CASE REPORT

"Why do I always see double?" A misdiagnosed case of ocular myasthenia gravis for 10 years

Uduman Ali Mohamed Yousuf,¹ B M Yashodhara,¹ Thevi Thanigasalam,² Heng Siang Ting³

¹Department of Medicine, Melaka Manipal Medical College, Melaka, Malaysia

²Department of Ophthalmology, Melaka General Hospital, Melaka, Malaysia

³Tuanku Ja'afar Hospital, Seremban, Malaysia

Correspondence to

Dr B M Yashodhara, bmyashodhara@gmail.com

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SUMMARY

A 58-year-old man presented with diplopia and partial ptosis for 10 years. It was non-progressive in nature, despite inadequate medical attention the patient received from non-specialists/general practitioners. He did not have fatigability or diurnal variation in weakness and was clinically stable without exacerbations of disease for a decade. He did not have features of Graves's disease, oculopharyngeal dystrophy, cranial nerve paralysis, polymyositis and stroke. The possibility of an atypical presentation of myasthenia gravis (MG) was considered and the patient was evaluated. Ice pack test was negative, Cogan's lid twitch (CLT) test was positive and high titres of acetylcholine receptor antibodies (AChR Ab) suggestive of MG were found. He was treated accordingly with a very good response.

BACKGROUND

Ocular myasthenia gravis (MG), in men, without progression to generalised disease and crisis in the absence of treatment for 10 years is rare, as most of the patients usually progress to generalised myasthenia in 2 years as evident in most of the studies.^{1,2} Ice pack test to the eyes usually results in improvement in eye signs in most patients with myasthenia.^{3,4} We report an atypical presentation of MG in a man in view of no diurnal variation in symptoms, no fatigability in muscle weakness, non-progression of disease or myasthenia crisis without treatment for 10 years and a negative ice pack test.

CASE PRESENTATION

A 58-year-old man had ptosis and diplopia for 10 years. He continued seeking treatment for 2 or 3 years, at presentation, but did not notice any improvement in symptoms and hence lost

follow-up for almost 8 years. There was no diurnal variation of ptosis or diplopia and no aggravating or relieving factors. The ptosis was of similar degree every day in the morning as it would be in the evening or rest of the day. There was no neck muscle weakness, no dysphagia and weakness of arms or legs. There was no history of difficulty in breathing. There was no history of fever, headache, fits, tuberculosis and swelling in the neck. The patient had diabetes, hypertension for 17 years and ischaemic heart disease for 2 years. He had repeated hospital visits for recurrent chest pain in the past 2 years, which was due to coronary artery disease (CAD); the treating doctors were focusing mainly on CAD and his eye symptoms were attributed to oculomotor nerve paralysis. There was no history of cataract surgery or any admissions to the hospital for eye symptoms in the past. Two years ago, he presented again to ophthalmology, outpatient department, for the eye symptoms. The ophthalmologist referred the patient to the neurologist, after the initial assessment. On examination, there were no scars of previous operations. There was partial ptosis in right eye, which did not fluctuate after 60s of continued upward gaze. There were full range of eye movements in all directions in both the eyes and no clinical evidence of extra-ocular movement (EOM) fatigability, but there was binocular diplopia in all directions. There were no clinical features of thyrotoxicosis. Pupils were equal in size, normally reacting to light and accommodation. There were no clinical features of third or sixth cranial nerve paralysis. There was ptosis and partial adduction of right eye in neutral position ([figure 1](#)), persistence of ptosis of right eyelid associated with lateral deviation right eye ball upon upward gaze ([figure 2](#)). A few reliable,

Figure 1 Ptosis and partial adduction of right eye in neutral position.

Figure 2 Persistence of ptosis of right eye lid on upward gaze associated with lateral deviation of the right eye ball upon upward gaze.

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Figure 3 Hess chart-1 showing reduced eye movements and diplopia in all directions at presentation. It shows underaction of right eye medial rectus with corresponding overaction of left eye lateral rectus.

easy, bedside tests could be performed to diagnose MG; Cogan's lid twitch (CLT) test and ice pack test. CLT test is a simple test; the patient is asked to look straight ahead, up, down and again look straight ahead. Twitching of upper eye lids indicates a positive test. It has sensitivity of 75% and specificity of 99% in diagnosing MG.⁵ Ice pack test is an important, simple, sensitive, specific bedside test to confirm the presence of features of MG.^{3 4 6} This is performed by applying ice to ptotic lids for 2–5 min and measuring the difference in palpebral fissures before and after the application of ice.^{3 4 6} A difference of two or more millimetres in improvement after ice application is considered a positive result.⁶ Five minutes of ice pack test is very sensitive test to diagnose MG,^{3 4} and has sensitivity of 76.9% for reducing diplopia and 96% sensitivity reducing ptosis in ocular MG patients.³ In our patient, ice pack test to the eyes was negative and CLT test was positive. The Hess chart assessment was performed and it showed reduced eye movements and diplopia in all directions at presentation, underaction of medial rectus with corresponding overaction of lateral rectus of right eye (figure 3), Hess chart-2, performed 2 weeks after

first chart demonstrated reduced eye movements and diplopia in all directions with underaction of medial rectus, inferior rectus, superior oblique of right eye with compensatory overaction of lateral rectus, inferior oblique and superior rectus of left eye (figure 4). Hence, the HESS chart assessment performed 2 weeks apart demonstrated variability of weakness of extraocular muscles. There was no fatigability of eye muscles or neck, arms and legs. Power, tone and reflexes in the limbs were normal. There were no sensory disturbances in any of the limbs. Thyroid signs were absent. There was no swelling in the neck. The acetylcholine receptor antibodies (AChR Ab) testing was performed and its titre was very high: 8.43 nmol/L (0–0.45 nmol/L). The patient was diagnosed with mild ocular MG with diabetes, hypertension, ischaemic heart disease and early chronic kidney disease.

TREATMENT

Oral pyridostigmine 60 mg twice daily, and prednisolone 5 mg once daily were started; the doses were gradually increased to 60 mg four times daily, 40 mg once daily, respectively. Over a

Figure 4 Hess chart-2, performed 2 weeks after first chart. Reduced eye movements and diplopia in all directions. Underaction of medial rectus, inferior rectus, superior oblique of right eye with compensatory overaction of lateral rectus, inferior oblique and superior rectus of left eye.

period of few months the symptoms gradually improved and the patient had full range of movements of extraocular muscles with persistence of mild partial ptosis and mild diplopia. The dose of prednisolone was tapered over months. The patient also received tablet aspirin, tablet simvastatin, tablet metoprolol and insulin. He had CAD symptoms and stress test was positive. Angiogram showed three vessel disease. The cardiology referral was performed. He underwent coronary artery bypass graft (CABG) for three vessel disease using left internal mammary vessel. During the same operation thymectomy was performed, even though he did not have generalised myasthenia or any myasthenia crisis.

Investigations

Routine blood tests full blood count, liver function tests were normal. His serum creatinine was mildly deranged: 133 $\mu\text{mol/L}$. Serum total cholesterol was 5.87 mmol/L, low-density lipoprotein was 3.68 mmol/L, glycated haemoglobin was 8.1% during early visits and levels were reduced to 3.99 mmol/L, 1.84 mmol/L and 7%, respectively, later on treatment. ECG ST segment depression in V3–V6, lead I and a VL. T3, T4 and thyroid-stimulating hormone were normal. CT of the brain was normal. Echocardiography showed mild left ventricular hypertrophy, no regional wall motion abnormalities and ejection fraction of 60%. Stress test was positive. AChR Ab antibody testing was performed and its titre was very high: 8.43 nmol/L (0–0.45 nmol/L).

DIFFERENTIAL DIAGNOSIS

- ▶ Abducens nerve palsy
- ▶ Oculomotor nerve palsy
- ▶ Diabetes
- ▶ Trochlear nerve palsy
- ▶ One and a half syndrome
- ▶ Graves ophthalmopathy
- ▶ Trauma
- ▶ Stroke
- ▶ Intracranial space occupying lesions
- ▶ Intracranial infections
- ▶ Trauma related eye surgery
- ▶ Giant cell arteritis

DISCUSSION

Diplopia could occur due to cranial nerve paralysis,^{7 8} micro-ischaemia involving sixth or third cranial nerves commonly due to diabetes,^{9 10} Graves' disease, trauma, MG,⁸ stroke, space occupying lesions, intracranial infections, related to eye surgery¹¹ or rarely due to temporal arteritis.¹² These conditions could be easily identified by clinical examination and with the help of investigations. MG is a rare, potentially serious but treatable autoimmune neuromuscular junction disorder that has a prevalence of 2–10/100 000 population.¹³ MG presents with painless, fluctuating, fatigable weakness involving specific muscle groups; the manifestations are due to antibody-mediated, T cell-dependent immunological attack against nicotinic AChR Ab and the muscle-specific tyrosine kinase (Anti MuSK Ab) on the end-plate region of the postsynaptic membrane. Commonly, it affects 29–40 years of age group; but occurs relatively early in women and later in men, although any age groups may be affected.¹⁴ It presents with asymmetric ptosis, binocular diplopia as an initial presentation, has a variable course, with progression to involve muscles of arms, legs or respiratory muscles in 50–80% of cases, if remains untreated in 2–3 years of onset,^{14–17} though early or isolated oropharyngeal or limb weakness is less common.¹⁵ The progression of MG to generalised disease is much less common

in children.¹⁸ Ten to twenty per cent of patients with ocular MG,¹³ will undergo spontaneous remission, more commonly if the age at presentation is in young age or in childhood.^{13 18} Male gender and later age at onset of the disease are associated with bad prognosis.¹³ Fifty to eighty per cent patients presenting with pure ocular MG at onset¹³ would eventually progress to generalised disease in 2 years.^{13–17} Fatigability and diurnal variation in the strength of muscles are important features of MG,¹⁹ suggested by drooping of lids on 60 s of prolonged upward gaze, progressive tongue weakness provoked by 'long, hasty or laborious speaking'. A range of bilateral, symmetrical, EOM weaknesses are common in ocular MG; typically higher degree of weakness in movements of elevator muscles (inferior oblique and superior recti).²⁰ Early diagnosis and treatment is important in MG to avert later complications. Our patient was a 58-year-old man. He had diplopia and ptosis for 10 years without treatment. He denied diurnal variation of symptoms. All the causes of diplopia were systematically ruled out by clinical examination and on investigations. His osserman staging of severity of MG,²¹ was stage 1 as the disease was confined only to eyes. He had significant improvement in symptoms and signs of the disease on treatment (vide supra). Thymectomy for ocular MG is controversial, but a recent study showed that it is effective and safe even in early stage non-thymomatous MG.²² Although our patient showed significant improvement on steroids and pyridostigmine, thymectomy was also performed, while he underwent CABG for his three vessel disease.

OUTCOME AND FOLLOW-UP

Patient did not have diplopia, had full range of EOMs and had mild partial ptosis 3 months after thymectomy.

Learning points

- ▶ Non-progression of ocular myasthenia gravis (MG) for 10 years in a middle-aged male patient is rare.
- ▶ Occurrence of stable ocular MG without treatment is also rare.
- ▶ Diplopia and ptosis with no fatigability, no diurnal variation and a negative ice pack test are unusual in a long-standing stable ocular MG.
- ▶ Early referral to a neurologist is vital for good outcome of disease.

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