Internal ophthalmoplegia and cranial neuropathy without external ophthalmoplegia

A report of 2 cases

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Summary

Two patients presented with an acute syndrome of internal ophthalmoplegia in the absence of external ophthalmoplegia, bilateral involvement of other cranial nerves, and minimal evidence of peripheral neuropathy. Cerebrospinal fluid protein was slightly raised, but diagnostic relevance in cluster headache.

Ophthalmoplegia in the Landry-Guillain-Barré syndrome is well described but unusual and is an essential feature of the variant of this disease known as Fisher's syndrome. In these conditions, external ophthalmoplegia may occur alone or in combination with internal ophthalmoplegia. Internal ophthalmoplegia alone is exceedingly rare.

Polyneuritis cranialis has been less well documented, but may represent another variant of the Guillain-Barré syndrome. Two cases in which features of polyneuritis cranialis were combined with internal ophthalmoplegia in the absence of external ophthalmoplegia are described.

Case reports

Case 1

A 61-year-old black man was admitted to hospital with a 72-hour history of difficulty with eye closure, blurring of vision, swallowing, and a mild gait disturbance. The symptoms had begun suddenly and had remained unchanged since onset. He denied headache, diplopia, nausea or vomiting. There was no history of vascular disease, toxin exposure or recent viral illness.

On examination, the patient had bilateral internal ophthalmoplegia with loss of pupillary responses to light and accommodation. The right pupil was 3.5 mm and the left 5 mm in diameter.


Distant visual acuity was 6/9 bilaterally and near vision was N9 on the right and N14 on the left. Eye movements were full and there was no evidence of associated ptosis on the right. There was complete lower motor neuron facial paresis with associated impairment of taste sensation. His speech was dysarthric because of facial paresis. The motor system was otherwise normal.

Sensory examination was normal initially, but 2 days after admission, slight impairment of position sense in his toes and diminished vibration sensation below his ankles were noted. Reflexes were intact except for absence of the ankle jerks. Gait was minimally ataxic with slight difficulty with tandem walking. General examination was normal; in particular there was no evidence of autonomic instability.

A lumbar puncture revealed clear fluid containing 2 lymphocytes and 3 erythrocytes per cubic mm, protein 1.71 g/l, glucose 3.5 mmol/l, chloride 124 mmol/l. Routine blood count and blood chemistry examination, protein electrophoresis, serum complement profile and angiotensin converting enzyme were normal. Syphilis serology, monospot test, antinuclear factor, rheumatoid factor and diphtheria antitoxin assay were negative. Visual and auditory brainstem evoked responses were normal.

Electromyography of orbicularis oris showed no volitional activity and no denervation activity 4 days after admission. Nerve conduction studies showed a motor conduction velocity of 33.6 m/s in the right peroneal nerve and a sensory conduction velocity of 18.7 m/s in the right sural nerve with a sensory action potential amplitude of 10 μV.

She improved on the day after admission with ACTH 60 U daily. Nine days later, an improvement was noted with sluggish pupillary reaction to light (but not accommodation) and slight improvement of facial weakness.

The patient was maintained on steroids, which were gradually tapered off over 6 weeks. At 8 weeks he had minimal residual facial weakness but complete resolution of other neurological deficit. Studies showed that nerve conduction had returned to normal.

Case 2

A 29-year-old black women developed lower abdominal pain, vomiting and diarrhoea. She had previously been well except for amenorrhoea for 16 months. After 4 days she suffered two grand mal seizures and was admitted to hospital, where she was found to be apyrexial with lower abdominal tenderness, guarding and normal bowel sounds. The cerebrospinal fluid was acellular with a protein content of 0.66 g/l. Her symptoms settled with penicillin, metronidazole and steroid therapy.

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Discussion

Both these patients presented with bilateral symmetrical cranial nerve dysfunction in association with isolated internal ophthalmoplegia. There was clinical and electrophysiological evidence of mild peripheral nerve involvement. In the absence of other causes of cranial neuropathy and in view of the raised cerebrospinal fluid protein it is proposed that these cases represent a variant of the Guillain-Barré syndrome. Cranial nerve involvement is a well-recognised feature of the Landry-Guillain-Barré syndrome; however, multiple or single cranial nerve dysfunction in association with minimal or no peripheral signs (polyneuritis cranialis) as a variation of the Guillain-Barré syndrome has been less well documented.

In 1938 Guillain classified the Guillain-Barré syndrome into four categories, the third of which, "la forme mesoschphalque pure", was limited to the cranial nerves. Subsequently several reports in the European literature described similar presentations with acute onset of multiple cranial neuropathies in association with minimal or no involvement of the extremities. The cranial nerves most commonly involved were the 7th, 9th and 10th. Ophthalmoplegia involving the 6th and less commonly the 3rd and 4th nerves was frequent, but complete ophthalmoplegia was rare.

In 1956 Fisher described 9 patients with a variant of acute polyradiculitis who presented with the triad of external ophthalmoplegia, ataxia and areflexia in the absence of significant ascending weakness or sensory loss. Over 50 such cases have subsequently appeared in the literature. Pupillary involvement may be found; this varies from complete iridoplegia to loss of either light reflex or accommodation to merely sluggish reactions. In a series of 52 cases taken from the literature 29 had pupillary involvement but in none were the pupils involved alone.

Munsat and Barnes reported 5 cases which presented with acute onset of bilateral lower motor neuron facial weakness with involvement of the 9th and 10th cranial nerves in 1. All cases had varying degrees of external ophthalmoplegia, but in all the pupils were spared. Involvement of the extremities was limited to mild parasthesiae in 2 cases and absent tendon reflexes in 3 cases. Mild ataxia was seen in 3 patients.

Gibberd and Kelly reported 8 cases with complete internal and external ophthalmoplegia, 2 with associated facial weakness and all with limb weakness involving primarily proximal muscles. Reflexes were diminished or absent and sensory involvement, if present, was minimal.

Ashworth reported a series of 51 patients, of whom 6 presented with ophthalmoplegia as the dominant feature. Four showed complete bilateral external ophthalmoplegia with ptosis; of these, 2 had normal pupillary reactions, 1 showed a sluggish response of the pupils to light and in 1 pupil reactions were absent at first but recovered within a week.
Elizan et al., reported a series of 11 cases in which 9 presented with ophthalmoplegia and the primary manifestation of an acute polyradiculitis. Ophthalmoplearesis — acute, bilateral and fairly symmetrical — progressed to subtotal or total external ophthalmoplegia with various degrees of internal ophthalmoplegia in 6 cases. Internal ophthalmoplegia did not occur in the absence of gaze paresis in any of these patients. Only 3 of the 11 patients demonstrated involvement of other cranial nerves. None had ataxia without appreciable motor weakness or sensory deficit. The course was benign with rapid and generally complete recovery within weeks to months.

The exact incidence of ophthalmoplegia in the full-blown Guillain-Barré syndrome varies in reported series (Table I). Gibberd20 described four types of ocul ar involvement in acute polyneuritis: complete ophthalmoplegia, complete external ophthalmoplegia with normal pupils, partial external ophthalmoplegia with partial pupillary involvement, and partial external ophthalmoplegia with complete pupillary involvement, but he encountered no case where the pupils were involved and the external muscles were spared. Strauss and Rabiner21 mention a patient with 'myeloradiculitis' (case 4) in which the right pupil was slightly enlarged and reacted sluggishly to light.

The most striking feature in our patients was the presence of an acute polyradiculitis. Ophthalmoplegias acute, bilateral and fairly symmetrical — progressed to subtotal or total external ophthalmoplegia with various degrees of internal ophthalmoplegia in 6 cases. Internal ophthalmoplegia did not occur in the absence of gaze paresis in any of these patients. Only 3 of the 11 patients demonstrated involvement of other cranial nerves. None had ataxia without appreciable motor weakness or sensory deficit. The course was benign with rapid and generally complete recovery within weeks to months.

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The pathological site of pupillary dysfunction in Guillain-Barré syndrome and the Fisher variant is controversial. Some authors24 have suggested underlying brainstem involvement, while others have favored a peripheral lesion.25,26

The lack of pupillary response to dilute (but not full strength) pilocarpine eyedrops in 1 of our patients might favour a central mechanism, but the normal brainstem auditory evoked responses in case 2 militate against this.

Both our patients complained of blurred vision. This may have been due to impaired accommodation, although this was not specifically proven. Near vision was, however, disproportionately impaired in case 1.

The most striking feature in our patients was the presence of a bilateral internal ophthalmoplegia in association with normal extra-ocular muscle functions. Review of the literature suggests that the association of an isolated internal ophthalmoplegia with an acute idiopathic polyneuritis cranialis has not previously been described. It is suggested that this represents a variant of the Landry-Guillain-Barré syndrome.

**REFERENCES**

10. Elizan JS, Spire JP, Andiman RM et al. Syndrome of ophthalmoplegia cranialis has not previously been described. It is suggested that this

**TABLE I. OPHTALMOPLEGIA IN REPORTS OF GUILLAIN-BARRÉ SYNDROME**

<table>
<thead>
<tr>
<th>Reports</th>
<th>Total No. cases</th>
<th>Ophthalmoplegia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haymaker and Kernohan</td>
<td>50 (24%)</td>
<td>External (2%)</td>
</tr>
<tr>
<td>Marshall</td>
<td>35 (17%)</td>
<td>Internal (0%)</td>
</tr>
<tr>
<td>Wiederholt et al.</td>
<td>97 (5%)</td>
<td>Not stated</td>
</tr>
<tr>
<td>McFarland and Grant</td>
<td>100 (13%)</td>
<td>'Several'</td>
</tr>
<tr>
<td>Ravn</td>
<td>127 (9%)</td>
<td>Not stated</td>
</tr>
<tr>
<td>Princeas</td>
<td>40 (17,5%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>McLeod et al.</td>
<td>50 (8%)</td>
<td>Not stated</td>
</tr>
<tr>
<td>Löffel et al.</td>
<td>123 (8,5%)</td>
<td>Not stated</td>
</tr>
</tbody>
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*Post-mortem series.*