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Myasthenia gravis masquerading as acute sixth nerve paresis following head trauma – or vice versa? A case report

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Abstract

Aim: **To report a case of sudden-onset diplopia, blurred vision and an inability of the left eye to fully abduct following trauma. Subsequent examinations showed significant variability leading to a possible diagnosis of myasthenia gravis.**

Methods: **This is a case report of a 7-year-old boy with a 2-day history of blurred vision, horizontal diplopia and headaches following a bump to the left side of his head that presented as a left sixth nerve paresis. The history, orthoptic findings, investigations and possible aetiologies are discussed.**

Results: **Orthoptic assessments initially revealed a marked left esotropia with restriction on left abduction. Computed tomography (CT) scans and magnetic resonance imaging (MRI) were both normal, as was monitoring of the patient's intracranial pressures. Further orthoptic assessments demonstrated normal ocular movements on some visits whilst on other visits a restriction of left abduction was still shown. The patient then developed a vertical element with ptosis with significant variability at each visit, leading to a possible diagnosis of ocular myasthenia gravis. He was started on pyridostigmine and improvement was observed. However, low-affinity acetylcholine receptor antibodies, MuSK antibodies, Tensilon test and nerve fibre stimulation were negative and pyridostigmine was stopped.**

Conclusion**: A question mark still hangs over the aetiology of this case. After a year of monitoring it was decided that the most suitable management for this patient was botulinum toxin. Following one injection the patient is currently straight and demonstrating stereopsis.**

Key words: Botulinum toxin, Childhood myasthenia gravis, Concomitant strabismus, Esotropia, Incomitant strabismus, Seronegative myasthenia gravis, Sixth nerve palsy, Sudden-onset strabismus

Introduction

Although the presentation of an acute concomitant strabismus in childhood is not an unusual one, those that present in later childhood, in association with a nerve palsy or any degree of incomitancy, should warrant further investigation. Head injuries cause the hospitalisation of 200–300 persons per 100 000 population per year,[1] and are a recognised cause of a central disruption of both motor and sensory fusion, and a major cause also of sixth nerve palsies.[2] Investigations into the causes and associations of sixth nerve palsy in children, mean age 4 years, were found to be: neoplasm (4 cases), idiopathic (3), trauma (2), congenital (2), viral (2) and inflammatory (1).[3] Those cases of strabismus that are incomitant in nature are generally indicative of an infranuclear cranial nerve lesion or mechanical limitation of movements due to extraocular muscle myopathy or an orbital lesion where the primary pathology needs to be thoroughly investigated.[4] Radiographic investigations such as computed tomography (CT) or magnetic resonance imaging (MRI) are principal elements of the investigation to rule out causes of a more sinister nature. One condition that might also need consideration in such cases of variability and sudden-onset strabismus with a nerve palsy and diplopia in a child is myasthenia gravis.

Myasthenia gravis is a neuromuscular disorder that affects skeletal muscles, especially the extraocular muscle.[5] The pathophysiology of the disorder requires an understanding of the neuromuscular junction (NMJ), which is the point at which the nerve fibre synapses on a muscle fibre. When a nerve impulse is initiated, it travels to the NMJ. Here the neurotransmitter acetylcholine (ACh) is released, passes through the NMJ, and ultimately attaches to receptors on the muscle surface, thereby resulting in muscular contraction. In myasthenia gravis, antibodies erroneously destroy ACh receptor sites, which are located at the postsynaptic membrane of the NMJ. This prevents ACh from binding to muscle cells, and hence inhibits muscle contraction. The result is a progressive muscle weakness that worsens with sustained activity.[6] Patients with purely ocular myasthenia gravis clinically have symptoms including diplopia, ptosis, weak eye closure, or a combination of these.

Case report

October 2010

A 7-year-old boy presented to the ophthalmology emergency clinic in October 2010 with a 2-day history of blurred vision and double vision. One day prior to the

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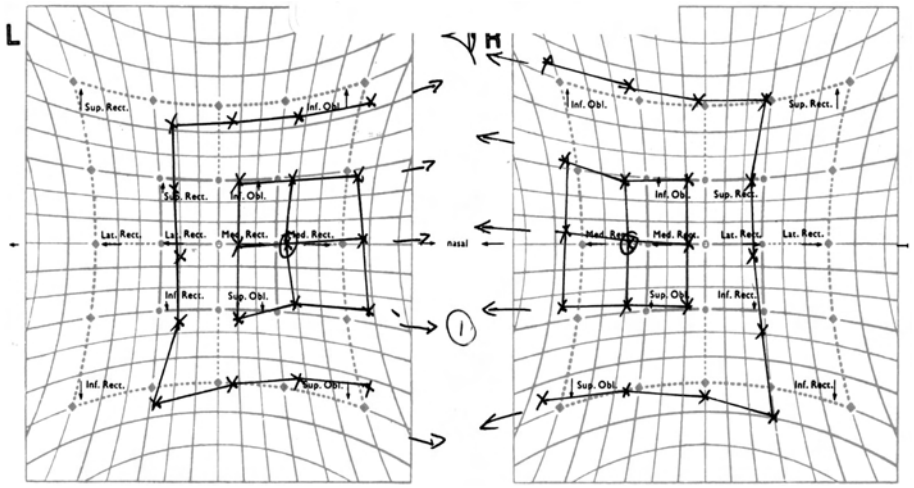

Fig. 1. Lees chart demonstrating lateral rectus restriction and bilateral underactions of the superior obliques.

onset of symptoms he had hit the left side of his head and face after being pushed into a tree. He was not unconscious or disorientated following the accident. The presence of a headache had coincided with the onset of his other symptoms.

The initial examination by the doctor reported that the patient had a normal eye examination with no papilloedema noted. Slight esophoria, full ocular movements and mild conjunctival injection were present, and an orthoptic assessment was requested. There was no other previous ocular history or family history to mention, and the only general health issue of note was mild asthma, for which he used a salbutamol (Ventolin, GlaxoSmithKline) inhaler.

November 2010

The patient was seen by the orthoptist in early November 2010. The patient's parents had noted deterioration in the squint, which had become constant 4 days prior to the appointment. The patient now reported constant diplopia, horizontal at all distances, and was still symptomatic with headaches. He additionally now complained of a shooting pain in the left eye.

The patient's vision was good either eye, with right being $6/7.5 + 2$ and left $6/7.5 + 1$, but cover test revealed a moderate left esotropia with diplopia measuring 35–40$^{\Delta}$ BO (prism dioptres) for near and 45$^{\Delta}$ BO for distance. Ocular motility revealed a slight restriction of the lateral rectus of the left eye, and also slight underaction of the left inferior oblique and equal overaction of the right superior rectus. A Lees chart was performed which demonstrated the lateral rectus restriction with full muscle sequelae and also bilateral underactions of the superior oblique (Fig. 1) which had not been noted on ocular motility testing.

The patient was seen by the consultant the same day and was sent for an MRI scan. The results were returned as normal.

The patient was seen again 10 days later. There was no change in the Lees chart and measurements were the same. The patient was therefore put on the waiting list for surgery for a decompensated esophoria due to trauma.

December 2010

The patient returned for his pre-operative assessment at the beginning of December 2010. Ocular motility was the same as at the previous visit; however, cover test and prism cover test revealed a reduction in the angle of strabismus to a slight left esotropia measuring 16–18$^{\Delta}$ BO for near and 20$^{\Delta}$ BO for distance. Surgery was cancelled in view of the findings and follow-up arranged for 2 weeks later.

At this point both the parents and the patient felt there had been deterioration in the squint. The parents reported the cosmesis to have declined, whilst the patient had noted the diplopia had changed and was now complaining of a horizontal and vertical separation in the images. No tilt was noted. Ocular motility appeared full, but prism cover test measurements had increased to 45$^{\Delta}$ BO for near and 50$^{\Delta}$ BO for distance and far distance, with no height seen.

Two days later the patient returned to the department for further investigations. Ocular motility assessment on this occasion revealed a small underaction of the left inferior oblique, small overaction of the right superior rectus, small overaction of the left inferior rectus, small underaction of the right superior oblique, and a slight underaction of the left superior oblique (Fig. 2).

Cover testing revealed a moderate left esotropia with left hypotropia measuring 35$^{\Delta}$ BO and 3$^{\Delta}$ R/L for near and 45$^{\Delta}$ BO and 3$^{\Delta}$ R/L. On the synoptophore the patient demonstrated fusion between $+5°$ and $-2°$, but no stereopsis was demonstrable.

A follow-up with the consultant was arranged, who organised an investigation of acetylcholine receptor antibodies to be carried out due to the variability in the deviation.

January 2011

At the beginning of January the patient's mother had

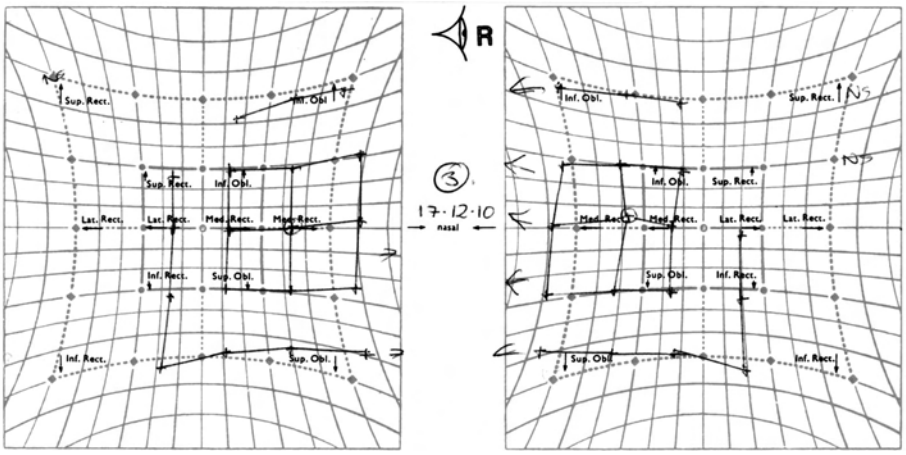

Fig. 2. Lees chart demonstrating a change in the muscle sequelae.

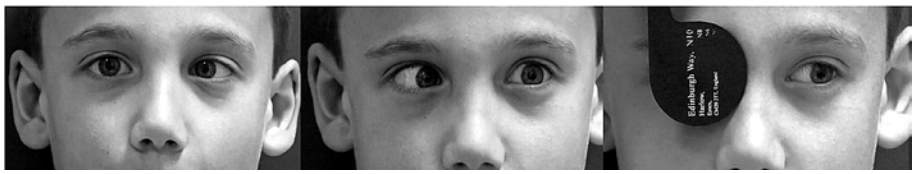

Fig. 3. *Left:* Patient in primary position. *Centre:* Patient in laevo-version. *Right:* Patient in laevo-duction.

been noticing intermittent ptosis of both eyes towards the end of the day and when the patient was tired. Diplopia remained horizontal and vertical, but the patient now noticed a slight tilt to the image on occasions. School work was becoming difficult due to the diplopia, headaches, and additional complaints of light-headedness and heavy legs. Measurements on this occasion were 40–45$^{\Delta}$ BO for near and 45$^{\Delta}$ BO for distance. Vertical deviation was noted on the cover test but not the prism cover test. Fusion was still present, whilst stereopsis was negative on the synoptophore. Ocular motility testing showed variability, left lateral rectus restriction once again (Fig. 3), along with bilateral slight overactions of the inferior obliques and slight underactions of the left superior rectus. Results of the blood tests had not been received at this point.

Following this visit an urgent referral to a consultant paediatrician was made in view of the possible diagnosis of ocular myasthenia gravis for the patient. He was subsequently referred on to a consultant paediatric neurologist off-site.

Assessment with the paediatric neurologist

Tensilon and nerve fibre stimulation tests were both carried out and found to be negative. It was felt there was a possibility of raised intracranial pressure; therefore, this too was investigated and found to be within normal limits. The patient was found to be hypermetropic (R: $+2.00/-0.75 \times 165$ and L: $+2.25/-0.50 \times 167$) and was prescribed glasses to try to eliminate any accommodative element that may have been present. In addition to the negative result of the acetylcholine receptor antibody test, MuSK antibodies were also tested for, with a negative result.

The diagnosis of myasthenia gravis was still suspected and, therefore, the patient was started on a trial of pyridostigmine. The patient's parents reported that on a dose of 20 mg three times daily there was a definite improvement of symptoms, especially after the third dose of the pyridostigmine in the afternoon. This treatment was continued for approximately 2 months, before being discontinued as it was felt there was no conclusive evidence for a diagnosis of ocular myasthenia gravis.

Six months after initial presentation

The patient returned to our department towards the end of April 2011 with a constant squint with headaches and diplopia; which was noted to still be very variable. The hypermetropic correction given to him was not tolerated and therefore not worn. On examination there was still a moderate left esotropia with minimal left hypotropia, measuring approximately 30$^{\Delta}$ BO for near and 35$^{\Delta}$ BO for distance, with minimal lateral rectus restriction on ocular motility testing. A cycloplegic refraction was also carried out, confirming the presence of hypermetropia.

Further assessment in May 2011 showed stable measurements but again variability was still seen on ocular movements during testing, and tests for fatiguability and Cogan's lid twitch were seen to be positive. Continued monitoring was decided on, and when the patient was seen again in June 2011 it was noted that his vision had become straight intermittently during testing.

One month later all the symptoms and complaints remained the same, as did the measurements, whilst the patient's vision was still spontaneously becoming straight during the investigations. After consultation with the doctor it was decided that following four

consecutive visits with stable measurements botulinum toxin (BT) would be used. This procedure was carried out on 10 August 2011 under sedation.

The patient returned following BT injection into the left medial rectus. Assessment revealed a slight esophoria, full ocular movements and stereopsis with Frisby value of 40 seconds of arc. His vision remains straight to date (November 2011).

Discussion

An acquired sixth nerve palsy in childhood is documented as being caused by: tumour (leukaemia), infection (meningitis), trauma, hydrocephalus, or possibly following an apparently benign viral illness.[2] The anatomy of the sixth nerve is such that after it has passed up the petrous-temporal bone to its upper border it then makes a right-angle bend under the petrosphenoid ligament; it is known that this is the point where the nerve is particularly prone to damage, either through traction or directly through a fracture of the base of the skull.[2] Evidence shows that following head trauma the most frequently encountered neuro-ophthalmic manifestation is ocular cranial injury, with the abducens nerve being the most commonly affected.[1]

The diagnosis of myasthenia gravis was also considered in this case. Although this condition is usually thought of as affecting adults, children can also have the disorder,[5] with myasthenia gravis in the paediatric population said to account for approximately 10–15% of cases annually.[7] However, reports of ocular myasthenia gravis in children are limited. Few studies have presented the clinical manifestations and ocular findings in children with ocular myasthenia gravis, visual and systemic outcomes, and treatment options in such cases.[5–13] On the whole, presentation of childhood ocular myasthenia gravis was similar to that in adults, with most patients having a ptosis (95–100%) and strabismus being present in 56–88%.[5,7–9] It has been suggested also that 50% of paediatric patients with ocular myasthenia gravis will go on to develop systemic or bulbar symptoms within 2 years.[14]

In a review of the literature, most patients were clinically identified as having ocular myasthenia gravis by abnormal repetitive nerve stimulation, acetylcholine receptor binding antibody level and a positive edrophonium test. In one case a patient was diagnosed based on clinical examination, history and a positive response to pyridostigmine therapy.[8] Another case report included a positive response to fatigue of the affected muscle with worsening of ptosis after prolonged upward gaze, or worsening of duction abnormality after prolonged gaze using the affected extraocular muscle.[7]

Botulinum toxin has been suggested to be of use in acute-onset esotropia and sixth nerve palsy. In a paper reporting on 14 patients with a mean age of 5.4 years, all except one showed considerable improvement in their manifest deviation after one injection of botulinum toxin A. Eight patients (57%) maintained high-grade stereopsis of 120 seconds of arc or better and long-term ocular alignment with toxin treatment alone. In total, 11 patients (79%) gained improved stereopsis and maintained satisfactory ocular alignment with toxin therapy and did not require squint surgery. Two patients (14%) did not maintain a stable ocular position after toxin treatment and later required squint surgery, gaining good ocular alignment and high-grade stereopsis.[16] In another study that reported the use of sub-Tenon injection of botulinum toxin 7 of 13 patients experienced recovery and regained binocular single vision; the overall recovery rate was 54%.[17] These results are suggestive that our patient has a considerable chance of maintaining good ocular alignment without the need for corrective surgery.

In this case, our patient initially appeared to be suffering from traumatic sixth nerve palsy but then subsequent signs suggested ocular myasthenia gravis. Clinical investigations, however, were all normal. The patient was seen on several occasions by a number of different clinicians and did demonstrate fatigue on sustained elevation. Also he had a positive response to a trial of pyridostigmine therapy, which is a treatment for myasthenia gravis; but then equally when he was treated with botulinum toxin all signs and symptoms improved.

This then poses the question: Do we diagnose from the clinical picture alone?

Conclusion

Due to the many contradictory features of the presentation, orthoptic investigation, clinical investigations and treatment of our patient, a question mark still hangs over the aetiology of this case. But the clinical presentation and treatment remain of interest.

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