MINI REVIEW

Neuro-ophthalmology

The most important neurone in the visual system is the second order neurone from the ganglion cell in the retina to the lateral geniculate body. Impairment of function is most likely to occur in the optic nerve. This review will therefore consider recent advances in knowledge in relation to the optic nerve. Three main aspects will be discussed – developmental, neuroradiological, and clinical advances.

DEVELOPMENT

One of the major challenges of the developmental neurobiologist is to understand what makes cells differentiate. The questions are beginning to be answered for neurones by some interesting work on the optic nerve.¹ The optic nerve is an excellent site to investigate because it contains no cell bodies and thus allows investigation of the neuronal supporting structure. Recent studies have shown that there are two types of astrocyte in the optic nerve, and these have been differentiated by morphology, antigenic phenotype, and response to growth factors. The astrocyte extends processes to the surface of the nerve, to the blood vessels forming a perivascular sheath, and to the nodes of Ranvier. Type I astrocytes are present before birth and send processes to blood vessels, whereas type II astrocytes occur in the second postnatal week and send processes to the nodes of Ranvier. The other glial cell in the optic nerve is the oligodendrocyte, which sends processes that concentrically wrap round the optic nerve to form an insulating myelin sheath.

Further investigation has shown that oligodendrocytes and type II astrocytes are derived from the same progenitor cell (0-2A progenitor cell). Evidence also suggests that platelet derived growth factor (PDGF) is secreted by type I astrocytes to stimulate 0-2A progenitor cells to proliferate. Similar studies in the retina have shown that retinal glial cells and Müller cells are derived from a similar cell line. Thus the scene is now set to investigate developmental abnormalities in the optic nerve (optic nerve glioma), optic disc anomalies (hypoplasia and drusen), and the retina (coloboma). We can therefore expect exciting advances in the next decade.

NEURORADIOLOGY

Assessment of the size of the optic nerve was virtually impossible 20 years ago, though information could occasionally be gained by the potentially hazardous procedures of injecting air into the orbit (orbital pneumography). The advent of the CT scan in the 1970s enabled clinicians for the first time to assess the optic nerve and the nerve sheath. The CT scan remains the investigation of choice for orbital diagnosis, and in particular for study of the optic nerve sheath.

ENLARGEMENT OF THE OPTIC NERVE AND SHEATH

Enlargement of the optic nerve sheath has been subdivided, depending on the CT appearances, into tubular, fusiform, and excrescent. Seventy-two cases of isolated optic nerve involvement were studied,² and the most common group was those with tubular enlargement. Common causes of tubular

enlargement were papilloedema (10), compressive neuropathy (7), meningioma (7), neuritis (7), glioma, lymphoma, or leukaemia and perineural haematoma (4), and patulous subarachnoid space (5), with, less commonly, optic perineuritis and metastases. The only condition producing fusiform or excrescent enlargements were meningiomas and gliomas. It is interesting that the commonest cause of an enlarged nerve sheath is raised intracranial pressure, and when an enlarged sheath is seen with chronic disc swelling the differential diagnosis is between benign intracranial hypertension and an optic nerve sheath meningioma. Enlargement of the nerve sheath is a common accompaniment of sight threatening papilloedema and it supports the decision of a surgeon considering an optic nerve sheath decompression to go ahead.

The clinician having forsaken the skull x ray and the optic canal view in the 1970s for the greater information of CT scanning, now in the 1980s has to adapt again to new technology. Magnetic resonance imaging (MRI) uses the resonance of protons to provide images. Since water is the main component of living tissue, including the nervous system and the orbit, a proton image of the brain and orbit is primarily a water content picture. Protons lined up in a large magnetic field can be forced to precess* by a field of appropriate frequency applied at right angles. If the second field is turned off, the protons revert to their former position and the return is described by two time constants – one longitudinal (T_1) and the other horizontal (T_2). Excellent definition is obtained, and the images are free of bony artefact, since bone contains little water. Thus MRI has at the moment a technological superiority in the diagnosis of intrinsic disease of the optic nerve, chiasm, brain, cerebellum, and spinal cord, whereas CT scanning detects meningiomas and bone defects.

In multiple sclerosis, plaques of demyelination are seen because there is an increase in water content, initially due to oedema and later to gliosis. In cases of optic neuritis MRI scans show plaques elsewhere in the brain in 50–70% of cases, and plaques can also now be visualised in the optic nerve.³ The MRI can be modified with a surface eye coil with coronal imaging of the optic nerve to produce the STIR sequence (short time inversion recovery).⁴ Leber's hereditary optic neuropathy has also been studied by the STIR sequence.⁵ Eight patients were studied, and in all cases the optic nerves showed an abnormal signal. In one case with monocular visual loss there was an abnormal signal in the affected optic nerve prior to involvement of the second eye. Thus MRI scanning has identified extensive involvement of the optic nerve in Leber's syndrome and hence provided a useful diagnostic role.

Further possible applications of MRI scanning include exploitation of drugs which traverse the blood-brain barrier (such as gadolinium), and its use for angiography and for metabolic mapping. At present CT reigns supreme for the detection of compressive and treatable lesions, whereas MRI scanning enables us to study intrinsic disease and has greater potential for future development.

*To precess: to spin about a cone shaped axis, as in a wobbling spinning-top.

CLINICAL FEATURES

It is surprising that so little headway has been made in understanding the pathogenesis or treatment of common conditions such as ischaemic papillopathy (anterior ischaemic optic neuropathy (AION)), optic neuritis, and nutritional amblyopia. Advances have, however, been made in some rare conditions, which I would therefore like to cover.

Leber's hereditary optic neuropathy

No devastation can be as great as the potential visual loss that occurs in this, the condition affecting young adults in their prime. Some interesting observations are furthering our knowledge about the subject.

Cardiac abnormalities. The high frequency of cardiac abnormalities (51% in one series⁶ indicates that this may be a multisystem disease.⁷ Cardiac abnormalities include the pre-excitation syndromes (the Wolff-Parkinson-White and the Lown-Ganong-Levine syndromes) which are associated with electrocardiographic abnormalities due to accessory A-V conduction tracts in the cardiac muscle, but are not usually symptomatic.

Enzymatic defects. Support for the cyanide toxicity theory has tended to falter over the past decade, but there does appear to be a deficiency of the enzyme thiosulphate sulphur-transferase (rhodanese) in these patients.⁸ This enzyme is used in the detoxification of cyanide.

Pathogenesis. A mutation has recently been described on the subunit 4 gene of mitochondrial DNA; one amino acid arginine is converted to histidine at codon 40.⁹ As a result of the amino acid substitution a restriction enzyme binding site is lost. The mutation affects DNA energy production and cell respiration. In a further paper analysis of mitochondrial DNA¹⁰ showed a mutation at base pair (bp) 11778, demonstrated by loss of a recognition site for the restriction enzyme endonuclease SfaNI. This mutation was accompanied by poor visual recovery, but patients without this mutation had regained useful vision. This therefore explains and will indeed predict the small number of patients (20%) with the potential for visual recovery. Further investigation may clarify the relationship of the microangiopathy to the disease, the incidence of visual loss, and the explanation for the greater incidence in males than females.

Optic neuropathy of sarcoidosis

Unexplained visual loss, often bilateral in association with enlargement of the optic nerve or nerve sheaths on CT scanning, may be attributed to granulomatous disease. Sarcoidosis is a multisystem disease in which non-caseating epithelioid cell granulomata occur in different sites. The optic nerves may rarely be affected without other clinical signs in the eye or in the nervous system. Visual loss may be acute or subacute and painful, or chronic and painless. Diagnosis was made by standard diagnostic criteria.¹¹ Cases are often steroid responsive, but, if high dosage is required, visual function may be retained by the use of azathioprine or chlorambucil.¹² In one recent case a man with progressive visual loss in one eye, with mild disc oedema and an expanded nerve on CT, was diagnosed as an optic nerve sheath meningioma. However, after several months a lesion on his forehead was biopsied and revealed sarcoidosis. Resolution of his visual symptoms with steroids leads me to reiterate the axiom that diagnosing the treatable is the most important part of the medicine.

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