-8.
5. Maggi G, Varone A, Aliberti F. Acute cerebellar ataxia in children. Childs Nerv Syst 1997; 13: 542-5.
6. Connolly AM, Dodson WE, Prensky AL, Rust RS. Course and outcome of acute cerebellar ataxia. Ann Neurol 1994; 35: 673-9.
7. Weiss S, Carter S. Course and prognosis of acute cerebellar ataxia in children. Neurology 1959; 9: 711-21.
8. Kesselring J, Miller DH, Robb SA, et al. Acute disseminated encephalomyelitis, MRI findings and the distinction from multiple sclerosis. Brain 1990; 113: 291-302.
9. Bain PG, O' Brien MD, Keevil SF, Porter DA. Familial periodic cerebellar ataxia: a problem of cerebellar intracellular pH homeostasis. Ann Neurol 1992; 31: 147-54.
10. Blass JP, Kark RAP, Engel WK. Clinical studies of a patient with pyruvate decarboxylase deficiency. Arch Neurol 1971; 25: 449-60.
11. Evans OB, Kilroy AW, Fenichel GM. Acetazolamide in the treatment of pyruvate dysmetabolism syndromes. Arch Neurol 1978; 35: 302-5.
12. Feeney GF, Boyle RS. Paroxysmal cerebellar ataxia. Aust NZJ Med 1989; 19: 113-7.
13. Lonsdale D, Faulkner WR, Price JW, Smeby RR. Intermittent cerebellar ataxia associated with hyperpyruvic acidemia, hyperalaninemia, and hyperalaninuria. Pediatrics 1969; 43: 1025-34.
14. Hill W, Sherman H. Acute intermittent familial cerebellar ataxia. Arch Neurol 1968; 18: 350-7.
15. Pennington RJT. Familial intermittent ataxia with possible X-linked recessive inheritance. J Neurol Sci 1984; 64: 89-97.
16. Herman A, Kappler JW, Marrack P, Pullen AM. Superantigens: mechanism of T-cell stimulation and role in immune responses. Ann Rev Immunol 1991; 9: 745-72.
17. Dalakas MC. Basic aspects of neuroimmunology as they relate to immunotherapeutic targets: present and future prospects. Ann Neurol 1995; 37 (Suppl I): S2-13.

การเกิดซ้ำของอาการเซอย่างเฉียบพลันจากซีรีเบลลัม ตามหลังการติดเชื้อทางเดินหายใจในผู้ป่วยเด็ก

อนันต์นิตย์ วิสุทธิพันธ์, พ.บ.,*
พงษ์ศักดิ์ วิสุทธิพันธ์, พ.บ., สุรางค์ เจียมจรรยา, พ.บ.**

อาการเซอย่างเฉียบพลันจากซีรีเบลลัมผิดปกติในเด็ก เป็นความผิดปกติที่พบได้ไม่บ่อยและมักจะหายเป็นปกติได้เอง คณะผู้รายงานได้นำเสนอการเกิดความผิดปกตินี้ที่เกิดซ้ำตามหลังการติดเชื้อของระบบหายใจในผู้ป่วยเด็ก 3 คน ที่พบในโรงพยาบาลรามาธิบดีในระหว่างปี พ.ศ.2523-2524 ซึ่งได้ติดตามการรักษาต่อเนื่อง 17, 16 และ 14 ปี พบว่าผู้ป่วยทั้งสามซึ่งแสดงอาการผิดปกตินี้เมื่ออายุ 2 ปี จำนวน 2 คน และ 18 เดือน จำนวน 1 คน มีอาการผิดปกติของการทรงตัวเกิดซ้ำอีก 6, 3 และ 5 ครั้งตามลำดับ ผู้ป่วยทุกคนตอบสนองต่อการรักษาด้วยคอร์ติโคสตีรอยด์และไม่มีความผิดปกติทางระบบประสาทหลงเหลือ นอกจากนี้ไม่พบว่ามีผู้ป่วยคนใดมีอาการเกิดซ้ำอีกภายหลังอายุ 5 ปี สาเหตุของการเกิดความผิดปกติของการทรงตัวที่เกิดซ้ำนี้ยังไม่แน่ชัด และคณะผู้รายงานเชื่อว่าปฏิกิริยาตอบสนองของระบบภูมิต้านทานของร่างกาย น่าจะเป็นสาเหตุหนึ่งของการเกิดความผิดปกตินี้

* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400