

Case Report

A Case of Miller Fisher Syndrome with Anti GQ1b in Thailand

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Miller-Fisher syndrome (MFS) is a rare variant of Guillain-Barré syndrome (GBS) and is characterized by the clinical triad of ataxia, ophthalmoplegia, and areflexia. The incidence rate in Thailand has not been established but it occurred approximately 1-5% that of GBS. Here, the authors report a Thai patient diagnosed as MFS that had a positive test of antibodies against the ganglioside GQ1b. These antibodies have diagnostic and pathogenic importance to MFS because of high sensitivity and specificity. All other investigations, such as cerebrospinal fluid analysis, electrophysiological studies, and imaging studies had no significant abnormalities. The patient was successfully treated with intravenous immunoglobulin and fully recovered within one month. After eighteen months follow-up, he is still healthy and has had no recurrent symptoms.

Keywords: Miller Fisher syndrome, Guillain-Barré syndrome, Anti-ganglioside, GQ1b, Immunoglobulin

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The Guillain Barré syndrome (GBS) is an acute inflammatory demyelinating polyneuropathy, usually associated with respiratory or gastrointestinal infection. Previously, it was considered as a single disorder. Nowadays, there are four main forms as follows: AIDP (acute inflammatory demyelinating polyneuropathy); the most common variation, AMAN (acute motor axonal neuropathy), AMSAN (acute motor-sensory axonal neuropathy), and MFS (The Miller Fisher syndrome). Electrophysiologic studies are the most sensitive and specific tests for GBS. However, there is no specific electro-physiologic abnormality in MFS. Anti-ganglioside GQ1b is now highly specific for diagnosis of the MFS. Here, the authors report a Thai patient diagnosed as MFS who had a positive test for AntiGQ1b.

Case Report

A 38 year-old Thai man presented with vertical diplopia and vertigo for three days. He had a history of myasthenia gravis for 20 years and had full remission after one year's treatment. He was previously

healthy and had no history of recent respiratory tract infection, alcohol consumption, or smoking. General physical examination was within normal limit. His consciousness was alert with normal speech. Both pupils were 8 mm in size and reacted sluggishly to light. Visual acuity was 20/20 both eyes. Bilateral ptosis was detected. The extra-ocular movements of both eyes were impaired in all directions. Gaze evoked horizontal nystagmus was demonstrated. There were no other cranial nerve abnormalities, no motor weakness, and no abnormal sensation. All deep tendon reflexes were absent. Romberg's sign was positive while other cerebellar signs were normal. The computed tomography of brain and magnetic resonance imaging of the brain, orbit and cavernous sinus were normal. The cerebrospinal fluid (CSF) was clear, without white blood cell. CSF protein and glucose was 22 and 68 mg/dL. The CSF/plasma glucose ration was 80%. The CSF India ink was also negative. The electrodiagnostic test demonstrated normal nerve conduction velocity, normal electromyogram, normal F wave, normal H reflex, normal repetitive nerve stimulation (RNS), and normal blink reflex. The magnetic resonance imaging of the whole spinal cord was normal. Serum for anti-ganglioside antibody was

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performed at Institute of Molecular Medicine, University of Oxford, United Kingdom. Additionally, the result was positive high titer 1600 (normal range 0-25). On the second day of admission, he developed nearly total ophthalmoplegia of both eyes. He was treated with intravenous immunoglobulin and gradually improved. At one month follow up, the pupil size of both eyes was 3 mm and responded to light normally. In addition, there was no ophthalmoplegia or gait abnormality. He is still healthy and has had no recurrent symptoms eighteen months after treatment.

Discussion

Miller Fisher syndrome (MFS), a Guillain Barré syndrome variant, was first reported in 1956 by Miller Fisher at Harvard Medical School⁽¹⁾. It is characterized by ataxia, ophthalmoplegia, and areflexia without significant weakness. In addition to this classical triad, some patients may have other neurological features such as ptosis, facial palsy, bulbar palsy, pupillary dilatation with pupillary areflexia, dysesthesia, generalized weakness, and micturition disturbance⁽²⁾. Some infectious agents and conditions are related to MFS. The preceding infection caused by Hemophilus influenza and Campylobacter jejuni is clearly associated with this rare disease⁽³⁾. In addition, some reports showed correlation of MFS with Epstein-Barr virus, Salmonella enteritidis, Chlamydia pneumonia, Mycoplasma pneumonia⁽⁴⁾, and Burkitt lymphoma⁽⁵⁾.

There is no specific pattern of electro-physiological study in MFS. In a serial multimodal neurophysiological study⁽⁶⁾ demonstrated abnormal H reflex and F wave, abnormal facial nerve conduction and blink reflex, abnormal somatosensory evoked potential (SEPs), and abnormal vibration perception threshold with normal electromyogram, electroencephalogram, and brainstem auditory evoked potential (BAEPs). However, abnormal jaw reflex⁽⁷⁾ or sensory impairment⁽⁸⁾ may be detected. MFS is generally thought to result from peripheral neuropathy. Several magnetic resonance imaging reports have indicated abnormalities at pons, brainstem, cerebellar tract, or posterior column⁽⁹⁾, which suggests that central lesions are also responsible for some clinical aspects of MFS. The CSF protein is increased in 60% of cases⁽³⁾. In this case, there was no abnormal finding in all investigations. However, anti-GQ1b antibody, a confirmation test, was positive.

Anti-GQ1b antibody is an immunoglobulin G (IgG1 antibodies) to gangliosides that are complex glycosphingolipids mostly in neuronal membranes. Different gangliosides are distinguished by both

number and position of sialyl residues, their main component⁽¹⁰⁾. The anti-GQ1b (IgG) has been found in 90% of cases of MFS⁽¹¹⁾. These antibodies also have high specificity for this benign syndrome because normal sera do not have them. However, they may be found in patients with related conditions that share the same pathogenesis, including the acute oropharyngeal palsy variant of GBS, Guillain-Barré-Fisher overlap syndrome, and benign brain stem encephalitis. Furthermore, the titer of the antibody indicates disease activity because it reduces with the clinical course of the disease. Several studies have found increased anti-GQ1b antibody titers in MFS^(12,13), with the immunoglobulin being of IgG class rather than IgM. At the presentation, the titer of anti-GQ1b was 1,600 (normal 0-25). Unfortunately, the level of these antibodies was not investigated after he had completely recovered.

MFS is a benign, self-limited disease. The average time of improvement of ataxia and ophthalmoplegia was 12 (range 3-41) and 15 (range 3-46) days, respectively. The patients will have full recovery from ataxia and ophthalmoplegia in 32 (range 8-271 days) and 88 (range 29-165) days, respectively. Within six months, all patients should be free of symptoms and areflexia will become normal by the end of follow-up. The presented patient recovered within these ranges.

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รายงานผู้ป่วยกลุ่มอาการ Miller Fisher ที่ตรวจพบภาวะภูมิคุ้มกันต่อ ganglioside GQ1b ในประเทศไทย

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กลุ่มอาการ Miller Fisher เป็นกลุ่มอาการผันแปรชนิดหนึ่งของกลุ่มอาการ Guillain-Barré syndrome (GBS) ซึ่งพบได้ไม่บ่อย กลุ่มอาการนี้ประกอบด้วยอาการแสดงหลัก 3 อย่างคือ อาการเดินเซ กล้ามเนื้อควบคุมการเคลื่อนไหวของตาเป็นอัมพาตและภาวะไม่มีปฏิกิริยาของเส้นเอ็น อัตราการเกิดกลุ่มอาการนี้ในประเทศไทยยังไม่ทราบแน่ชัด แต่มีการประมาณว่าพบได้ประมาณร้อยละ 1-5 ในผู้ป่วยกลุ่มอาการ GBS รายงานนี้ต้องการรายงานผู้ป่วยกลุ่มอาการ Miller Fisher ชาวไทยที่ตรวจพบภาวะภูมิคุ้มกันต่อ ganglioside GQ1b ซึ่งเป็นภูมิคุ้มกันสำคัญที่ช่วยในการวินิจฉัยกลุ่มอาการนี้เนื่องจากมีความไวและความจำเพาะสูง การตรวจทางห้องปฏิบัติการอื่น ๆ อาทิ การตรวจน้ำไขสันหลัง การตรวจโดยวิธีคลื่นไฟฟ้าและสรีรวิทยา การตรวจทางรังสีวิทยาของผู้ป่วยรายนี้ไม่พบความผิดปกติ ภายหลังจากการรักษาด้วย immunoglobulin ทางหลอดเลือดดำพบว่าผู้ป่วยมีอาการดีขึ้นเป็นลำดับ และอาการเป็นปกติภายใน 1 เดือนและไม่พบว่ามีการกลับเป็นซ้ำอีกภายหลังการติดตามการรักษาเป็นระยะเวลา 18 เดือน