DISORDERS OF THE ANTERIOR VISUAL PATHWAYS

S A Madill, P Riordan-Eva

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Clinical assessment remains the crucial step in management of disorders of the anterior visual pathways. Once the patient has been examined, or in the majority of cases once the history has been obtained, the clinician should have a clear idea of the site of the disease process and its likely pathogenesis. Only then can appropriate and timely investigations be organised and their results interpreted correctly.

DISTINGUISHING BETWEEN RETINAL AND OPTIC NERVE DISEASE

Although fundal examination is diagnostic in many patients with retinal disease (see fig 7 in Lueck *et al*, p iv9), initial assessment by optometrists generally results in such patients being referred to ophthalmologists. In neuro-ophthalmic practice fundal abnormalities are usually absent or non-specific, such that other clinical features must be relied upon. They may be subtle so requesting repeat examination by an ophthalmologist may be helpful when other clinical features indicate retinal disease.

Symptoms

Photopsia (flashes or sparks of light) are most commonly caused by vitreo-retinal traction, in which case they are often induced by eye movements and do not last for more than a few weeks. Persistent photopsia are a feature of retinal disease, either degenerative, inflammatory (for example, acute zonal occult outer retinopathy (AZOOR) that characteristically presents acutely with unilateral visual field loss, photopsia, and normal fundal examination but abnormal electroretinograms (ERGs)), or paraneoplastic (cancer or melanoma associated retinopathy). Photopsia induced by eye movements or change in illumination occasionally occur in optic nerve disease. Metamorphopsia and micropsia (distortion and minification of the visual image) most commonly indicate retinal disease, respectively caused by retinal distortion and separation of photoreceptors by oedema. (Particularly photopsia but also metamorphopsia can occur in posterior visual pathway disease.) Night blindness (nyctalopia) indicates rod photoreceptor dysfunction, characteristically occurring in retinitis pigmentosa but also in melanoma associated retinopathy. Light intolerance ("day blindness" or hemeralopia) is a feature of cone photoreceptor dysfunction. Temporary exacerbation of visual impairment with increased body temperature (Uhthoff's phenomenon) occurs in optic neuropathies, usually but not necessarily in progressive or relapsing remitting multiple sclerosis.

Visual function and pupillary responses

Macular disease tends to impair near more than distance visual acuity, whereas in optic nerve disease near and distance acuity are equally reduced. Although acquired red/green colour blindness (dyschromatopsia) traditionally is associated with optic nerve or posterior visual pathway disease and acquired blue/yellow or blue dyschromatopsia with retinal disease, there are a number of conditions that contradict this such as autosomal dominant optic atrophy and chronic papilloedema. More reliable is the relative impairment of colour vision and visual acuity. In optic nerve disease, particularly caused by demyelinating disease or compression, colour vision tends to be more severely affected—that is, there may be profound dyschromatopsia with relatively preserved visual acuity. Usually in retinal disease visual acuity is equally or more notably impaired than colour vision.

Peripheral scotomas with borders that do not conform to the organisation of the retinal nerve fibre layer, such as a ring pattern or having an irregular outline, usually indicate retinal disease. (Homonymous irregular scotoma may be caused by a lesion of the primary visual cortex.) Field loss respecting the horizontal meridian, such as altitudinal or arcuate defects, usually indicate anterior optic nerve disease but may be caused by a retinal lesion involving the retinal nerve fibre layer, in which case there is likely to be a corresponding abnormality on fundal examination.

Central field loss occurs in both retinal and optic nerve disease but not if it respects the vertical meridian, in which case scotomatous bitemporal hemianopia caused by chiasmal disease or

See end of article for authors' affiliations

Correspondence to:
Mr Paul Riordan-Eva,
Department of
Ophthalmology, King's
College Hospital, Denmark
Hill, London SE5 9RS, UK;
paul.riordan-eva@kingsch.
nhs.uk

scotomatous homonymous hemianopia caused by post-chiasmal disease needs to be considered. Enlargement of the blind spot may be due to optic disc swelling or peripapillary retinal pathology, including myopic degeneration. Pronounced bilateral blind spot enlargement can be mistaken for bitemporal hemianopia, reinforcing the importance of determining whether the vertical meridian is respected.

A relative afferent pupillary defect (RAPD) caused by retinal disease requires extensive asymmetric disease with macular involvement—for example, subtotal retinal detachment. Thus in most cases there will be obvious fundal changes but retinal disease may not be apparent on fundoscopy. Conversely if there is only localised disease, including maculopathy, the possibility of coincidental optic neuropathy needs to be considered. RAPD in the presence of a normal fundus, particularly if visual function is relatively preserved, is highly suggestive of optic nerve disease.

Fundal examination

Rarely is it possible to determine the underlying aetiology solely from the appearance of the optic disc, whether it is swollen or atrophic.¹ An exception is exposed optic nerve head drusen (fig 1). Even optic atrophy associated with cupping may not be caused by glaucoma. It is particularly important to remember that optic atrophy can result from

retinal disease, such as previous central retinal artery occlusion or cone dystrophy.

Some neurological conditions are associated with pigmentary retinopathy. The most common example is mitochondrial myopathy, in which a granular (“salt and pepper”) retinopathy, often difficult to differentiate from normal variation, with little visual impairment is most common (fig 2).² A “bone spicule” appearance associated with night blindness and visual field constriction, as typically seen in retinitis pigmentosa, or diffuse atrophy with severe visual loss may also occur.

Visual electrophysiology

When clinical assessment is inconclusive, visual electrophysiology is usually the best method of distinguishing between retinal and optic nerve disease, as long as it is performed and interpreted correctly. Full field ERGs assess retinal function, particularly of the rod and cone photoreceptors (see fig 8C in Lueck *et al*, p iv10). The P50 and N95 components of the pattern electroretinogram (PERG) reflect macular and retinal ganglion cell function, respectively. Flash and pattern visual evoked potentials are often thought to be solely measures of optic nerve function, but this depends upon the presence of normal retinal function. In the electrophysiological investigation of visual loss, visual evoked potential (VEP) abnormalities can only be interpreted in combination with the results of full field and pattern ERGs.

COMMON OPTIC NEUROPATHIES

Correct assessment of optic disc abnormalities necessitates experience of normal variation, as well as the spectrum of congenital anomalies and other entities that can be mistaken for optic disc swelling or optic atrophy.³ Glaucoma rarely presents to neurologists, usually being detected by optometrists or ophthalmologists, and will not be discussed.

Acute demyelinating optic neuropathy (“optic neuritis”)

Acute demyelinating optic neuropathy is rare over the age of 50 years. Visual loss usually develops over a few days. It should have stabilised by two weeks from onset and begun to recover by six weeks. In almost all cases there is pain around the eye and/or pain on eye movements. Visual acuity is 6/12 or better in 36% and 6/60 or worse in 35%, with no perception of light (NPL) in 3%. There is reduced colour vision, central field loss usually manifesting as diffuse loss on conventional computerised perimetry, and RAPD unless there has been previous involvement, symptomatic or subclinical, of the fellow optic nerve. In two thirds of cases the optic disc is normal in the acute stage (retrobulbar optic neuritis) and in one third it is swollen (papillitis).

Without treatment final visual acuity is 6/12 or better in 95% of cases. There is comparable recovery of colour vision, contrast sensitivity, and visual field. Frequently there is persistent RAPD and prolongation of the latency of the pattern VEP, as well as development of optic atrophy.

Acute demyelinating optic neuropathy can be diagnosed clinically, without the need for further investigations, unless there are atypical clinical features (see below).⁴ It is particularly associated with relapsing remitting multiple sclerosis, either as a first manifestation or as part of a relapse. It may be a component of acute disseminated encephalomyelitis. It may also be precipitated by a viral

Figure 1 Exposed optic nerve head drusen. (A) Colour photograph. (B) Autofluorescence.

Figure 2 Pigmentary retinopathy in mitochondrial myopathy. (A) Granular ('salt and pepper') retinopathy. (B) Bone spicule appearance. (C) Diffuse retinal atrophy.

illness or immunisation, in which cases there is no risk of developing multiple sclerosis.

The optic neuritis treatment trial (ONTT) found no improvement in visual outcome with systemic steroid treatment, intravenous or oral, in patients with a first episode of idiopathic acute demyelinating optic neuropathy.⁵ Steroid treatment did, however, accelerate recovery of vision and may be particularly indicated in certain instances (table 1). The overall risk of developing multiple sclerosis at 10 years was 38%, increasing to 56% if there were any white matter lesions on brain magnetic resonance imaging (MRI) at presentation, and decreasing to 22% if the baseline brain MRI was normal, in which case the risk was further reduced in male patients or if there was optic disc swelling in the acute stage (table 2). The controlled high-risk Avonex (interferon- β 1a) multiple sclerosis prevention study (CHAMPS) found that among patients with a first episode of acute demyelinating optic neuropathy and abnormal brain MRI at presentation initially treated with systemic steroids, interferon treatment reduced the risk of developing multiple sclerosis at three years from 50% to 33%.

Ischaemic optic neuropathy

Ischaemic optic neuropathy is divided into non-arteritic, which is more common, and arteritic, usually caused by giant cell arteritis but possibly other systemic vasculitides, such as systemic lupus erythematosus, requiring systemic steroid treatment.⁶ Anterior ischaemic optic neuropathy (AION), in which the optic disc is swollen during the acute stage (see fig 7A in Lueck *et al*, p iv9), is much more common than posterior ischaemic optic neuropathy (PION), in which the optic disc is normal during the acute stage.

In non-arteritic anterior ischaemic optic neuropathy (NAION) there is infarction of the retrolaminar optic nerve, just posterior to the lamina cribrosa, caused by perfusion deficit in the short posterior ciliary arteries. Visual loss is painless and usually sudden in onset, although in some cases

Table 1 Particular indications for steroid treatment in acute demyelinating optic neuropathy

- ▶ Poor vision in the fellow eye
- ▶ Severe visual loss in the affected eye
- ▶ Severe pain

Table 2 Ten year risk of multiple sclerosis after an initial episode of acute demyelinating optic neuropathy

White matter lesions on brain MRI at presentation		10 year risk (%)
0	Overall	22
	Female	31
	Swollen optic disc	16
	Male	15
1	Swollen optic disc	5
1 or more		51
Overall		56
		38

Adapted from: Optic Neuritis Study Group. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis. Experience of the optic neuritis study group. *Arch Ophthalmol* 2003;121:944–9.

there is progression over the first two weeks. Visual acuity is from normal to NPL, but 33% of eyes retain 6/18 or better. Colour vision tends to be relatively preserved. Visual field loss is typically inferior altitudinal, reflecting the anatomy of the anterior optic nerve vascular supply, but other patterns of monocular field loss may occur. There is an RAPD, unless the fellow optic nerve has previously been affected. By definition the optic disc is swollen in the acute stage, often with disc or peripapillary haemorrhages.

As long as optic disc swelling is documented in the acute stage and there are no atypical features (see below), NAION in patients under age 55 can be diagnosed clinically without the need for further investigation.⁴ Giant cell arteritis must be excluded in patients over the age of 55 years.

The predominant risk factor for NAION is congenitally small optic discs, which also predisposes to optic nerve head drusen. Other risk factors are systemic hypertension, diabetes mellitus, hypercholesterolaemia, and nocturnal arterial hypotension, which may be caused by overzealous antihypertensive treatment. Visual acuity spontaneously improves in over 40% of eyes by six months but without improvement in the visual field loss. The optic disc swelling resolves to leave optic disc pallor, often segmental. NAION does not recur in the same eye but there is about 15% risk of fellow eye involvement. Low dose aspirin may reduce this risk and is usually recommended, together with control of risk factors amenable to treatment.

Arteritic ischaemic optic neuropathy caused by giant cell arteritis results from multiple occlusions of arteries supplying

the optic nerve.⁷ Visual loss is usually more severe than in NAION, with many eyes presenting with visual acuity worse than 6/60. Optic disc swelling in the anterior type tends to be more pallid and less frequently associated with haemorrhages than in NAION. The combination of ischaemic optic neuropathy and central retinal artery occlusion is highly suggestive of giant cell arteritis (fig 3). Recognition of PION caused by giant cell arteritis can be very difficult. The patient presents with poor vision, an RAPD and normal fundus. Fluorescein angiography will, however, show notably impaired choroidal perfusion.

Clinical diagnosis of giant cell arteritis depends upon identification of symptoms of cranial arteritis, of which jaw claudication is the most specific, polymyalgia rheumatica and constitutional disturbance, and examination for tenderness or absence of pulsation of the superficial temporal arteries. Erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) are usually raised, above 45 mm/hour and 25 g/l, respectively, being highly suggestive. However some patients have “occult GCA”, in which there are no apparent clinical features other than the visual loss, some have normal ESR and CRP, and rarely there are neither clinical features nor raised inflammatory markers.

Temporal artery biopsy, with a specimen of at least 2 cm in length, should be performed in all cases of suspected giant cell arteritis. Sequential bilateral biopsy should be considered if there is high clinical suspicion and the first biopsy is negative. Recent studies have shown that concerns about having to perform biopsies within a few days of starting steroid treatment are not warranted, with biopsies still positive in the majority of cases after four weeks of high dose steroid treatment.

Giant cell arteritis with visual loss requires emergency systemic steroid treatment if bilateral blindness is to be avoided. Standard initial treatment is oral prednisolone (1–1.5 mg/kg/day). A single dose of intravenous hydrocortisone (250–500 mg) should be considered as soon as the clinical diagnosis has been made, particularly if there is likely to be delay in starting oral prednisolone. Whether initial treatment with intravenous methylprednisolone improves outcome remains uncertain, but it is particularly indicated under certain circumstances (table 3). Subsequent gradual tapering

Figure 3 Combined anterior ischaemic optic neuropathy (swollen optic disc with haemorrhages) and central retinal artery occlusion (pallid swelling of the retina with cherry red spot).

Table 3 Particular indications for intravenous methylprednisolone in giant cell arteritis
▶ Bilateral involvement
▶ Symptoms of impending visual loss in the fellow eye
▶ Pre-existing poor vision in the fellow eye
▶ Inadequate response to oral prednisolone

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of systemic steroid treatment is adjusted according to clinical and laboratory response. Steroid treatment is likely to last at least six months and usually 12 months. Steroid related complications need to be anticipated. There is no evidence that other immunosuppressants provide better control of the disease process, but they can be used as steroid sparing agents.

PION also occurs as a late complication of radiotherapy, in which there is a characteristic pattern of gadolinium enhancement of the optic nerves and optic chiasm on MRI, and in association with non-ocular, especially spinal surgery, or massive blood loss when hypotension, blood loss, anaemia, and risk factors for arteriosclerosis play variable roles. Spontaneous non-arteritic PION is rare and the diagnosis necessitates thorough exclusion of other possibilities, including compression by tumour and meningeal disease.

Nutritional/toxic optic neuropathy

The nutritional optic neuropathies, including tobacco-alcohol amblyopia, have largely been attributed to deficiency in the B vitamins, particularly thiamine and B12, and/or folate. In most cases B vitamin or folate deficiency cannot be identified, but the response to empirical treatment suggests that there may be impaired utilisation rather than deficiency. Optic neuropathy caused by vitamin B12 deficiency, most commonly secondary to pernicious anaemia, may occur before other neurological manifestations, and both may develop in the absence of macrocytosis. Drugs (for example, ethambutol, amiodarone (see below), or chloramphenicol), heavy metal poisoning, or chemicals such as methanol may cause toxic optic neuropathy.

Nutritional/toxic optic neuropathy presents with painless, subacute, symmetrical, progressive visual loss. Visual acuities and particularly colour vision are reduced, usually without an RAPD. Characteristically there are subtle central or caeco-central field defects, best identified with a small red target on confrontation or tangent screen testing (fig 4). In some cases, particularly in methanol poisoning, there is peripapillary

Figure 4 Small central scotomas to red target in nutritional/toxic optic neuropathy detected by tangent screen perimetry.

Figure 5 Pseudopapilloedema caused by congenitally small optic disc (without buried optic nerve head drusen) associated with anomalous branching of the central retinal artery (arrow).

nerve fibre layer swelling in the acute stage. Temporal optic disc pallor develops with time and is a poor prognostic sign. Bilateral central field defects, assuming that scotomatous bitemporal hemianopia has been excluded, are rarely caused by optic nerve compression but neuroimaging is prudent, especially if there is no response to treatment.

Treatment of nutritional/toxic optic neuropathy comprises removal of any causative factors, treatment of any identified vitamin deficiencies, and if necessary empirical treatment with parenteral hydroxocobalamin (1 mg intramuscularly per week for four weeks), oral B vitamins including thiamine (for example, vitamin B compound strong 2 tabs three times daily) and oral folate (5 mg per day).

Compressive optic neuropathy

Compressive optic neuropathy usually causes chronically progressive visual loss with signs of an optic neuropathy but it may present acutely—for example, when caused by ophthalmic artery aneurysm or acute thyroid orbitopathy. Proptosis indicates disease involving the orbit. Although thin slice CT scanning, including orbital views, will identify most compressive lesions, dedicated MRI views of the optic nerves

with gadolinium enhancement are often required and may need to be repeated. They will also exclude intrinsic optic nerve disease. Treatment is relief of the compression, usually surgically but possibly by endovascular therapy if caused by aneurysm or with systemic steroids in thyroid orbitopathy.

Papilloedema

The term papilloedema should be reserved for optic disc swelling caused by raised intracranial pressure, either confirmed by measurement of cerebrospinal fluid (CSF) opening pressure or highly likely given the results of neuroimaging. Although blurred disc margins, lack of spontaneous venous pulsation, and enlargement of the blind spots are frequently cited as the most useful signs of optic disc swelling, they may be misleading. Haemorrhages or cotton wool spots on or around the optic disc, capillary dilatation on the disc surface, nerve fibre layer thickening with obscuration of the larger vessels on and around the disc, peripapillary retinal (Paton's) folds, choroidal folds, "vintage" spots, comparison with the fellow eye, and changing appearance of the disc, are more reliable signs. Fluorescein angiography may also be helpful but needs to be interpreted by an experienced observer. However normal the appearance of the optic discs is, symptoms suggestive of raised intracranial pressure necessitate urgent neuroimaging.

Papilloedema is usually associated with normal visual function apart from induced long sightedness and enlarged blind spots. Impaired visual function usually indicates an alternative or additional optic neuropathy—for example, direct optic nerve involvement as well as raised intracranial pressure in cryptococcal meningitis—or may be caused by secondary optic nerve infarction. Impaired visual function caused by papilloedema necessitates urgent treatment of the raised intracranial pressure.

Pseudopapilloedema should be considered when the optic discs are thought to be swollen in the absence of other clinical features of raised intracranial pressure. It should be

Table 4 Diagnostic criteria for idiopathic intracranial hypertension

- ▶ No abnormal symptoms, signs, or neuroimaging abnormalities that cannot be explained by raised intracranial pressure
- ▶ Confirmation of increased CSF pressure, usually by lumbar puncture (>25 cm in obese patients) but occasionally necessitating intracranial pressure monitoring
- ▶ Normal CSF constituents
- ▶ Exclusion of other potential causes of raised intracranial pressure, including:
 - drug treatment, particularly tetracyclines or vitamin A
 - cerebral venous sinus occlusion, particularly if there is a predisposition (for example, oral contraceptive therapy, mastoid disease, inherited or acquired thrombophilia, Behçet's disease), or jugular venous occlusion, suggested by history of neck surgery
 - dural arteriovenous malformation, suggested by pulsatile tinnitus with an objective bruit
 - sleep apnoea
 - congenital or acquired disease of the spine or spinal cord

Table 5 Features atypical for acute demyelinating optic neuropathy or non-arteritic anterior ischaemic optic neuropathy

- ▶ Progressive visual loss more than 2 weeks after onset
- ▶ Temporal field defect in the fellow eye
- ▶ Optic atrophy at presentation
- ▶ History of sarcoidosis or systemic vasculitis
- Additional features atypical for acute demyelinating optic neuropathy*
 - ▶ Age over 50
 - ▶ Absence of pain
 - ▶ Severe headache localised to the vertex suggestive of sphenoid sinusitis
- ▶ Failure of vision to recover, necessitating further investigation to exclude:
 - compressive lesion
 - other types of inflammatory disease ("atypical optic neuritis")
 - infiltrative optic neuropathy
 - Leber's hereditary optic neuropathy
- Additional features atypical for non-arteritic anterior ischaemic optic neuropathy*
 - ▶ Pain
 - ▶ No optic disc swelling in the acute stage
 - ▶ Signs of retinal infarction
 - ▶ Large optic disc cup in the fellow eye
 - ▶ Clinical or laboratory features of giant cell arteritis or other systemic vasculitis

particularly considered when the optic discs are incidentally noted to be abnormal, such as by an optometrist. Although the discs are elevated with indistinct margins, there is no capillary dilatation, nerve fibre layer thickening to obscure the major blood vessels, superficial haemorrhages, or cotton wool spots (fig 5). The underlying abnormality is congenitally small ("crowded") optic discs, which are usually associated with long sightedness, compounded in some cases by buried optic nerve head drusen. There is often anomalous branching—for example, trifurcation rather than bifurcation—of the central retinal vessels, and tortuosity of the retinal vessels.

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (IIH) is a diagnosis of exclusion, the criteria being listed in table 4.⁸ It is generally a disease of overweight young adult females. It occurs in children. It is uncommon in adult males. The major morbidities are headaches and visual loss, the latter necessitating regular monitoring with formal visual field testing, measurement of visual acuities, and optic disc assessment. Treatment is adjusted according to symptoms and risk of progressive visual loss, primarily judged on visual fields and appearance of the optic discs. The mainstay of treatment is usually weight loss. Acetazolamide (0.5–2.0 g/day) is the preferred drug to reduce intracranial pressure. Furosemide or bendrofluazide are alternatives if acetazolamide is not tolerated or is contraindicated—for example, sulfonamide hypersensitivity. Management of headaches is determined by how much they are thought to be related to raised intracranial pressure or other factors, such as muscle tension, and otherwise on empirical grounds. Surgical treatment by CSF shunting or optic nerve sheath fenestration is indicated if there is risk of progressive visual loss that is not likely to be controlled by medical treatment, due to lack of effect, intolerance, or non-compliance. All the surgical options have a significant failure rate. If CSF shunting is being considered, a ventriculoperitoneal shunt is preferred if the cerebellar tonsils are relatively low. Repeated lumbar puncture is not indicated as a therapeutic measure except as a short term temporising measure before surgery or possibly during pregnancy. High dose steroid treatment has been advocated for acute severe visual loss but more important is urgent control of the intracranial pressure by CSF shunting.

Figure 6 Optic atrophy with retino-choroidal collaterals (arrows) caused by optic nerve sheath meningioma.

Traumatic optic neuropathy

Optic nerve trauma may occur in association with fractures of the optic canal or medial orbital wall, caused by blunt trauma to the forehead without any fracture, or rarely due to penetrating orbital injury. There is no conclusive evidence in favour of high dose systemic steroid treatment or surgery.⁹

UNCOMMON OPTIC NEUROPATHIES

Errors in the management of optic neuropathies are usually due to failure to recognise atypical features, of which the common ones are listed in table 5. In any anterior optic neuropathy associated with macular exudates ("macular star") or retinal vascular abnormalities, infectious disease including cat scratch disease, Lyme disease, or syphilis needs to be considered. In any retrobulbar optic neuropathy the visual field of the fellow eye must be carefully examined for temporal field loss indicative of a lesion at the junction of the optic nerve and optic chiasm, since there is a high likelihood of a mass lesion.

"Atypical optic neuritis"

Inflammatory optic neuropathy with clinical features atypical for acute demyelinating optic neuropathy (see above) may be caused by sarcoidosis or systemic lupus erythematosus. Sometimes no underlying aetiology is identified in which case the terms granulomatous optic neuropathy or chronic relapsing inflammatory optic neuropathy (CRION) have been used. In the immunosuppressed, cytomegalovirus, herpes zoster, and cryptococcal infection need to be considered. When bilateral disease, simultaneous or sequential, is associated with transverse myelitis, the term Devic's neuromyelitis optica may be applied. This is best considered a syndrome, since it may be a manifestation of multiple sclerosis, sarcoidosis, systemic vasculitis, or a distinct entity with a specific immunopathogenesis, and management should be determined accordingly. Gradually progressive optic neuropathy, often bilateral, may be a manifestation of progressive multiple sclerosis, either primary or secondary.

Infiltrative optic neuropathy

Primary optic nerve sheath meningioma usually presents in middle aged women, but may present as early as childhood. There is slowly progressive visual loss, sometimes with mild proptosis, pain, or limitation of eye movements. The

Figure 7 CT scan showing bilateral optic nerve sheath calcification caused by optic nerve sheath meningiomas.

characteristic optic disc appearance is atrophy with retino-choroidal collaterals (previously known as optico-ciliary shunts) (fig 6). More commonly there is chronic swelling progressing to atrophy. Optic nerve sheath calcification, best demonstrated on computed tomography (CT), is pathognomonic (fig 7). MRI with gadolinium shows a normal optic nerve with thickening and enhancement of the meninges (see fig 8A in Lueck *et al*, p iv10). Frequently there is intracranial extension encasing the anterior clinoid process and internal carotid artery. Occasionally optic nerve sheath meningiomas are bilateral and it is important in all cases to look for other intracranial meningiomas. Treatment is fractionated stereotactic radiotherapy, although it is not clear whether this should be undertaken as soon as the diagnosis is made or only once there is evidence of progressive visual loss. Optic nerve sheath infiltration should also be considered in skull base meningioma with visual loss that fails to respond to surgical excision or progresses despite the absence of intracranial anterior visual pathway compression.

Optic nerve glioma usually presents in childhood, with visual loss, squint, proptosis, or acquired nystagmus. It is associated with neurofibromatosis type 1 and the pathology is usually benign pilocytic astrocytoma. The optic disc may be normal, swollen, or atrophic. On CT there is usually fusiform enlargement of the optic nerve. MRI shows expansion of the optic nerve with heterogeneous signal. Management of glioma confined to the optic nerve is usually conservative. Excision may be considered if there is severe proptosis, particularly if the eye is blind, or progressive disease confined to the optic nerve. Chemotherapy or radiotherapy may be indicated if there is progressive disease with involvement of the optic chiasm.

Optic nerve infiltration caused by non-Hodgkin's lymphoma or leukaemia, more commonly acute than chronic leukaemia, usually occurs in patients with an established diagnosis, but occasionally is the presenting feature. Visual loss may be slowly progressive or occasionally acute. There may be optic disc swelling. Imaging usually shows optic nerve expansion and enhancement.

Leber's hereditary optic neuropathy

Leber's hereditary optic neuropathy (LHON) usually presents in males between 11–30 years of age with painless, sequential

Figure 8 Coronal MRI showing expansion of the optic chiasm (arrow) caused by benign glioma in neurofibromatosis type 1.

visual loss. Visual acuities decline to 6/60 or counting fingers with large dense central scotomas. Pupillary light responses may be relatively preserved. In the acute stage there may be swelling of the nerve fibre layer and dilated telangiectatic vessels in the peripapillary retina together with optic disc swelling, but without leakage on fluorescein angiography. In all cases the optic discs become atrophic.

LHON is a maternally inherited disease caused by point mutations in mitochondrial DNA, of which the most common are located at base positions 11778, 3460, and 14484. Affected males do not transmit the genetic mutation to any of their children. Relatives most at risk of visual loss are matrilineal nephews—that is, sisters' sons. The reason for the male propensity for visual loss remains unexplained. LHON is associated with a multiple sclerosis-like illness, particularly in females with the 11778 mutation. There is no treatment of proven benefit. Spontaneous visual improvement may occur, most often in individuals with the 14484 mutation who develop visual loss before the age of 20 years.

Autosomal dominant optic atrophy

Autosomal dominant optic atrophy (ADOA) usually produces very gradually progressive, painless, relatively symmetrical visual loss. The typical story is mildly reduced vision noted in childhood, but not sufficient to hinder schooling, little restriction on adult employment but failure to fulfil DVLA requirements for driving, and dependence on magnifying aids later in life. There are central field defects sometimes mistaken for bitemporal hemianopia. Reduced colour vision, predominantly affecting the blue-yellow axis, and optic disc pallor are prominent even when visual acuity is good. In the absence of a family history, detection of these abnormalities in asymptomatic relatives, of which the biological father is most useful, are often enough to make the diagnosis. There may be optic disc cupping, occasionally leading to misdiagnosis of glaucoma. Visual electrophysiology shows reduced N95 of the pattern ERG indicative of retinal ganglion cell dysfunction. Genetic analysis has identified a mutation on chromosome 3, the protein product being involved in mitochondrial membrane stability, but this may not be the only mutation responsible. There is no specific treatment.

Mimics of ischaemic optic neuropathy

Diabetic papillopathy and amiodarone optic neuropathy occur in patients at risk of NAION and the optic disc swelling of the three entities is difficult to distinguish clinically or on fluorescein angiography. However, diabetic papillopathy and amiodarone optic neuropathy usually develop insidiously, often with relatively mild visual impairment. Diabetic papillopathy is frequently identified incidentally during routine retinal screening. It may be unilateral or bilateral. It occurs in both type 1 and type 2 diabetes mellitus, with no definite correlation with stage of retinopathy or tightness of glycaemic control. Occasionally dilation of the disc capillaries is mistaken for neovascularisation. The disc swelling lasts for several months but visual outcome is usually good. Amiodarone optic neuropathy is usually bilateral and slowly resolves after discontinuation of treatment.

OPTIC CHIASMAL DISEASE

Chiasmal dysfunction is usually caused by compression from a suprasellar mass. The most common cause is pituitary macroadenoma, which must have enlarged upwards by 1 cm before contact is made with the chiasm and must have

Table 6 Causes of pseudo-bitemporal hemianopia

- ▶ Astigmatism
- ▶ Tilted optic discs
- ▶ Inferior retinal detachments
- ▶ Sector retinitis pigmentosa
- ▶ Dermatochalasis (droopy eyelids)

significantly elevated and distorted the chiasm before vision is impaired. Thus presentation with visual loss usually occurs with non-functioning tumours, prolactinomas, or pituitary apoplexy. Other causes of a suprasellar mass include meningioma, craniopharyngioma, Rathke’s cleft cysts, suprasellar epidermoids, supraclinoid aneurysm, and metastasis, which commonly also causes diabetes insipidus from involvement of the posterior pituitary.

Typically pituitary adenoma, by approaching the chiasm from below, causes predominantly upper bitemporal hemianopia, with relatively preserved colour vision and visual acuity, and normal discs in the early stage. If the chiasm is relatively post-fixed there will be optic nerve dysfunction, usually unilateral with an upper temporal field loss in the fellow eye. If the chiasm is relatively pre-fixed there will be posterior chiasmal dysfunction, manifesting as scotomatous bitemporal hemianopia, or optic tract dysfunction (see below). Particularly craniopharyngioma but also other suprasellar lesions tend to present with less clear-cut clinical syndromes.

Acute chiasmal compression from pituitary apoplexy typically presents with severe bilateral visual loss, headache, and collapse. Chronic chiasmal compression leads to progressive bilateral visual loss, also with the potential for complete blindness. There may be headache, ocular motor cranial nerve palsies caused by lateral tumour expansion, and features of endocrine dysfunction. The pattern of optic atrophy classically has a horizontal band (“bow-tie”) pattern in each eye, retinal ganglion cell axons entering the upper and lower poles of the optic disc, predominantly subserving the retina temporal to a vertical line through the fovea, being preserved.

Thin slice CT scanning should identify a suprasellar lesion large enough to compress the optic chiasm. MRI is usually required to characterise the lesion. MR, CT, or catheter angiography may be required to exclude aneurysm and to aid surgical planning.

Acute chiasmal compression from pituitary apoplexy requires urgent treatment of the endocrine failure and surgical decompression. Treatment of chronic chiasmal compression is generally surgical in the first instance, except for aneurysms that may be amenable to endovascular therapy and prolactinomas that are initially treated medically. It is important that serum prolactin is checked early in the course of investigation of pituitary macroadenomas.

Intrinsic chiasmal disease may be caused by inflammatory disease, neoplastic disease, or radionecrosis (see above). Chiasmal dysfunction is rare in demyelinating disease except in ADEM. Sarcoidosis may present with intrinsic disease alone, as a suprasellar mass lesion, or a combination of the two. Benign anterior visual pathway glioma may arise in the chiasm (see above) (fig 8). Malignant anterior visual pathway glioma, usually a disease of middle aged males, presents with rapidly progressive painful bilateral visual loss with

optic disc swelling, sometimes associated with widespread retinal haemorrhages. Pathology is grade IV malignant astrocytoma and death usually ensues within 6–12 months despite radiotherapy.

Severe head injury with skull base fracture through the pituitary fossa may be accompanied by optic chiasmal damage resulting in complete bitemporal hemianopia.

Pseudo-bitemporal hemianopia

In any patient with bilateral temporal visual field loss, particularly when discovered incidentally, it is important to determine whether the field loss respects the vertical meridian before it is assumed to be caused by chiasmal compression. There are a number of ocular entities that produce predominantly upper temporal field loss not respecting the vertical meridian (pseudo-bitemporal hemianopia) (table 6).

OPTIC TRACT DISEASE

Pure lesions of the optic tract are uncommon because optic tract disease is most commonly caused by tumours that usually also cause optic chiasmal or optic nerve dysfunction. The clinical features of a pure optic tract lesion are normal visual acuities and colour vision, contralateral homonymous hemianopia (complete, incongruous or scotomatous), RAPD and horizontal band optic atrophy (see above) in the contralateral eye with the temporal field loss and diffuse optic atrophy in the ipsilateral eye. Other causes of optic tract lesions are vascular processes, demyelinating disease, and trauma.

Authors’ affiliations

S A Madill, P Riordan-Eva, Department of Ophthalmology, King’s College Hospital, London, UK

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