Case Report: A young man with progressive weakness, double vision and breathlessness

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A 17 year old man presented in November 2010 to Queen Elizabeth Central Hospital (QECH) with acute shortness of breath and bilateral leg weakness.

His symptoms had started gradually in July 2010 with weakness of his right leg . After two weeks his left leg also became weak. He found it particularly difficult to get up from a chair. Despite his weakness, he was still able to walk independently. At this point he sought medical advice at QECH; a definitive diagnosis was not made.

By August 2010 his weakness also involved both his arms, so that he was unable to raise them above his head. He noticed that he fatigued easily, especially at the end of the day, and he became breathless when doing simple tasks like walking to the toilet. He again went to QECH; on this occasion he had a series of investigations which included a normal Chest X-ray and X-ray of his spine. Blood examination showed that he was HIV negative and his full blood count was unremarkable.

By September, his voice was slurred and he frequently lost control of his speech; he described this as "speaking in tongues". Sometimes by the end of the day he could see two images when looking to the side, and occasionally he had difficulty swallowing liquids. A presumptive diagnosis of peripheral neuropathy was made and he was given a week trial of 20mg of prednisolone. He showed very little improvement during treatment with steroids.

Approximately 2 weeks after his trial of steroid therapy, he noted a rapid deterioration in his symptoms; he was particularly concerned about his breathlessness and bilateral leg weakness. He denied symptoms of numbness / paraesthesiae, he had no sphincter disturbance and he suffered no fever, night sweats or unintentional weight loss.

He was well prior to the onset of his symptoms in July 2010; he had been performing well at school and had normal developmental milestones. He did not use any illicit drugs and there was no family history of any neurological conditions.

On examination

The patient was lethargic and was unable to hold his head up. He was afebrile, normotensive and had a pulse rate of 75 beats per minute. He had a respiratory rate of 16 breaths per minute and his oxygen saturation while breathing air was 96%. Cardiovascular, respiratory and abdominal examinations were unremarkable. Cranial nerve examination revealed double vision during lateral gaze in either direction. There was, however, no overt evidence of opthalmoplegia. The remainder of his cranial nerves were normal. He had symmetrical proximal muscle weakness of his upper and lower limbs; this included neck flexion (MRC score 3/5), abduction and adduction of his shoulders (MRC 3/5), flexion of his elbows (MRC 4/5), flexion and extension of his hips (MRC 3/5) and flexion and extension of his knees (MRC 4/5). His reflexes were intact, plantars were downgoing and all his sensory modalities were normal. There was no evidence of mal-coordination, muscle wasting or muscle fasciculation.

One striking observation was that he was easily fatigable after repeated movement of his shoulder (Figure 1).

Investigations

Full blood count: Hb 13.4g/dl, wbc 6.0x109/L, platelets 300x109/L. A repeat HIV test was negative and Chest X-ray normal. CSF analysis: WCC 0, RCC 0, glucose 3.28mmol/l, protein 0.33g/l.

We administered a drug that resulted in a full (transient) recovery of his muscle weakness; this response revealed the diagnosis (Figs 1 and 2)

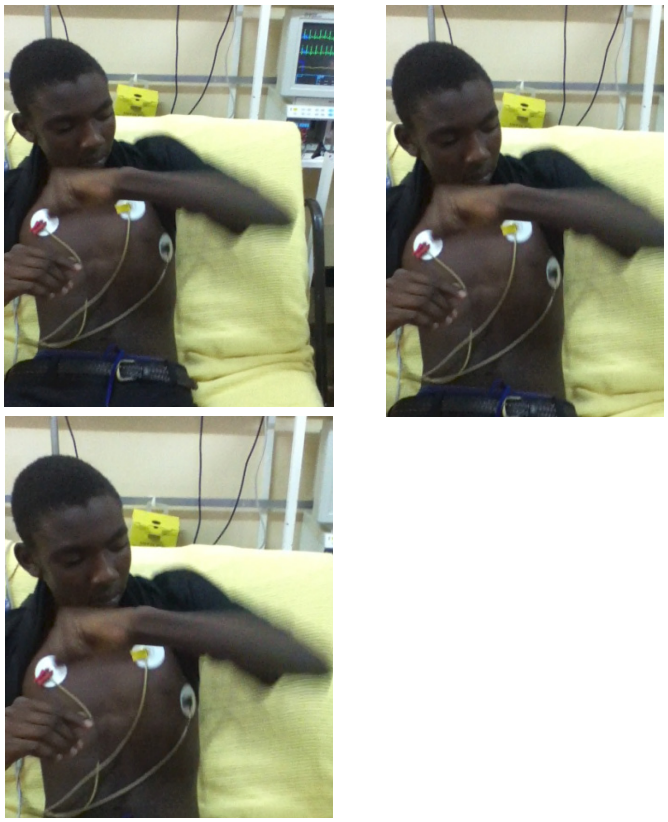

Figure 1. (a) and (b) The patient makes repeated movements of the left arm; (c) He is now asked to raise the left arm, and is unable to do so.

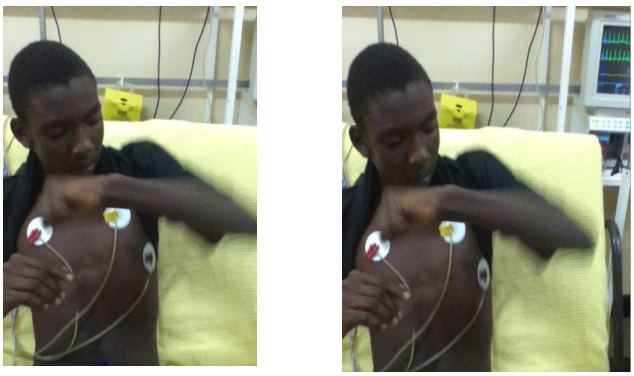

Figure 2. After the administration of a drug, the patient develops full transient recovery. He is now able to lift his left arm above his head and can resist the examiner pushing the left arm down.

What was the drug? What is the name of the test? What is the diagnosis?

Discussion

1) Edrophonium (Tensilon). This is a short acting acetyl cholinesterase inhibitor

2) 'Tensilon test'; the test is usually performed in a double blinded setting (i.e. placebo - usually 0.9% saline - versus edrophonium, with the clinician unaware of which substance is being injected), monitoring for a transient improvement in muscle strength following the administration of edrophonium but no improvement after saline. If this occurs, the test is positive. This test is usually done in an intensive care setting because edrophonium can cause bradycardia; cardiac monitoring, a prepared dose of atropine and resuscitation equipment is usually advocated.

3) Myasthenia Gravis (MG)

MG is an autoimmune disease affecting the neuromuscular junction. It is caused by auto antibodies against neuromuscular junction receptors (acetylcholine nicotinic receptors) which are essential for the contraction of muscle.

The incidence of this condition worldwide is approximately 100 per million in a population. The incidence of MG in sub-Saharan Africa is unknown. The condition is probably under-recognised because of its heterogeneous clinical presentation and also because of the sophisticated diagnostic tests necessary to make a diagnosis. Our case report indicates that MG does exist in a sub-Saharan setting and should always be considered in patients presenting with exclusively motor symptoms.

MG has a bimodal age of onset. It can present early, as in our case, or late in life; the latter tends to be more common in men. Patients typically present with extraocular muscle weakness and later limb and bulbar muscle weakness. This disease has a heterogeneous clinical syndrome and does not always follow a typical course, making the diagnosis sometimes difficult. In our case, the patient's symptoms predominately affected his limbs; his extraocular muscles and bulbar symptoms were less obvious.

Worsening of weakness after prolonged contraction or use (fatigability) is the hallmark of this condition.

There are many methods used to make a definitive diagnosis of MG, some of which can be used in a resource-limited setting like Malawi:

1) identifying serum antibody to acetylcholine receptor (these antibodies are found in 80-85% with generalised myasthenia gravis);

2) neurophysiology testing; repetitive nerve stimulation shows a decremental response, indicating a neuromuscular transmission blockade ;

3) edrophonium (Tensilon test) – which was the definitive test used in our case. Edrophonium is a drug that is often used to reverse anaesthetic medications; where there is an anaesthetic department, this drug or its equivalent should also be available.

Our patient was started on symptomatic treatment with a cholinesterase inhibitor (pyridostigmine) and definitive treatment with high dose corticosteroid (an immunosuppressive agent). After 6 months of treatment he went into remission with a low maintenance dose of steroid, and he did not require symptomatic treatment with pyridostigmine after 3 months.

In some patients it can take many months on high-dose steroids to achieve maximal benefit. That is probably why there was minimal improvement following the initial trial of steroid in our patient. A paradoxical worsening with steroids can be observed during its initiation – an effect thought to be due to a transient depletion of acetylcholine stores. This complication can be kept to a minimum by increasing the dose gradually and giving it on alternate days. It may well be that the short cause of steroid given for the presumptive diagnosis of peripheral neuropathy may have exacerbated our patient's symptoms.

A life–threatening complication of MG is 'myasthenic crisis'; this is a medical emergency that may progress to respiratory failure. There are important correctable conditions that should be treated and drugs that should be used with caution in patients with MG to avoid such a crisis (Table 1).

This case is an example of a non-HIV related, treatable neurological condition that is probably often un-diagnosed. We have demonstrated that in a resource-limited setting we were able to make a definitive diagnosis of MG and start appropriate treatment, which led to our patient's full recovery.

Acknowledgement

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References

1.Jacob S, Viegas S, Lashley D, Hilton-Jones D. Myasthenia gravis and other neuromuscular junction disorders. Pract Neurol. 2009 Dec;9(6):364-71.

2. Vincent A, Clover L, Buckley C, Grimley Evans J, Rothwell PM. Evidence of underdiagnosis of myasthenia gravis in older people. J Neurol Neurosurg Psychiatry. 2003 Aug;74(8):1105-8

Table 1. Exacerbating factors of MG and potential triggers of myasthenic crisis (modified from Jacob et al)

Infection	Viral, bacterial, mycobacterial, fungal
Metabolic conditions	Electrolyte imbalance (hypo-ka laemia, hypophoshataemia); intoxications Anaemia
Drugs	Withdrawal of cholinesterase inhibitors (when symptoms not fully recovered) Rapid introduction or increase of steroids antimicrobials (e.g. gentamicin, ciprofloxacin, chloroquine) Anti-hypertensives (e.g. beta-blockers and calcium chan nel blockers) Neuropsychiatric drugs (e.g. lithium, chlorpromazine, pheny toin) Botulinum toxin