the three patients with myasthenia with bilateral EOM atrophy reported by Okamoto *et al*,[4] who were positive for only acetylcholine-receptor antibodies, our patient was seronegative for these antibodies but positive for MuSK antibody. In ocular myasthenia, only 50% of patients are found to have anti-acetylcholine receptor antibodies,[6] and of 38 patients with seronegative ocular MG, none show increased titres of the anti-MuSK antibody.[9 10] Between 38% and 47% of patients with seronegative MG have increased anti-MuSK antibodies.[9 10] Similar to the clinical course of patients in the study by Okamoto *et al*,[4] our patient had an approximately 15 year duration of limited ocular motility that did not improve with medication or thymectomy.

Diplopia and ptosis are well-recognised signs of MG, but bilateral EOM atrophy is exceedingly rare. Although ocular involvement is a less common presentation of the anti-MuSK MG syndrome, it may be reasonable to check for anti-MuSK antibody in any patient who presents with progressive external ophthalmoplegia.

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Botulinum toxin injection causing lateral rectus palsy

A 35-year-old woman with brow spasms, treated in the past with Botox, was referred for increasing tightness in the brow. She reported having experienced an episode of difficulty focusing after a previous injection of Botox by another physician. The patient had no response to a subcutaneous injection consisting of 10 units of Botox above the eyebrows, nor to a subsequent injection of 20 units in the same location 2 months later. A third injection of 35 units of Botox resulted in improvement of her brow spasms, but only for 48 h. Accordingly, 2 months after the third injection, she was injected with 75 units of Botox, with 30 units injected in three separate locations above each eyebrow and 7.5 units injected just lateral to each lateral canthus. At 1 week after this injection, the patient had difficulty focusing, and shortly thereafter noted horizontal binocular double vision, worse on left gaze.

On examination 48 h after the onset of her symptoms, the patient had normal visual acuity of 20/20 OU, with normal colour vision and full visual fields. She had anisocoria, with the right pupil being 0.5 mm larger than the left, but both pupils reacted briskly to light stimulation and both dilated equally well after topical administration of a 10% cocaine solution. The right eye moved fully in all directions. The left eye had mild limitation of abduction, but otherwise moved fully. Duction measurements revealed 60° of abduction of the right eye versus 50° of the left eye. In primary position, the patient had an esotropia of 9 prism diopters (PD) at distance and 2 PD at near. The esotropia was incomitant, and increased on left gaze to 15 PD. Corneal and facial sensation were equal and normal bilaterally. Slit-lamp examination and fundoscopy were normal. MRI of the brain and orbit were normal.

The patient was treated with a 6-PD Fresnel prism placed base out on her left spectacle lens for temporary symptom relief. One month later, her diplopia had resolved and she was able to remove the prism.

Comment

This is the first reported case of lateral rectus paresis after an injection of Botox into the lateral canthal region. Inferior oblique paresis is an uncommon adverse effect of Botox injection into the lower lid,[1] with a reported incidence of 1.7%.[2] The mechanism is postulated to be diffusion of the medication to the underlying inferior oblique muscle. Diffusion of botulinum toxin to surrounding muscles has also been reported after treatment of dystonia with large doses of the drug.[3] We believe that, in our case, Botox spread from the lateral canthus to the left lateral rectus muscle, producing a transient paresis of the muscle characterised by an incomitant esotropia and a mild left abduction deficit. It is interesting that patients who experience diplopia after a periorbital injection of Botox tend to have recurrence of diplopia when they are reinjected, suggesting that they have some predisposition to this complication.[2] Our patient had an episode of difficulty focusing after a previous periorbital injection of Botox by another physician, which was similar to the prodrome that she experienced just before she developed diplopia after the injection we gave her. Fortunately, the diplopia was transient, resolving as the effects of the botulinum toxin dissipated. We believe that patients who experience diplopia or have difficulty focusing after an injection of botulinum toxin should be counselled as to the potential recurrence of such an effect with subsequent injections of the drug, regardless of the care taken to avoid these sequelae.

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Abducens palsy and Sjögren's syndrome induced by pegylated interferon therapy

Interferons (IFNs) and their pegylated forms (PEG-IFNs) are widely used in the treatment of viral hepatitis and some neoplasms. Although ophthalmic symptoms are common among their various side effects,[1 2] abducens palsy is rarely observed. Here, we describe a case where abducens palsy developed during PEG-IFN therapy, and discuss the management.

Case report

A 65-year-old man had undergone removal of stage IV renal cell carcinoma 5 years ago. He had been managed with IFNα therapy (6×10^6 IU three times a week) for recurrence. Although the therapy suppressed tumour growth effectively, it had moderate side effects including influenza-like symptoms, erythema and depression. After 4 years of conventional IFN therapy, PEG-IFNα became available for the patient.

On the first day of PEG-IFN therapy (3×10^6 IU), the patient had the expected fever and malaise. The next day he developed diplopia, which worsened gradually. After 1 week, the patient was referred to ophthalmologists and was diagnosed as having right abducens palsy (fig 1, upper panel). IFN-induced retinopathy was absent. Diabetes mellitus was negative with fasting glucose (73 mg/dl) and haemoglobin A1c (5.5%). He did not have hypertension. MRI showed no evidence of metastasis or intracranial hypertension, but showed enhancement of the right abducens nerve (fig 2).

After 1 month of onset of diplopia, painful swelling of the right parotid gland was noted. In another 1 month, dry eye and dry mouth sensations developed. The result of Schirmer's test (3 mm) and fluorescent corneal staining suggested presumable Sjögren's syndrome (SS). Furthermore, serum examination showed increased SS A and SS B antibody levels (128

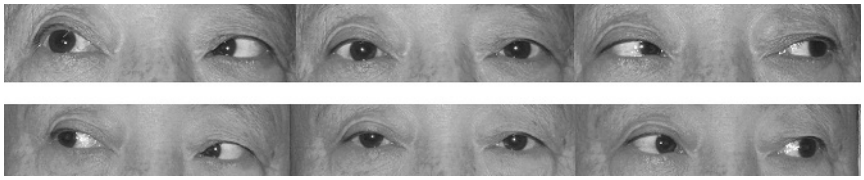

Figure 1 Upper panel: detail of the patient, primary position and lateral gaze at the initial examination. Note that abduction of his right eye is limited. Lower panel: eye position of the patient 5 months after the onset of symptoms. Abducens palsy resolved completely and the diplopia disappeared. Informed consent was obtained for the publication of this figure.

and 23.2 U/ml, respectively) and antinuclear antibody with speckled pattern. Other autoantibodies and cryoglobulinaemia were absent. Although lymphocytic sialoadenitis in salivary glands did not fulfil the focus score criteria, he was diagnosed as having primary SS by the revised European–American classification criteria.[3]

Considering the poor prognosis of the carcinoma and lack of alternative treatments, the patient returned to conventional IFN therapy. He did not receive steroids. His diplopia improved gradually and resolved in 5 months (fig 1, lower panel).

Comment

The patient presented abducens palsy soon after the initiation of PEG-IFN therapy. Two similar cases have been described to date.[4 5] CT or unenhanced MRI were performed, which failed to detect an abnormality. Both cases recovered completely, with steroid use in one case. The mechanism by which IFN induces abducens palsy is unclear.

The enhancement of the abducens nerve is seen in disseminated tumour, inflammation, trauma, venous congestion or autoimmune disease, but less likely in diabetic microinfarcts.[6] We assume that the IFN-activated immune system induced an acute inflammatory process in the abducens nerve, which appeared as the enhancement, and led to ensuing development of SS. In fact, IFNs have complex immunomodulating effects and frequently induce or exacerbate autoimmune disease.[7 8]

The symptom resolved spontaneously as abducens palsy usually does. The cessation of IFN and/or the use of steroids may not be necessary for such patients. Careful monitoring enabled us to detect SS. Searching for autoimmune disease might be considered when faced with unexplained symptoms during IFN therapy. Unrecognised autoimmune diseases may affect the therapeutic course.

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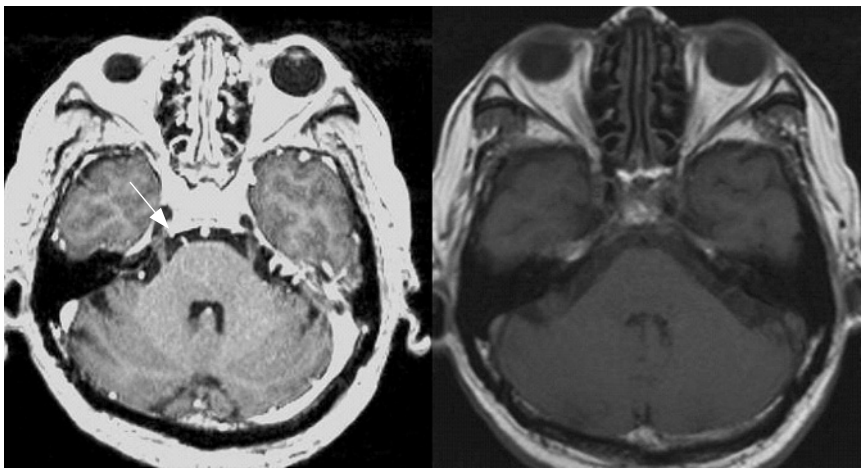

Figure 2 MRI scans of the axial section of the patient's brain. Magnetisation-prepared rapid gradient echo images (left) show the enhancement of right sixth nerve (arrow). An unmodified plain T1 image is also shown (right).

MAILBOX

Secondary paracentral retinal holes after removal of the internal limiting membrane

We read with interest the article by Steven *et al*[1] on their finding of secondary paracentral retinal holes after internal limiting membrane (ILM) peel. We have also reported on four eyes of four patients that developed iatrogenic eccentric macular holes after vitrectomy with ILM peeling for idiopathic macular holes.[2] In their report, Steven *et al* treated three of the seven patients with argon laser photocoagulation. Haritoglou *et al*[3] reported paracentral scotomata after vitrectomy with ILM peeling for macular holes. Treatment of these paracentral holes with argon laser photocoagulation could therefore make these scotomas worse. The pathogenesis of these iatrogenic holes is unclear. We believe that there must be an element of mechanical trauma involved in the formation of these secondary holes, despite the fact that it is not visible at the time of surgery. Their speculation of weakening of the glial structure of the retina caused by decapitation of the Muller cells is interesting and may also play an important role, as all the holes reported are in the ILM-denuded area. We note that, in the series by Steven *et al*, all the reported holes appear temporal to the fovea. In our series, the holes were reported inferior as well as nasal to the fovea. We used trypan blue to assist in the peeling of the ILM, and no obvious areas of retinal trauma were apparent at the time of surgery. The secondary holes became apparent in the follow-up period; none of them have had any treatment and have not caused any problems after long-term follow-up (6 years). We recommend that these holes should not be treated, as they do not appear to lead to retinal detachment.

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