ACUTE BULBAR PALSY WITHOUT OPHTALMOPLEGIA DUE TO ANTI- GD3 IGM ANTIBODIES

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Introduction

The **acute bulbar palsy (ABP)** is a rare regional variant of Guillain-Barré syndrome (GBS) that usually affects oropharingeal muscles in the absence of prominent limb weakness. ABP can occur as either isolated form (ABPi) or associated with other symptoms ABP-plus syndrome (ABPp). [1] The **anti-GD3 antibody** has a significant association with oculomotor nerves involvement but it has never been associated with ABP variant of GBS. [2] We describe a case, never described before, of **ABPp syndrome with positivity of anti-GD3 antibodies without ophtalmoplegia.**

Case report

A 37-year-old male developed progressive acute **difficulty swallowing and hypophonia** 15 days after an episode of diarrhea. The day after the events, he showed distal numbness of the four limbs and gait ataxia. He had unremarkable past medical history. He then was admitted to our neurology department and his neurological examination showed (four days after the onset of symptoms) ataxia, positive Romberg sign, severe dysphagia to both solids and liquids and nasal quality of voice. Extraocular movements were fully preserved. The deep tendon reflexes exam showed hyporeflexia of upper limbs and areflexia of lower limbs. The strength examination was normal (Medical Research Council grade, 5) in all four limbs and in the neck muscles. A slight tactile hypoesthesia was present in the palms of hands and the soles of feet. The complete blood count and blood chemistry results were normal. His cerebrospinal fluid, obtained five days after the onset of the symptoms, showed normal protein and cell content. Brain and spinal cord MRI with gadolinium was normal. The patient's serum was tested for the presence of anti-gangliosides immunoglobulin IgG and IgM antibodies against GM1, GM2, GM3, GM4, GD1a, GD1b, GD2, GD3, GT1a, GT1b, GQ1b and Sulfatides (Immuno-Dot-Blot Assay). **The serological test was positive for IgM anti-GD3 antibodies** and hypothetical cross-reaction with anti-GT1a or anti-GQ1b antibodies were excluded because the patient's serum was examined even at lower dilution factors.

Five day after the onset of the symptoms, nerve conduction studies [Table] showed prolonged distal motor latencies (left Median nerve and both common Peroneal nerves); H reflex was bilaterally pathological. Sensory conduction velocities were reduced in both Median nerve and left Sural nerve. Repetitive Nerve Stimulation (on Facial, Spinal Accessory and Ulnar nerves) and Single Fiber Examination (on Extensor Digitorum Communis) were normal. **Electrophysiological data were suggestive of a mild demyelinating sensorimotor polyneuropathy.** A diagnosis of **Acute Bulbar Palsy with ataxia** was made based on clinical examination, serological test and electrophysiological findings. A nasogastric tube was inserted because of severe dysphagia. **Intravenous immunoglobulin was administered at dose of 0.4 mg/Kg/day for five days.** Three days later the patient showed a dramatic improvement of his symptoms and a full recovery was achieved in ten days. The nasogastric tube was removed the day after the end of therapy with Immunoglobulin. **At follow-up (one month) nerve conduction studies and neurologic exam were normal. The repeated antibodies assay at the follow-up serum was negative.**

Table
Nerve conduction studies before treatment with immunoglobulin and after one-month follow-up

	Before IVIg	After IVIg	Normal values
MOTOR NERVES STUDIES			
Right Median			
DML (ms)	3.52	3.42	≤3.60
CMAP amplitude (mV)	12.9	11.4	≥5.0
CV wrist-elbow (m/s)	60.5	64.0	≥49.96
Left Median			
DML (ms)	**3.73**	3.58	≤3.60
CMAP amplitude (mV)	12.4	12.4	≥5.0
CV wrist-elbow (m/s)	67.2	67.7	≥49.96
Right Ulnar			
DML (ms)	2.52	2.50	≤2.52
CMAP amplitude (mV)	14.9	15.9	≥5.0
CV wrist-elbow (m/s)	63.1	62.0	≥50.61
Left Ulnar			
DML (ms)	2.44	2.35	≤2.52
CMAP amplitude (mV)	14.3	15.1	≥5.0
CV wrist-elbow (m/s)	60.7	66.3	≥50.61
Right Peroneal			
DML (ms)	**5.59**	3.81	≤4.78
CMAP amplitude (mV)	8.3	9.0	≥4.0
CV ankle-fibula (m/s)	43.4	53.0	≥41.65
Left Peroneal			
DML (ms)	**6.02**	3.94	≤4.78
CMAP amplitude (mV)	4.6	9.1	≥4.0
CV ankle-fibula (m/s)	45.8	47.4	≥41.65
SENSORY NERVES STUDIES			
Right Median			
SNAP amplitude (μV)	22.9	26.4	≥10.0
CV (m/s)	**39.0**	41.9	≥41.26
Left Median			
SNAP amplitude (μV)	20.9	47.6	≥10.0
CV (m/s)	**38.3**	41.2	≥41.26
Right Ulnar			
SNAP amplitude (μV)	16.0	25.0	≥8.0
CV (m/s)	40.8	43.0	≥39.26
Left Ulnar			
SNAP amplitude (μV)	22.8	22.8	≥8.0
CV (m/s)	44.1	44.2	≥39.26
Left Sural			
SNAP amplitude (μV)	9.8	6.8	≥6.0
CV (m/s)	**31.3**	34.7	≥34.68

Abbreviation: CMAP= compound muscle action potential; CV= conduction velocity; DML= distal motor latency; IVIg= intravenous immunoglobulin; SNAP= sensory nerve action potential. Abnormal values are highlighted in bold.

Discussion

It has been recently highlighted that ABP without limb weakness can be considered a regional variant of GBS either isolated or plus (ABPi and ABPp) [1]. The most common neurologic findings accompanying ABPp syndrome are areflexia/hyporeflexia (91%), ophtalmoplegia (82%) and gait ataxia (82%). Our patient indeed showed two out of the three signs, ataxia and areflexia/hyporeflexia. Of note, there are few reports that describe acute oropharingeal palsy with positivity of anti-gangliosides antibodies [3]; the antibodies most frequently detected in this form are anti-GT1a and anti-GQ1b. **The anti-GD3 antibody is rarely found in GBS (4%)** and most frequently in Miller-Fisher syndrome (26%) [4]. This antibody is distributed in high percentage in every cranial nerve and his role in GBS variants remains unclear [5]. Although a significant association exists between the anti-GD3 antibody and the dysfunction of ocular motor nerves (III, IV and IV) [4]; **we described the first case of a patient with ABPp associated to anti-GD3 antibodies and without ophtalmoplegia or diplopia**.

Conclusions

This report suggests **expanding the spectrum of clinical syndromes associated with anti-GD3 antibodies**. Furthermore, it highlights the need for identifying a **wider anti-ganglioside screening panel** in patients with atypical forms of GBS and apparent negativity of the frequent antibodies against GT1a and GQ1b.

References:

1. Kim JK, Kim BJ, Shin HY, Shin KJ, Nam TS, Oh J, Suh BC, Yoon BA, Park HT, Huh SY, Oh SI, Bae JS, Korean Inflammatory Neuropathy Consortium. Acute bulbar palsy as a variant of Guillain-Barré syndrome. Neurology. 2016 Feb 23;86(8):742-7
2. Wang Y, Sun S, Zhu J, Cui L, Zhang HL. Biomarkers of Guillain-Barré Syndrome: Some Recent Progress, More Still to Be Explored. Mediators Inflamm. 2015;2015:564098. doi: 10.1155/2015/564098. Epub 2015 Sep 16
3. Onodera M, Mori M, Koga M, Kamitsukasa I, Fukutake T, Hattori T, Yuki N, Kuwabara S (2002). Acute isolated bulbar palsy with anti-GT1a IgG antibody subsequent to Campylobacter jejuni enteritis. J Neurol Sci. 15;205(1):83-84
4. Koga M1, Yuki N, Ariga T, Hirata K. Antibodies to GD3, GT3, and O-acetylated species in Guillain-Barré and Fisher's syndromes: their association with cranial nerve dysfunction. J Neurol Sci. 1999 Mar 15;164(1):50-5
5. Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I (1997). Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. Brain Res 16;745(1-2):32-36.

XLVII CONGRESSO DELLA SOCIETA' ITALIANA DI NEUROLOGIA
Venezia, 22-25 ottobre 2016