항 GQ1b 항체 양성인 급성 양측 동공산대 및 외전신경 마비

부산대학교 의학전문대학원 소아과학교실

김경민 · 송귀정 · 이윤진 · 남상욱 · 김영미

Acute Bilateral Mydriasis and Abducens Nerve Palsy with anti-GQ1b Antibody

Ophthalmoplegia without ataxia has various etiologies. An atypical Miller Fisher syndrome implies an ophthalmoplegia without ataxia, areflexia or both. The presence of anti-GQ1b antibody supports the diagnosis of an atypical Miller Fisher syndrome. A 4-year-old Russian girl visited our hospital because of acute bilateral abducens nerve palsy and mydriasis. Although the muscle power of extremities was normal and she didn't show an ataxia, the deep tendon reflex of both knees and ankles was absent. The results of nerve conduction study and cerebrospinal fluid analysis were normal. Magnetic resonance imaging (MRI) showed an enhancement of the bilateral abducens nerve. The anti-Gq1b antibody titer was elevated. The diagnosis of atypical Miller Fisher syndrome was made and a therapy with intravenous immunoglobulins led to the clinical recovery. We report a girl with atypical Miller Fisher syndrome with acute bilateral abducens nerve palsy and mydriasis, diagnosed by of anti-GQ1b antibody positivity.

Key Words: Miller Fisher syndrome, GQ1b ganglioside, Ophthalmoplegia

Kyung Min Kim, M.D., Gui Jeong Song, M.D.,
Yoon Jin Lee, M.D., PhD, Sang Ook Nam, M.D.,
PhD, Young Mi Kim, M.D., PhD

Department of Pediatrics, Pusan National
University School of Medicine, Busan, Korea

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Correspondence to Young Mi Kim, M.D., PhD.
Department of Pediatrics, School of Medicine, Pusan
National University Hospital 10, 1-Ga, Ami-dong,
Suh-gu, Busan, 602-739, Korea
Tel: +82-51-240-7298, Fax: +82-51-248-6205
E-mail: pink2129@naver.com

Introduction

Miller Fisher syndrome (MFS) is an unusual variant of Guillain-Barre syndrome (GBS)¹⁻³⁾. MFS is characterized by external ophthalmoplegia, areflexia and ataxia. The diagnosis may be supported by two laboratory findings: an elevated cerebrospinal fluid (CSF) protein and the detection of anti-GQ1b antibodies¹⁾. Chiba et al.⁴⁾ first reported about MFS patients with the presence of anti-GQ1b antibodies during the acute phase of disease and more than 90% of those patients were reported to have this antibody in their serum during this phase²⁾. So the anti GQ1b antibody is useful for the diagnosis of MFS²⁾.

We report about a 4-year-old Russian girl with atypical MFS that presented with acute bilateral mydriasis without ataxia. The MFS was confirmed by an anti GQ1b antibody positivity.

Case report

A 4-year-old Russian girl presented with a history of fever and cough one month ago and esotropia for two weeks. She was admitted to a hospital in Russia and was checked by a brain MRI. The brain MRI only showed sinusitis and she had been treated with antibiotics for two weeks. There was no improvement on her esotropia and so she visited our outpatient clinic.

On examination, she was alert, oriented and her reactions were appropriate. Vital signs including blood pressure, pulse rate, body temperature and respiration rate were stable. The neurologic examination revealed a lateral gaze palsy of both eyes and both mydriasis. Both pupils were non-reactive to light. Other cranial nerve functions were normal. The deep tendon reflex of both knees and ankles was decreased. The muscle tone was normal and there was no evidence of atrophy or fasciculation. She had no ataxic gait. Also the cerebellum function test was normal.

The initial blood tests were normal, including white blood cell count, hemoglobin, platelet, C-reactive protein, liver function test, renal function test and blood sugar level. Chest radiography, urine examination and electrocardiography were normal also. The lumbar puncture showed a sterile CSF without white blood cells as well as normal protein level (22.8 mg/dL). Herpes simplex virus, cytomegalovirus and varicella zoster virus, Epstein-Barr virus and mycoplasma were negative in the

serological tests. No respiratory virus was detected in the nasopharyngeal swab. The enterovirus polymerase chain reaction was negative in CSF and there was no bacterial growth found in blood, urine, stool or CSF. All motor and sensory nerve conduction studies were normal. An orbit MRI showed an enhancement of the bilateral abducens nerve (Fig.1). The anti-GQ1b antibody IgG titers were positive (>100%).

The girl underwent a 5 day course of intravenous immunoglobulin therapy (400 mg/kg per day) and was discharged after this treatment. The patient was doing well at 7 days follow-up, esotropia and areflexia were still present but the esotropia was mildly improved. She went back to her country. She was free of symptoms, such as mydriasis and esotropia at three months after disease onset.

Discussion

MFS is a clinical variant of GBS and is very rare in children¹⁻³. The triad of ophthalmoplegia, ataxia and areflexia was first described by Charles Miller Fisher, a Canadian stroke specialist in 1956³. Approximately 80% of patients with MFS are concerned with infections including viruses of the upper respiratory tract and enteritis due to *Clostridium jejuni*. Other pathogens including *Haemophilus influenzae*, *Mycoplasma pneumoniae*, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella-zoster virus (VZV) and mumps virus have been reported as antecedent infectious agents in MFS⁵. The diagnosis of MFS is based on the clinical manifestations of the triad (ophthalmoplegia, ataxia and areflexia). Increased cerebrospinal fluid protein levels and the presence of anti-GQ1b antibodies in serum are useful markers to support the diagnosis of MFS^{1,2}. The anti-GQ1b antibody is very specific for MFS and is present in more than 90% of MFS patients^{2,5-8}. An increased CSF protein level is found in 65% of MFS patients. The anti-GQ1b antibody represents in the first week after the onset of symptoms, while the CSF albumin-cytologic dissociation mostly represents in the first 2 weeks after the onset of symptoms⁶⁻⁸. Therefore, a serum anti-GQ1b antibody test is better for the diagnosis of MFS than an albumin-cytologic dissociation in CSF within 1 week⁷⁻⁹. However, anti-GQ1b antibody doesn't only appear in Miller Fisher syndrome. In 2001, Odaka et al.¹⁰ named following diseases with ophthalmoparesis and ataxia including Miller Fisher syndrome: muscle paralysis associated Guillain-Barre syndrome, Bickerstaff's brainstem encephalitis (BEE) and acute ophthalmoparesis as the "anti-GQ1b IgG antibody syndrome".

GQ1b ganglioside mainly has been localized in the oculomo-

Fig. 1. MRI of orbit show the enhancement of bilateral 6th cranial nerve (arrows).

tor nerve (III), trochlear nerve (IV) and abducens nerve (VI) of cranial nerves²⁾. A MRI of brain or spinal cord shows an enhancement of the cranial nerve roots⁶⁾. An absence of an abnormality in brain and spinal MRI should not negate the involvement of brain and spinal cord. MRIs of brain and spine are frequently normal. Tests of nerve conduction may show diminished activities of nerves usually carrying sensory information to the spinal cord and brain⁵⁾. Electrophysiological tests are not specific in MFS, however, they are important to diagnose the disease and to determine the prognosis¹¹⁾.

The Miller Fisher syndrome usually shows a benign course of disease. Most patients with Miller Fisher syndrome completely improve within 8 to 12 weeks and may be almost recovered within 6 months^{7,8,12)}. However, residual deficits can be left in some patients and relapses may occur very rarely¹³⁾. The treatment with intravenous immunoglobulin or a plasma exchange may be effective in case of severe disease courses. Today, an intravenous immunoglobulin infusion is recognized to be the most effective treatment^{13,14)}. In our study, IVIG had not been found to be effective because of improvement of symptoms 3 months later.

Studies in the Miller Fisher syndrome of children are still insufficient. But, a Miller Fisher syndrome should be considered first if children have an ophthalmoplegia associated with infection. The detection of anti-Q1b antibody in the serum is thought to be helpful for the diagnosis of MFS during the acute phase of disease, if this disease shows occurs atypically.

요약

비정형 Miller Fisher 증후군은 보행실조나 건반사 소실을 동반하지 않는 외안근 마비를 보이는 환자에서 진단할 수 있으며, 혈청 항 GQ1b 항체가 검출되는 경우 진단에 도움을 받을 수 있다. 평소 건강했던 4세 러시아 소녀가 급성 양측 외전 신경 마비와 동공산대를 주소로 내원하였다. 운동실조는 없었지만, 심부건반사가 소실되었고, 혈청 항 GQ1b 항체가가 상승되었으며, 뇌 자기공명영상에서 양측의 외전신경의 조영증강이 관찰되었다. 정맥 면역 글로불린 투여 하였고 3개월후에 임상적 증상이 호전되었다. 저자들은 급성 외안근 마비, 동공산대와 심부건 반사 소실 증상을 보인 4세 여아에서 항 GQ1b 항체가 양성인 비정형 Miller Fisher 1례를 경험하고 치료하였기에 보고하는 바이다.

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