Reminder of important clinical lesson

Bedside testing for myasthenia gravis: the ice-test

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Summary

A 67-year-old man presented to the acute medical take with a history of droopy eyelids and difficulty swallowing. A diagnosis of myasthenia gravis was suspected from the clinical history. The patient's symptoms were progressive, raising concerns of aspiration pneumonia or respiratory compromise if untreated. Definitive diagnosis of myasthenia gravis relies upon a combination of serological and electrophysiological investigations, the results of which are not immediately available in an acute situation. Bedside tests are therefore of practical clinical importance to enable prompt and effective initiation of treatment, particularly where critical symptoms are present. The ice-test is a straightforward and non-invasive investigation with a high sensitivity for myasthenia gravis and is a useful alternative to edrophonium testing. It is especially helpful in patients with cardiac and respiratory co-morbidities for whom acetylcholinesterase inhibitors are contraindicated. We describe a case where this simple bedside test successfully expedited the correct treatment and improved patient care.

BACKGROUND

Myasthenia gravis can present to the acute take with a diverse range of symptoms, including generalised skeletal muscle weakness, diplopia, dysphagia and respiratory compromise. We describe a case where an underused but extremely useful bedside test expedited the management of this condition and potentially prevented life-threatening complications.

The diagnosis of myasthenia gravis is generally made on the basis of clinical history and examination with subsequent confirmation by testing for the presence of antiacetylcholine receptor antibodies and electrophysiological investigation. However, the ice-test is a useful bedside test (with a high sensitivity) which can help to differentiate myasthenia gravis from other similarly presenting conditions and is a helpful adjunct to more definitive serological and electrophysiological investigations. A positive ice-test result can allow the prompt initiation of treatment.

CASE PRESENTATION

A 67-year-old man was referred by his general practitioner to the acute medical take with a 2-day history of worsening dysphagia. Six weeks previously he had developed ptosis, diplopia and slurred speech. These symptoms were worse at the end of each day. No additional neurological or respiratory symptoms were described. The patient recalled an episode of globus 15 years prior to the current admission. The patient felt that his current symptoms were different in character. The patient denied choking, but described difficulty chewing and swallowing. His work, which involved heavy lifting and manual work above head height, was also compromised.

Medical history included bilateral carpal tunnel release but no personal or family history of autoimmune disease. He was taking indapamide and felodipine for hypertension but no additional medications.

On examination the patient was comfortable at rest. He was afebrile with a blood pressure of 139/32, a

regular heart rate of 110 beats/min, a respiratory rate of 18 breaths/min and oxygen saturations of 98% measured by pulse oximetry. There was marked bilateral ptosis, more pronounced on the right. Clinical examination of cranial nerves II–XII showed no other abnormalities. Clinical examination demonstrated marked fatigability of the proximal limb musculature. All tendon reflexes were intact, with equivocal plantar flexes bilaterally. Tone, coordination and sensation were normal and there was no abnormal gait. No muscular fasciculations were seen. There was no lymphadenopathy.

INVESTIGATIONS

Blood tests revealed mild hypokalaemia (3.3 mmol/l). All other investigations (including full blood count, urea and electrolytes, serum Ca^{2+} , thyroid function, rheumatoid factor, C reactive protein, chest x-ray and electrocardiogram) were within normal limits.

A clinical diagnosis of oculobulbar myasthenia gravis was suspected and, on this basis, a bedside ice-test was performed. This involved holding ice packs over the patient's closed eyes for 1 min and monitoring for resolution of ptosis. Prior to the test, the patient demonstrated a marked ptosis, more prominent on the right (figure 1A). After the application of ice, the ptosis showed a marked improvement (figure 1B). This effect persisted for several minutes.

The patient was subsequently shown to be positive for antiacetylcholine receptor antibodies. CT imaging of the chest did not reveal the presence of a thymoma.

DIFFERENTIAL DIAGNOSIS

- Myasthenia gravis
- Acute neurological event
- Lambert–Eaton syndrome
- Guillain–Barré syndrome
- Demyelinating neuropathy.

Figure 1 (A) The patient before the ice-test. (B) The patient immediately after the ice-test.

TREATMENT

Following a neurology review, the patient was commenced on oral pyridostigmine 30 mg three times per day. We liaised closely with the patient's general practitioner and made a plan to titrate this to 60 mg three times per day as tolerated.

OUTCOME AND FOLLOW-UP

We subsequently learnt that the patient reported an improvement in his symptoms following the instigation of treatment and that subsequent serological testing confirmed the diagnosis of myasthenia gravis. Arrangements were made together with the neurology team for his continued follow-up under their care.

DISCUSSION

Myasthenia gravis can present with ocular, bulbar, respiratory and limb weakness. Although it is an uncommon condition, it is the most common disorder of neuromuscular transmission (reviewed in Drachman¹ and in Vincent *et al*²). Myasthenia gravis can present to an acute medical take, particularly where critical symptoms develop, for example, dysphagia and respiratory compromise. Definitive diagnosis is not straightforward and generally depends on a combined clinical, serological and electrophysiological approach – this can be even more difficult in the acute situation.^{3,4}

Confirmatory bedside tests allow a more rapid and definitive diagnosis than is possible from history and clinical examination alone. The Tensilon test is commonly used.⁵ This involves observing the response to the administration of intravenous edrophonium, an acetylcholinesterase inhibitor. Edrophonium potentiates muscarinic transmission and is contraindicated in patients with cardiac conditions and bronchial asthma; it also requires resuscitation equipment to be readily available.⁶ Furthermore, there are reports that, although the sensitivity is high, the Tensilon test can result in false negatives.^{5,7,8}

An alternative to edrophonium testing is the ice-test, as described here. It is most useful in patients with ptosis. Both edrophonium and the ice-test are less useful in patients who present with limb weakness only due to the difficulty in quantifying any response.

Cooling improves muscarinic neuromuscular transmission, possibly by decreasing the activity of acetylcholinesterase, and this explains the resolution of ptosis in patients with myasthenia gravis.^{9–11} For appropriately selected patients, the test is approximately 80% sensitive for myasthenia gravis – this is comparable to the sensitivity of the Tensilon test and actually exceeds the sensitivity of testing for antiacetylcholine receptor antibodies for ocular myasthenia gravis.^{10–12} The specificity is not known, although it is reported that patients with ptosis not related to myasthenia gravis do not improve with the ice-test.^{9,12}

Learning points

- ▶ Early diagnosis of myasthenia gravis allows prompt initiation of treatment.
- ▶ Definitive diagnosis of myasthenia gravis requires serological and electrophysiological investigations which are not generally available in the acute setting.
- ▶ In appropriate patients, the ice-test is a non-invasive and sensitive bedside test which can be used to aid diagnosis and direct initial treatment.
- ▶ For patients with potentially critical symptoms, starting treatment early is important.

Acknowledgements We extend our utmost thanks to our patient for allowing us to prepare this interesting and useful clinical case for publication.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Browning J, Wallace M, Chana J, Booth J. Enterovirus—a double act. *BMJ Case Reports* 2010;10.1136/bcr.06.2010.3091, date of publication

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