A PATIENT THAT CHANGED MY PRACTICE

Visual loss in a young man

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THE STORY

A 29-year-old man presented in the winter of 1973/4 to the Emergency Department of the Moorfields Eye Hospital, London, complaining of painless and increasing blurring of monocular vision over several days. He was referred to the physician's clinic where he was seen two weeks later. There had been no improvement. There was moderately severe (6/24) impairment of left eye vision with a central scotoma and a relative afferent pupillary defect. The fundi were normal. A diagnosis of acute optic neuritis was made, the only slightly unusual feature being the absence of pain on eye movement; but this is so in about 20% of cases. A plain X-ray of the skull was normal. A CT scan (the availability of which was very restricted at that time) was not performed.

At follow up a month later vision had returned virtually to normal, in keeping with the diagnosis of optic neuritis. The patient was reviewed again some nine months after the onset of symptoms. He reported that over the previous few months the blurring of vision had returned in the left eye, not acutely as on the first occasion, but gradually. Such a course is distinctly rare in optic neuritis (though it does occur) and sounded alarm bells. My disquiet was increased when it emerged that he had also noticed blurring of vision in the other eye over the previous four weeks.

On examination, the left eye vision was reduced to perception of hand-movements and the right eye vision to 6/12. There was a temporal defect in the right visual field, sparing central vision, suggesting compression of the optic chiasm. At that time Martin Halliday and I were exploring the clinical role of pattern evoked visual potentials in a variety of disorders. In this patient we found that the response was (as expected) absent from the left eye and reduced with an asymmetrical distribution from the right eye, but the latency was normal. This pattern was clearly abnormal but not of the type we had recently reported in optic neuritis. But we had seen similar asymmetries in several recent cases of chiasmal compression. Further investigation did indeed reveal a suprasellar mass, which at operation proved to be a craniopharyngioma.

It was successfully removed. The visual acuities returned rapidly to normal (left 6/5, right 6/5), as did the visual evoked potentials, apart from a trace of residual asymmetry (Fig. 1).

LESSONS LEARNED

This case taught me a number of lessons about optic neuritis and about compression of the visual pathways.

Though the diagnosis of optic neuritis is easy in most cases, one must be alert to alternative possibilities, especially when there is even one atypical feature. In this case there were four: lack of pain in the first episode; the later development of progressive visual loss after initial recovery; the appearance of an unusual field defect in the newly affected eye; and on later investigation a visual evoked potential from the better eye that was not delayed and was asymmetrically distributed. Though each of these clinical and investigative features occurs rarely in optic neuritis, seeing them all together was so unusual as to make an alternative diagnosis probable.

On the other hand, visual loss due to compression is usually progressive. A central scotoma is exceptional, though it is encountered occasionally. The present case (together with others seen at about the same time) made the point that space occupying lesions affecting the optic nerve and chiasm can rarely present with rapid visual loss as in optic neuritis. The normal skull X-ray was unhelpful as in adults (unlike children) calcification is seen only in about 20–30% of craniopharyngiomas. This case also illustrated the point that if the pituitary fossa is intact in a patient with typical visual features of chiasmal compression, pituitary tumour is unlikely and meningioma or craniopharyngioma probable.

Furthermore, the case illustrated an important aspect of management: while long standing compression leads almost inevitably to permanent visual loss, early treatment – even when visual loss is severe – can restore virtually normal vision. This latter clinical point, and the recovery of the evoked potentials, in the present patient (who was one of the original series that established the role of this technique – now largely superseded by MRI – in the detection of

compression of the anterior visual pathways) also raised basic questions about the mechanism of visual loss and recovery in these circumstances. What are the pathological changes in the compressed nerve fibres? What is the mechanism by which vision is restored so rapidly – a common enough observation in such cases?

The standard accounts of the pathology of anterior visual pathway compression were largely restricted to the features of the tumours and contained little or no reference to any changes in the nerve fibres, which, after all, cause the symptoms. We therefore undertook an experimental electron microscopic study of incremental chronic compression of the optic nerve and found that the characteristic change was not degeneration but demyelination. Moreover, remyelination started while compression was still present. The new myelin sheaths had all the known morphological prerequisites for saltatory conduction and given that the axons appeared normal (though some were constricted) it seemed likely that when the known ischaemic effects of compression were relieved the nerve fibres would be able to conduct again. Parallel experiments on the spinal cord had shown similar changes and in a related model it was proved directly that conduction was indeed possible in remyelinated central nerve fibres.

Returning to patients, the finding of normal optic discs in the present case indicated that axonal loss must have been limited. The occasional finding of delayed evoked potentials with compressive lesions provides evidence for demyelination in such cases. That conduction can be restored rapidly (as in peripheral nerve) was shown in an American patient in whom the visual evoked potential was restored within three hours when an unresectable craniopharyngiomatous cyst was drained externally. Taken together these clinical and experimental observations led to the following conclusions about the pathophysiology of reversible compression of the visual pathways:

- Visual loss is produced by conduction block, partly due to de-

myelination and partly to ischaemia, in fibres that would be able to conduct if the pressure were relieved. These include both histologically normal fibres and fibres undergoing remyelination while the tumour is still present.

- The early rapid phase of recovery can be accounted for by restoration of conduction in these fibres.
- In most patients there is a further, slower phase of recovery in which progressive remyelination is likely to play a part.
- There is much current interest in the possible contribution of adaptive synaptic changes, but that is another story.

ACADEMIC MEDICINE, AND BEING ALERT TO THE DISCREPANCY

The case of this young man taught me two things. Firstly, it illustrated the importance of the academic medical unit in which (as Derek Denny-Brown, professor of neurology at Harvard used to emphasize), the physician having identified a problem in the clinic could take it to the laboratory, investigate it rigorously and bring back to the clinic the new insights gained. Secondly, the practical lessons illustrated a favourite adage of one of my first and most influential teachers in neurology, Keith Macleod of the University of Otago, New Zealand: 'Be alert to the discrepancy'. The insights gained from pursuing the analysis of a discrepancy are often the key to diagnosis and they may play an important part in developing the best possible plan of management.

FURTHER READING

References to the background literature, both clinical and experimental, are contained in:

- Clifford-Jones RE, McDonald WI, Landon DN (1985) Chronic optic nerve compression: an experimental study. *Brain*, 108, 241–262.
Powell MP, Lightman SL, Laws ER (eds) (2003) *Management of pituitary tumours: the clinician's practical guide*, pp. 318. Humana Press, Totowa New Jersey.

Figure 1 Pattern-reversal visual evoked responses from an array of electrodes (1–5) over the parieto-occipital region. Time scale along the x axis at 10, 50 and 100 ms. Note the restoration of the visual evoked potential from stimulation of the left eye and the increased amplitude of that from the right eye postoperatively. With permission from Halliday *et al.* *Brain* 1976; 99; 357–74.