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LETTER TO THE EDITOR

A case report of Fisher syndrome with the detection of anti-GM3 and anti-GD1b IgG antibodies

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Introduction

Antiganglioside antibodies play an important role in the pathogenesis of Guillain–Barré syndrome (GBS) and Fisher syndrome (FS) [1]. FS is a variant form of GBS and is characterized by the triad symptoms of opthalmoplegia, ataxia, and areflexia. While serum anti-GQ1b IgG antibody is positive in almost 90% of cases of FS, associations with the other antiganglioside antibodies are rare [2]. The anti-GD1b IgG antibody is reported to be associated with ataxia in a few GBS cases [3]. The pathogenesis associated with anti-GM3 IgG antibody in GBS or FS remains unknown, but is reported to be associated with narcolepsy-cataplexy [4]. However, there has been no report of typical FS associated with anti-GD1b and anti-GM3 IgG antibodies. Here, we report for the first time a FS case that developed the triad symptoms and was anti-GQ1b IgG antibody negative but anti-GD1b and anti-GM3 IgG antibody positive.

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Case presentation

A 48-year-old healthy man suddenly developed ophthalmoplegia, mild numbness in his bilateral upper and lower limbs, and ataxia. The patient's symptoms worsened and he was admitted to our hospital 3 days after the onset of symptoms. There was no history of preceding diarrhea or respiratory infection. He had no medical treatment.

On admission, severe ophthalmoplegia was present (Fig. 1a). While bilateral lateral rectus impairments of the ocular movement were mild, there was almost no mobility in other extraocular muscles. As a result, he reported severe diplopia in all views. Direct or indirect light reflexes were prompt in both eyes. Dysarthria was present. Although there was no muscle weakness, he was not able to sit, stand, or walk due to severe truncal ataxia. Both the finger-nose test and heel-knee test results were poor. According to the sensory disturbance, numbness was only present in his distal limbs. His deep tendon reflexes showed generalized areflexia. Autonomic failure such as arrhythmia, orthostatic hypotension, and urinary disturbance did not appear. His Hughes functional grade scale at admission was 4.

Laboratory examination showed no remarkable abnormality except for antiganglioside antibodies. Cerebrospinal fluid analysis showed normal data including cell number (4/μl) and protein level (27 mg/dl). Neither cranial nor spinal magnetic resonance images showed any abnormalities. However, sensory nerve action potentials of the median and sural nerves could not be evoked (Fig. 1b). Motor nerve conduction studies showed that muscle nerve action potentials were preserved and muscle conduction velocities were at the lower limit of normal. His acute phase serum was investigated for antiganglioside antibodies by an enzyme linked immunosorbent assay (ELISA), as previously described [5]. The ELISA was performed for IgG antibodies to 10 single ganglioside antigens, GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b, GQ1b, Gal-C, and

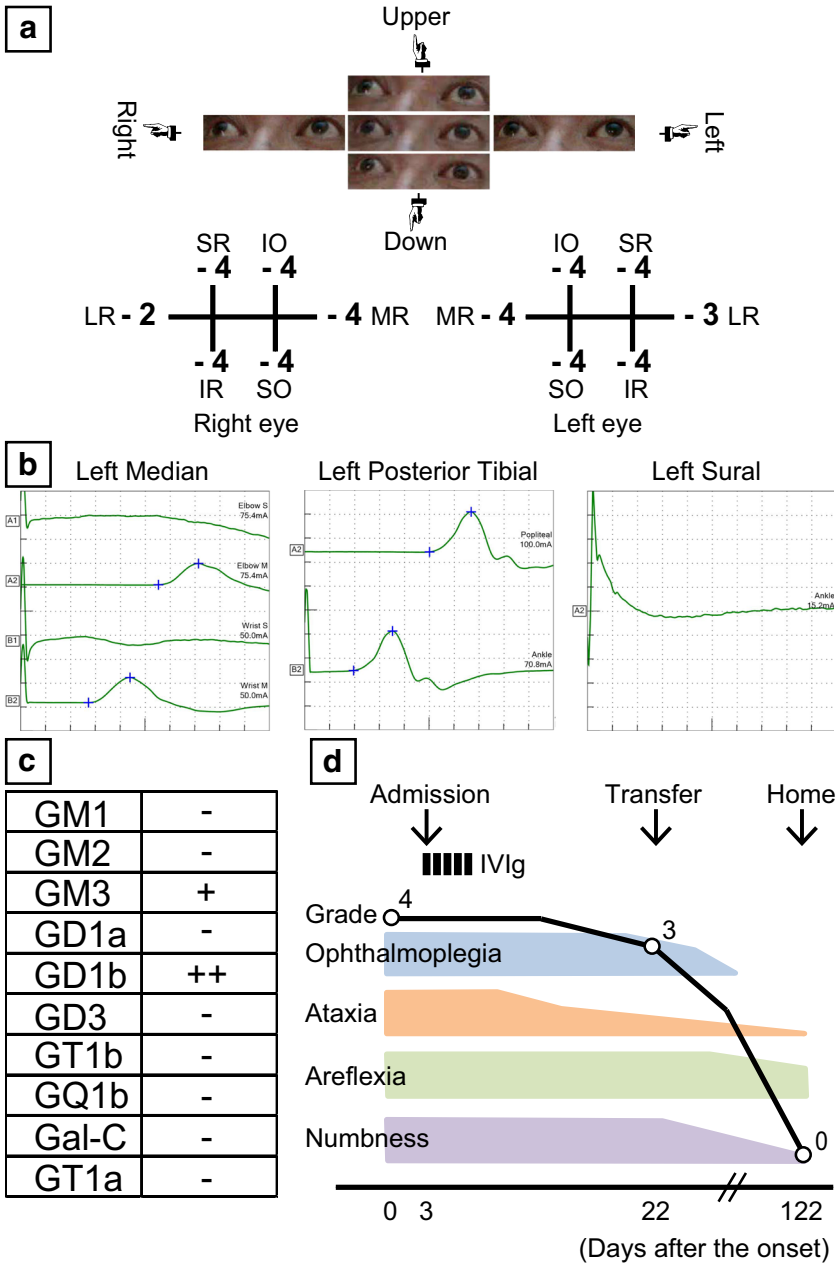

Fig. 1 Severe ophthalmoplegia at all distances, but with mild bilateral lateral rectus impairments. Photograph recording in the upper column and the conventional clinical recording of the ocular motility in the lower column. The grade of the ocular motility is from 0 (no limit) to −4 (no motility). IO, inferior oblique; IR, inferior rectus; LR, lateral rectus; MR, medial rectus; SO, superior oblique; SR, superior rectus (**a**). The nerve conduction study showing SNAPs of median and sural nerves could not be evoked, whereas CMAPs of median and posterior tibial nerves were evoked (**b**). Results of IgG antibodies to 10 single ganglioside antigens by ELISA (**c**). The antibody activity of IgG anti-GD1b was stronger than that of IgG anti-GM3. A summary of the patient's clinical course showing the relationship among events, changes in the Hughes functional grade scale, and IVIg (**d**)

GT1a, and positive results were only obtained for anti-GM3 and anti-GD1b IgG antibodies (Fig. 1c). On the basis of the patient's symptoms, he was diagnosed with FS. Owing to severe followed by acute symptoms, a 5-day course of high-dose intravenous immunoglobulin treatment was initiated at admission. Although his deep tendon areflexia remained, ataxia gradually improved and he was transferred to another hospital for rehabilitation 22 days after the onset of symptoms. His Hughes functional grade scale at transfer was 3. His symptoms without areflexia completely disappeared and he returned home 148 days after the onset of symptoms. A summary of the patient's clinical course is shown in Fig. 1d.

Discussion

Here, we present a case study involving clinical FS triad symptoms along with sensory polyneuropathy. However, FS did not progress to GBS because no muscle weakness or autonomic failure occurred during the clinical course, and the results of the motor nerve conduction studies were different from those of GBS. Thus, we report a pure case of FS, which was anti-GQ1b IgG antibody negative but anti-GD1b and anti-GM3 IgG antibody positive.

Ataxia in anti-GQ1b IgG antibody-positive FS is considered to be due to sensory disturbance because many GQ1b proteins exist in large dorsal root ganglia neurons [6].

However, in our case, we consider that ataxia mainly resulted from cerebellar ataxia because dysarthria was present and sensory disturbance was mild.

There have been a few cases of ataxic GBS presenting with sensory neuropathy with monospecific anti-GD1b IgG antibody [7, 8]. In these cases, ophthalmoplegia was specifically reported not to be present. Our case therefore differed because severe ophthalmoplegia was present, which was a major distinction with the previously reported cases. Ophthalmoplegia and cerebellar ataxia pathogenesis are difficult to explain by the monospecific anti-GD1b IgG antibody alone. We suggest that both anti-GD1b and anti-GM3 IgG antibodies played an important role in the pathology of the current case.

In summary, we report the first case of FS with anti-GD1b and anti-GM3 IgG antibody pathogenesis.

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Authors' contributions K.M. and T.O. were the attending doctors for the present case. K.Y. and S.K. investigated for antiganglioside antibodies. K.M. and K.Y. drafted the manuscript. S.K. and S.F. conceived the study, participated in its coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical standards Informed consent was obtained from the patient described in this article.

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