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Acute Complex Neuroplegia and Ophthalmoplegia Associated with Anti-GQ1b Antibodies

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ABSTRACT

A 24-year-old gentleman presented with a history of severe throbbing headache preceded by sore throat. He was noted to have a nasal twang and dysphagia. He progressively developed weakness of all four limbs associated with ophthalmoplegia. He, subsequently, had to be intubated and ventilated in view of the involvement of the respiratory muscles. His anti-GQ1b antibodies were positive and the diagnosis of Bickerstaff brainstem encephalitis associated with Miller Fisher Syndrome overlapping with Guillain-Barre syndrome was confirmed. He was treated with intravenous Immunoglobulins 0.4 gm/kg/day for 5 days which resulted in a gradual recovery from his neurologic weakness.

Key words: *Ophthalmoplegia, Miller Fisher, Guillain-Barre syndrome, Bickerstaff encephalitis*

Anti-Gq1b Antikorları ile İlişkili Akut Kompleks Nöroloji ve Oftalmopleji

ÖZET

Yirmi dört yaşında bir erkek boğaz ağrısını takip eden zonklayıcı tarzda şiddetli baş ağrısı şikayeti ile başvurdu. Burundan konuşma ve disfaji şikayetleri olduğunu belirtti. Hastada progresif olarak tüm dört ekstremitede güçsüzlükle birlikte oftalmopleji gelişti. Ardından solunum kasları tutulumu nedeniyle entübe edildi ve ventilasyon yapıldı. Hastanın anti-GQ1b antikorları pozitif geldi ve hastada Guillain-Barre sendromunun üstüne eklendiği Miller Fisher Sendromu ile birlikte Bickerstaff beyinsapı ensefaliti tanısı teyit edildi. Hasta 5 gün intravenöz immünüglobin 0.4 mg/kg/gün ile tedavi edildi ve nörolojik zayıflığı yavaş yavaş düzeldi.

Anahtar kelimeler: *Oftalmopleji, Miller Fisher, Guillain-Barre sendromu, Bickerstaff ensefaliti*

INTRODUCTION

Guillaine-Barre syndrome (GBS), also known as acute inflammatory demyelinating polyneuropathy (AIDP) is a relatively uncommon disease with a worldwide incidence of 0.75 – 2.0 cases per 100,000 population (1). Miller Fisher Syndrome (MFS) is a rare variant of GBS, which occurs in about 1 - 5% of all cases in the Western population (2). MFS is characterized by an acute onset of ataxia, areflexia and ophthalmoplegia (3) and when there is associated disturbance of consciousness the condition is known as Bickerstaff brainstem encephalitis (BBE) (4-6). This suggests that the different syndromes are in fact part of a spectrum of immune-mediated disorder involving the peripheral nerves at one end and the central nervous system at the other. The present report describes a young gentleman who presented with an unusual neurology and had rapid deterioration but was managed appropriately on intensive care unit.

CASE

A 24-year-old man was admitted to our hospital with a history of generally feeling unwell for 3 days. He developed severe throbbing headache associated with numbness of the hands and extreme fatigability, making it difficult for him to get out of bed without help. He had

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a history of sore throat a week prior to admission. His father noticed a nasal twang in his speech. He found it difficult to swallow food, both solids as well as liquids. He was getting progressively weak and was referred to the hospital by his General Practitioner. On examination by the attending physician, he was drowsy but arousable. He was haemodynamically stable and apyrexial. On neurological examination, there was no cognitive impairment. He had dysarthria with a prominent nasal twang. Cranial nerve examination revealed bilateral small pupils with absent light reflexes. He could not gaze upwards and his horizontal and downward gaze were mildly limited. He had bilateral sixth nerve palsy with limited movement of medial recti suggestive of involvement of second, third and probably fourth cranial nerve. He also had bilateral facial weakness along with ninth, tenth, eleventh and twelfth nerve palsy. The upper limb examination revealed a power of 2/5 bilaterally with a grip of 0/5 on the right and 1/5 on the left side on the Medical Research Council (MRC) scale. All the tendon reflexes were absent and the plantars were flexor bilaterally. There was no sensory loss. The examination of the fundus as well as of the rest of the systems was unremarkable. Routine laboratory investigations were normal. His cerebrospinal fluid examination was clear in appearance with normal pressure, protein and glucose. Cell count showed White Cell Count (WCC) 65/mm^3 with 95% lymphocytes and 5% neutrophils. His CT head was unremarkable.

We considered differential diagnoses of Miller Fisher syndrome (MFS), GBS and meningitis/encephalitis, botulism, Bickerstaff brainstem encephalitis (BBE) and HIV encephalitis with MFS. He was commenced on Ceftriaxone and Aciclovir. Whilst on the ward, he deteriorated and developed complete flaccid paralysis with difficulty in breathing due to respiratory muscle weakness. He was, therefore, intubated and ventilated and transferred to the intensive care unit. Further investigations including antinuclear antibodies, anti-nuclear cytoplasmic antibodies, Ebstein Bar virus, Parvovirus, toxoplasmosis and botulinum toxin were negative. His serological tests for syphilis, HIV and Lyme were negative as well. The blood cultures did not grow any micro-organism. Anti ganglioside antibodies were sent to Southern General Hospital, Glasgow. He was subsequently commenced on IV IG 0.4 gm/kg/day for 5 days as per neurologists' advice. Seeing his very gradual recovery, percutaneous tracheostomy was performed on day 6. On day 8 on intensive care unit, he started bringing up greenish sputum and spiked temperature. His repeat chest X-ray confirmed a diagnosis of ventilator-associated pneumonia. He was treated with Timentin. His anti-GQ1b antibodies came back as positive (Table 1) and the diagnosis of Bickersatff brainstem encephalitis associated with Miller Fisher Syndrome overlapping with Guillain-Barre syndrome was confirmed. On day 19 on intensive care unit, he was making gradual but good recovery. He was fully conscious and oriented. His conjugate eye movements recovered partially and the strength in the arms and legs was 3 on the MRC scale.

DISCUSSION

Our patient presented initially with a history of severe headache, dysphagia and drowsiness on admission. He developed ophthalmoplegia and flaccid weakness of all four limbs along with weakness of the respiratory muscles. The classic presentation of ophthalmoplegia, ataxia and areflexia was described by Miller Fisher in 1953 (3), who regarded it as an unusual variant of GBS resulting from peripheral nerve injury (3). One of his patients was noted to have drowsiness. Bickerstaff reported eight patients with acute ophthalmoplegia, ataxia and drowsiness, and considered this syndrome as a form of encephalitis (4). Later on, an antibody that reacts with peripheral nerve ganglioside GQ1b was found in patients with MFS (7) and in some cases of BBE (8). Further observations related anti-GQ1b to the presence of ophthalmoplegia and ataxia. Greater amounts of ganglioside GQ1b have been found in cranial nerves III, IV and VI (7). These syndromes have been related to GBS since the first description of Bickerstaff and Fisher and supported by several overlapping cases (8,9) describing the presence of muscle weakness and albumino-cytologic dissociation in addition to the classic triad of Fisher and/or altered consciousness. The prognosis is usually benign, especially in the 'classic, MFS (10) and while in GBS treatment with plasmapheresis or immunoglobulin is widely recommended,(11) in MFS these are not always necessary (10). In BBE or MFS/BBE overlapping cases, this treatment has been associated with beneficial effects. However, randomized controlled trials are needed to establish the value of immunotherapies or other treatments (12).

The relationship of BBE to MFS or GBS remains controversial (13). Serum anti-GQ1b IgG antibody levels can be elevated in all these diseases (14). Moreover, some clinical findings such as areflexia and CSF albumino-cytologic dissociation can be detected in all these diseases. Clinically

***Table 1**. Anti-Glycolipid antibody titres of the patient*

Glycolipid	*IgG*	*IgM*	*Normal range*
GM1	*Negative*	*Negative*	*< 1/500*
GM2	*Negative*	*Negative*	*< 1/500*
GM3	*1/300*	*Negative*	*< 1/500*
GA1	*Negative*	*1/200*	*< 1/5000*
GD1a	*1/2200*	*1/200*	*< 1/500*
GD1b	*1/1500*	*1/200*	*< 1/500*
GT1b	*1/2100*	*1/200*	*< 1/500*
GQ1b	*1/10000*	*1/300*	*< 1/500*
GD3	*1/12500*	*1/300*	*< 1/500*
Sulphatides	*1/4000*	*Negative*	*< 1/10000*
Globoside	*Negative*	*Negative*	*< 1/500*

BBE, MFS and GBS are characterized by similar features. It is suspected that BBE,MFS and GBS form continuous spectrum; BBE is a distinct disease entity or a variant of MFS and GBS (15,16).

The presence of Anti GQ1b IgG suggests that a common autoimmune mechanism functions in the pathogenesis of GBS, MFS and BBE. It is worth checking Anti GQ1b antibodies in patients who present with a complex neurology and ophthalmoparesis. Always consider overlap of different disorders in patients presenting with bizarre neurology. Patients who present with rapidly deteriorating neurology needs very close monitoring as they do often develop respiratory muscles weakness requiring ventilatory support as was the case in our patient. Patients presenting with unexplained ophthalmoparesis a fortiori if it is associated with a general complex clinical picture, may benefit from testing for anti-GQ1b antibodies.

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REFERENCES

1. *Ropper AH. The Guillain-Barre Syndrome. N Engl J Med 1992; 326:11306.*
2. *Mori M, Kuwabara S, Fukutake T, Yuki N, Hattori T. Clinical features and prognosis of Miller Fisher syndrome. Neurology 2001; 56:1104-6.*
3. *Fisher M. An usual variant of acute idiopathic polyneuritis (Syndrome of ophthalmoplegia, ataxia and areflexia) N Eng J Med 1956; 255: 57-65.*
4. *Bickerstaff, ER. Brainstem Encephalitis: further observations on a grave syndrome with benign prognosis. Br Med J 1957; 1: 1384-7.*
5. *Bickerstaff ER, Cloake PC. Mesencephalitis and rhombencephalitis. BMJ 1951; ii:77-81.*
6. *Al-Din AN, Anderson M, Bickerstaff ER, Harvey I. Brainstem encephalitis and the syndrome of Miller Fisher: a case study. Brain 1982; 105: 481495.*
7. *Chiba A, Kusunoki S, Obata H, et al. Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher Syndrome and Guillain-Barre syndrome: clinical and immunohistochemical studies. Neurology 1993; 43: 1911-7.*
8. *Odaka M, Yuki N, Yamada M, et al. Bickerstaff's brainstem encephalitis : clinical features of 62 cases and a subgroup associated with Guillain-Barre syndrome. Brain 2003; 126: 2279-90.*
9. *Snyder LA, Rismondo V, Miller NR. The Fisher variant of Guillain-Barré syndrome (Fisher syndrome). J Neuroophthalmol 2009 Dec;29(4):312-24.*
10. *Overell JR, Willison HJ. Recent developments in Miller Fisher Syndrome and related disorders. Curr Opin Neurol 2005; 18: 562-6.*
11. *Hughes RA, Cornblath DR. Guillain-Barre syndrome. Lancet 2005; 366: 1653-66.*
12. *Overell JR, Hsieh ST, Odaka M, et al. Treatment of Fisher syndrome, Bickerstaff's brainstem encephalitis and related disorders. Cochrane Database Syst Rev 2007; 1; CD004761.*
13. *Ogawara, K; Kuwabara, S; Yuki, N. Fisher syndrome or Bickerstaff brainstem encephalitis? Anti-GQ1b IgG antibody syndrome involving both the peripheral and central nervous systems. Muscle and Nerve 2002; 26 (6):845-9.*
14. *Matsuo, M; Odaka, M; Koga, M; Tsuchiya, K; Hamasaki, Y; Yuki, N. Bickerstaff's brainstem encephalitis associated with a IgM antibodies to GM1b and Gal-NAcGD1a. J Neurol Sci 2004; 217 (2): 225-8.*
15. *Ogawara , K; Kuwabara, S; Mori, M; Hatori, T; Koga, M; Yuki, N. Axonal Guillain-Barre syndrome: relation to anti-ganglioside antibodies and Compylobacter jejuni infection in Japan. Ann Neurol 2000; 48 (4): 624-31.*
16. *Odaka, M; Yuki, N; Hirata, K. Anti-GQ1b IgG antibody syndrome: clinical and immunologic range. J Neurol Nerosurg Psychiatry 2001; 70 (1):50-5.*