Ocular Flutter, Generalized Myoclonus, and Trunk Ataxia Associated With Anti-GQ1b Antibodies

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Objective: To describe a movement disorder characterized by ocular flutter, trunk ataxia, and mild generalized myoclonus associated with anti-GQ1b antibodies.

Design: Case report.

Setting: University hospital.

Patient: A 37-year-old woman presented with rapid, conjugated, and periodic oscillations of the eyes with a strict preponderance for the horizontal plane (ocular flutter); trunk ataxia; and occasional arrhythmic muscle jerks (myoclonus) most pronounced at the neck.

Results: Brain magnetic resonance imaging results were normal. Cerebrospinal fluid examination revealed mild lymphocytic pleocytosis. Results of extensive serological tests on viral, bacterial, and fungal infections from blood and cerebrospinal fluid samples were unremarkable. Results of screening examinations for neoplasms and paraneoplastic antibodies, including whole-body fludeoxyglucose F18 positron emission tomography, were normal. Positive titers of IgG and IgM anti-GQ1b antibodies were found.

Conclusions: This is the first description of an association between the clinical syndrome of ocular flutter, mild stimulus sensitive myoclonus, and trunk ataxia and anti-GQ1b antibodies. The association with ganglioside antibodies lends further support to the notion of an autoimmune-associated pathology of the syndrome.

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Ocular Flutter is a rare oculomotor syndrome that is clinically defined by intermittent bursts of involuntary conjugate eye oscillations with a strict preponderance for the horizontal plane and without intersaccadic interval.1 Ocular flutter has been considered to be a subform of opsoclonus, probably caused by a loss of tonic stimulation of omnipause neurons.2 In the healthy brain, omnipause neurons inhibit burst neurons within the paramedian pontine reticular formation.1,2 A recent case of ocular flutter after a circumscribed pontine lesion due to multiple sclerosis strongly supports the role of the paramedian pontine reticular formation within the current pathophysiological concept of ocular flutter.3 Cogan4 and Baringer and colleagues5 are credited for the first descriptions of a movement disorder characterized by brief jerks of conjugated eye movements and postural body tremor. Although ocular flutter and opsoclonus probably share a common pathophysiology, the syndromes are clinically distinct. Whereas the conjugate oscillations of the eyes are strictly horizontal in ocular flutter, irregular oscillations in both the horizontal and vertical planes are observed in opsoclonus.1,2 Hankey and Sadka6 reported a case of ocular flutter associated with postural body tremor and trunk ataxia. In each of these early descriptions, cerebrospinal fluid examination revealed a mild lymphocytic pleocytosis, suggesting a parainfectious origin. Despite the frequent lack of direct serological evidence, the etiology of ocular flutter has been

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small-cell lung cancer.11,12

with several forms of cancer, such as breast cancer10 and ever, ocular flutter has also been reported to be associated

lieved when the patient was in a recumbent position. The

stimulus sensitive myoclonus (which was most 

associated with anti-GQ1b antibodies. Our case descrip-

ter infection with viruses,5-10 such as the mumps virus,5
to the patient for 5 days together with the antiviral and

acetate (1000 mg once a day intravenously) was given

mg once a day intravenously) for 14 days. Prednisolone

left to right (100 mg once a day orally) for 11 days. Plasma-

ersis therapy began 21 days after admission, with daily

mphilus influenzae, Neisseria meningitidis, Campylobacter
to the patient for 5 days together with the antiviral and

ther: tests included screenings for infection with Eb-

mycolus associated with anti-GQ1b antibodies. Our case description strengthens the autoimmune response hypothesis of this rare syndrome.

 Three days before admission, a 37-year-old woman de-

cular flutter, trunk ataxia, and mild generalized myoclonus

3.12 Chlamydia pneumoniae, Borrelia burgdorferi, Haemophi-

serous infection (oscillopsia), diz-

inclusions of horizontal external motion (oscillopsia), diz-

neuronal, acoustic, and visual evoked potentials and

type A and B, cytomegalovirus,

rhus simplex virus type 1 and 2, varicella-zoster vi-

stein-Barr virus, mumps, measles, rubella virus, adeno-

CMV, EBV, measles, rubella virus, adenovirus, influenza virus type A and B, cytomegalovirus,

and anti-amphiphysin, were negative. Ganglioside anti-

infections. Tests included screenings for infection with Eb-

of gadolinium–diethylenetriamine pentaacetic acid. Analy-

s) and ataxia of the trunk and gait being more pronounced.

Red and white blood cell counts and biochemistry were 

were normal on admission. Cerebrospinal fluid examination on

made normal opening pressure and mild pleocytosis (75 lymphocytes/mm³). Cerebrospinal fluid

protein, lactate, and glucose levels were within the normal

range. Oligoclonal bands were positive and quantita-

tive cerebrospinal fluid IgG and IgM indexes were posi-

tive. Results of a cerebrospinal fluid examination repeated

10 days later were unremarkable (3 lymphocytes/mm³).

Brain magnetic resonance imaging, including 2-mm

sections through the brainstem and the cerebellum, showed

no abnormality before or following application of gadolinium–diethylenetriamine pentaacetic acid. Analysis of ocular movements using electrooculography revealed bursts of rapid horizontal, symmetric, and sinusoidal movements without intersaccadic interval (Figure).

Results of electrophysiological examinations, such as somatosensory, acoustic, and visual evoked potentials and electroencephalography, were normal. Results of duplex Doppler ultrasonography of the extracranial and intracranial vessels were also normal.

Serological tests, cultures, and polymerase chain re-

actions performed on blood and cerebrospinal fluid

samples were negative for viral, bacterial, and fungal in-

fections. Tests included screenings for infection with Eb-

stein-Barr virus, mumps, measles, rubella virus, adeno-

virus, influenza virus type A and B, cytomegalovirus,

herpes simplex virus type 1 and 2, varicella-zoster vi-

rus, enterovirus, human immune deficiency virus type

1 and 2, Chlamydia pneumoniae, Borrelia burgdorferi, Haemophilus influenzae, Neisseria meningitidis, Campylobacter jejuni, Mycoplasma pneumoniae, Yersinia, Listeria monocytogenes, Streptococcus pneumoniae, Mycobacterium tuberculosis, and Treponema pallidum.

Results of screening examinations for neoplasms, in-

cluding abdominal ultrasonography, computed tomog-

raphy of the abdomen and chest, as well as whole-body

fluorodeoxyglucose F18 positron emission tomography, were all unremarkable. Serological tests of blood and cerebrospinal fluid for paraneoplastic antibodies, such as anti-Ri (ANNA-2), anti-Hu (ANNA-1), anti-Yo (PCA1), anti-

Ma2, anti-CV2 (collapsin response mediator protein 5), and anti-amphiphysin, were negative. Ganglioside anti-

bodies were negative for GM1, GM2, GM3, GD1a, GD1b, GD3, GT1a, GT1b, GT3, and asialo GM1. IgG and IgM antibodies against GQ1b were found.

The patient was initially treated with acyclovir (750

mg, 3 times a day intravenously) and ceftriaxone (2000

mg once a day intravenously) for 14 days. Prednisolone

acetate (1000 mg once a day intravenously) was given
to the patient for 5 days together with the antiviral and

antibiotic therapy and then was switched for an oral regi-

men (100 mg once a day orally) for 11 days. Plasmapheresis therapy began 21 days after admission, with daily

immunoabsorption of 500 mL of plasma for 2 days but had to be discontinued owing to low fibrinogen levels.

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Twenty-three days after admission, immunoadsorption therapy was started (3 L) for 3 days. Twenty-six days after admission, the patient was given intravenous immunoglobulins (10 g, 3 times a day for 5 days). The symptoms gradually resolved after the second day of immunoadsorption and continued to improve after the administration of intravenous immunoglobulins during the following 2 weeks.

**COMMENT**

This is the first description of an association between anti-GQ1b antibodies and the clinical syndrome of ocular flutter, stimulus sensitive myoclonus, and truncal ataxia. The association of ocular flutter with elevated serum titer for ganglioside antibodies lends further support to the notion of an autoimmune-associated pathology of the syndrome. The origin of ocular flutter appears to be related to a malfunction of the inhibitory control of saccadic burst neurons in the paramedian pontine reticular formation. Postural ataxia of the trunk in the absence of limb ataxia may be associated with a circumscribed dysfunction of the vestibulocerebellum, including the flocculus and the nodulus, the nucleus fastigii, the ventral uvula, and the ventral paraflocculus. Generalized myoclonus most likely results from a dysfunction within the Guillaumin-Mollaret triangle between the nucleus ruber, the inferior olive, and the dentate nucleus of the cerebellum.

It is typical of the syndrome that brain imaging does not demonstrate an anatomical lesion, and therefore the clinical symptomatology is probably caused by a functional rather than a structural disturbance within the network of areas specified. The brainstem and cerebellar features found in our patient suggest that anti-GQ1b antibodies target central nervous system epitopes in these neuroanatomical regions. Indeed, an association between ganglioside antibodies and central nervous brainstem malfunction causing oculomotor deficits (not cranial nerve dysfunction as obvious as in Miller-Fisher syndrome) has recently been described. Generally, this syndrome has a benign course, and an appropriate treatment regimen remains to be established given its rare occurrence. Intravenous high-dose immunoglobulin and plasmapheresis have been recommended, while oral steroids are less effective. In our case, antibiotics and steroid treatment did not result in profound clinical improvement. The favorable course in many reported cases is probably caused by spontaneous remission. An association with anti-GQ1b antibodies should be considered when confronted with a movement disorder that is related to dysfunction of the brainstem (ocular flutter and myoclonus) and the vestibulocerebellum (trunk ataxia), and additional clinical or instrumental data suggesting other etiologies are lacking.

**REFERENCES**