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Isolated bulbar palsy with anti-GM3 and GT1b antibodies

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Abstract

Isolated acute bulbar palsy has been described as one of the more rare variants of Guillain-Barré syndrome. IgG anti-ganglioside antibodies are associated with axonal subtypes of Guillain-Barré syndrome as well as Fisher syndrome. However, IgG against GM3 and GT1b in relation to bulbar palsy is uncommon. In this case report, we describe a 64 year-old male patient presenting with isolated bulbar weakness and generalized hyporeflexia without limb weakness. Serological testing for antiganglioside antibodies was positive for IgG anti-GM3 and -GT1b, suggesting the association of these antibodies with isolated bulbar palsy.

INTROUDUCTION

Gangliosides are a family of glycosphingolipids containing sialic acid that are commonly found in the nervous system, and IgG anti-ganglioside antibodies have been associated with the pathogenesis of Guillain-Barré syndrome (GBS) and its variant Fisher syndrome (FS). FS is characterized by external ophthalmoplegia, ataxia and areflexia. However, patients with FS and GBS can also demonstrate bulbar weakness. Isolated bulbar palsy has been described to be a lesser variant of FS although both conditions are rare.[1] Another rare variant of GBS, pharyngeal–cervical–brachial weakness is associated with bulbar palsy and proximal upper limb weakness. These conditions are associated with ganglioside antibodies, specifically GT1a, GQ1b and GD1a.[2]

Rojas-Garcia *et al*.[3] retrospectively reviewed the association of antiganglioside antibodies against terminal NeuNAc (alpha2-3) Gal in over 3,000 patients from 1998 to 2007. The anti-GM3, GD1a and GT1b combination was found in only 10 patients (Table 1). Eight of out of 10 patients had symptoms of bulbar involvement. All 10 patients were male with an average age of 60.4 years (range 35-74 years). Five patients (no. 1-5) who presented with acute symptoms, had a history of upper respiratory tract infection, and were positive for IgG antibodies, while the other 5 patients (no. 6-10) had chronic symptoms with positive IgM antibodies on testing. Frequent symptoms were dysphagia or dysphonia. Other symptoms included vocal cord paralysis, nasal voice, ophthalmoplegia, ptosis, and bilateral facial paresis. The patients with acute symptoms (cases 2, 3, 5) received intravenous immunoglobulin (IVIG) and recovered. Case no. 4 received IVIG, prednisolone and had plasma exchange with no improvement. The three patients (no. 8-10) with chronic presentations were treated. Case no. 8 received IVIG and fully recovered. Cases 9 and 10 received IVIG, prednisolone and plasma exchange, but neither showed improvement. Their antibodies against terminal NeuNAc (alpha2-3) Gal epitope were rare and may relate to bulbar involvement.

Rojas-Garcia *et al*.[4] reported a patient with acute oropharyngeal, facial diplegia and tongue palsy in 2006. CSF examination revealed albumin-cytological dissociation following infection of the upper respiratory tract. High titers of anti-GM3, GD1a and GT1b IgG were detected suggesting the association with acute bulbar palsy. Koga *et al*.[1] compiled data from clinical records of 602 patients who were diagnosed as having GBS,FS, Bickerstaff's brainstem encephalitis, and acute ophthalmoparesis in order to find a correlation between early bulbar palsy and antiganglioside antibodies. They found that anti-GT1a and anti-GM-1b antibodies supported the diagnosis of GBS and GBS variant. Anti-GM1b IgG and IgM, however, did not significantly correlate with bulbar palsy.[1]

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Table 1: Serological and clinical data reported in the literature

Patient	Clinical diagnosis	Gangliosides	Ig Class
1	Acute bulbar palsy[3]	GM3,GD1a,GT1b	IgG
2	Acute ataxic neuropathy, bulbar palsy[3]	GM3,GD1a,GT1b	IgG
3	GBS[3]	GM3,GD1a,GT1b,GQ1b,GD3,GD1b,GT1a	IgG
4*	GBS[3]	GM3,GD1a,GT1b,GQ1b,GD3,GD1b,GM1,GM2	IgG
5	GBS[3]	GM3,GD1a,GT1b,GQ1b,GD3,GD1b,GT1a	IgG
6	Chronic ataxic neuropathy[3]	GM3,GD1a,GT1b,GQ1b, GD3,GD1b,GT1a,GM1,GM2	IgM
7*	Chronic ataxic neuropathy[3]	GM3,GD1a,GT1b,GQ1b,GD3,GD1b	IgM
8*	Chronic ataxic neuropathy[3]	GM3,GD1a,GT1b,GQ1b,GD3,GD1b,GM1,GM2	IgM
9*	CIDP[3]	GM3,GD1a,GT1b,GD3,GD1b	IgM
10*	CIDP[3]	GM3,GD1a,GT1b,GM1,GM2	IgM
11	GBS (arm dominant)[9]	GT1a,GT1b, GD1a, GQ1b	IgG
12**	Isolated bulbar palsy	GM3,GT1b	IgG

*GT1a was not tested; **present case; GBS, Guillain-Barré syndrome; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy.

In this report, we describe the rare presentation of a patient with isolated bulbar palsy associated with anti-GM3 and anti-GT1b antibody.

CASE REPORT

A 64 year-old male patient presented with dysarthria and difficulty in swallowing both liquids and solid food. There was no facial or limb weakness. He had a background history of diabetes mellitus for the last 20 years and was also in complete remission from diffuse large B cell lymphoma which was treated with chemotherapy for one year.

He reported numbness of both hands and feet which had been present for many years, likely related to his underlying diabetes. The patient denied a history of fever or any other antecedent illness. The bulbar symptoms had a slow progression and, at one month, the patient started to develop diplopia when looking to the left and mild ptosis of the right eye. The symptoms remained stable and did not progress pass the one month. On examination, his pupils were 2 mm and reactive to light. There was mild ptosis of the right eye, left lateral rectus palsy, reduced gag reflex bilaterally and weakness of tongue movement. Examination of the limbs revealed normal muscle power, absent deep tendon reflexes bilaterally and decreased pinprick sensation in a glove and stocking pattern.

Cerebrospinal fluid (CSF) examination showed a protein level of 135 mg/dL (normal range 15-45 mg/dL), sugar of 121 mg/dl, red blood cell (RBC) of 40 cell/ml, and white blood cell (WBC) of 3 cell/mm^3. Magnetic resonance imaging (MRI) of the brain showed no significant abnormalities. Serological testing for anti-ganglioside IgG antibodies against GQ1b, -GT1b, -GD1b, -GD1a, -GM3, -GM2 and -GM1 were performed (Euroimmun®).[5] The patient's serum was positive for anti-GT1b and GM3 antibodies.

Nerve conduction study showed evidence of demyelinating polyneuropathy and no evidence of axonopathy. Diagnosis of GBS variant was made. IVIG was not given because there was no evidence of respiratory failure or limb weakness and all of symptoms were stable for 2 months. Dysarthria was also not severe and showed improvement at 3 months follow-up.

DISCUSSION

In this report, we describe a patient with acute presentation and slow progression of isolated bulbar palsy followed a month later by ophthalmoplegia. There was areflexia but no limb weakness. Nerve conduction studies revealed demyelinating neuropathy whereas CSF revealed albumin-cytological dissociation. Serological testing was positive for IgG against

the gangliosides, GM3 and GT1b. Although the clinical presentation was unusual, the findings would suggest a less extensive variant of FS, in view of the absence of ataxia.[6]

In a recent review[2], IgG anti-ganglioside antibodies commonly associated in GBS subtypes and variants include GM1, GD1a, GT1a, GQ1b, GQ1b, and GT1a. In contrast, anti-GM3 and anti-GT1b are rare.[2,5] At present, the antigens in acute inflammatory demyelinating polyneuropathy variant of GBS remain unknown. In acute motor axonal neuropathy, anti-GM1 or GD1a may be detected whereas FS is strongly associated with anti-GQ1b antibodies. Caudie *et al*[7]. reported that only 9 out of 249 patients with GBS had anti-GT1b and polysialoganglioside antibodies but not anti-GM3 in patients with ophthalmoplegia and lower cranial nerve involvement.[7] Anti-GM3 antibodies have been detected in patients with non-insulin-dependent diabetes mellitus and neuropathy the association with neuropathy was no significant.[8]

To our knowledge, there is only one other case report of isolated bulbar palsy with a positive anti-GM3 and -GT1b antibodies in the literature[3]. The current report of our patient adds further to the literature and highlights the usefulness of comprehensive antiganglioside antibody testing to aid in understanding the pathogenesis of this rare condition.

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