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Doyne Lecture: Current Concepts in Orbital Disease

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It is now nearly 20 years since the inception of the Orbital Clinic at Moorfields Eye Hospital. During these years tremendous changes have taken place in the investigation and management of patients with orbital disease. The clinical application of Computerised Tomography in 1973 gave clinicians, for the first time, a view of the soft tissues within the orbit so that the shape and position of lesions could be seen. More recently Nuclear Magnetic Resonance has produced views of the orbit which are to a certain extent complementary to CT but its true role has yet to be defined. The concentration of patients, with what is a comparatively rare condition, in a number of centres has also proved beneficial. Previously unrecognised patterns of disease have become apparent and groups of clinicians in related specialities have gained experience and expertise in dealing with many difficult, unusual and puzzling problems.

In 1968 conventional radiography and orbital venography together with Massiot tomography were the main radiographic investigations for orbital lesions. Conventional radiographs showed extension of disease into the orbit from adjacent structures particularly if axial tomography was used to outline the ethmoids and medial orbital wall. I visited Passerini in Milan in 1967 and learned his technique of orbital venography. The orbital veins were filled with radiographic contrast and an orbital tumour was suspected if the veins were displaced from their normal position. There were several disadvantages to the technique. Tumours had to be fairly large to displace the veins and if the intraorbital pressure was high then contrast would not enter the orbital veins. In 1970 the combination of clinical examination, conventional radiography and orbital venography enabled us to diagnose the presence of a space occupying lesion with an accuracy of about 84 per cent.[1]

Ultrasound was a more direct method of examining the orbital contents. In 1968 orbital A and B scans were being used in a number of centres with reports of excellent results. At this time several research laboratories including the AERE at Harwell were experimenting with the application of ultrasonic holography. The technique involved mixing the echoes from ultrasonic scans with a reference signal to produce an ultrasonic hologram. The hologram was recorded on photographic film, thus converting it from an ultrasonic to a visual hologram. The image of the scanned object could then be recreated by shining a laser beam through the hologram. Aided by a generous grant from the MRC, we embarked on a research and development programme with the AERE to develop apparatus capable of examining the eye and orbit. The resulting prototype was installed at Moorfields Eye Hospital in 1974, the foundation of the present Ultrasound Department. The apparatus produced excellent A, B and C scans[2] which were useful in delineating the intraocular structures particularly in the presence of opaque media but its use within the orbit was constrained by the inability of the ultrasound to define structures in the most posterior part of the orbit.[3] Within a few years the use of orbital ultrasonography was overshadowed by a new development in the use of X-rays.

Computerised tomography was discovered by Dr. Hounsfield working at the EMI research laboratories in London. The first machine was installed at the Maudsley Hospital and Dr. Glyn Lloyd and I were privileged to work with Dr. J. Ambrose with both this and subsequent prototype scanners.[4,5] Each new scanner improved the resolution and

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accuracy of the images. It was a most exciting period in the development of our speciality for normal and abnormal orbital anatomy could be readily viewed prior to surgery. The position, extent and morphological features of a tumour together with the history and physical signs gave the experienced surgeon a good idea of the likely nature of a lesion prior to biopsy or total removal.

A new method of imaging structures within the body has been devised recently using the alteration in the alignment of hydrogen nuclei when they are in a strong magnetic field (NMR). When the magnetic field is switched off the nuclei return to equilibrium and emit a radio signal. The radio signals emitted by the nuclei can be recorded and a spatial display produced. The image is of the hydrogen protons of water and fat and their concentration determines the contrast of the images (Fig. 1). NMR has not supplanted CT which is cheaper, quicker and defines structures with great accuracy. NMR does, however, provide some additional information but the technique is still being developed and its role in orbital investigation has yet to be determined.

Lacrimal Gland Tumours

The benefit of collecting together patients with a relatively uncommon lesion is well illustrated in cases of lacrimal gland tumours. An analysis of 40 patients seen in the clinic up to 1979 revealed a pattern of clinical presentation which led to the publication of a method of distinguishing between benign and malignant lesions on clinical grounds.[6] Patients with a pleomorphic adenoma were noted to have a painless mass which had been present for at least a year (Fig. 2). Carcinomas of the lacrimal gland had a much shorter history with pain and a clinical picture indistinguishable from inflammatory lesions. In subsequent years this method of separating benign and malignant lesions has been shown to be accurate in over 80 per cent of patients. High resolution CT scans help the differentiation[7] but the history and physical signs are much more important. Lesions arising in the palpebral lobe of the lacrimal gland do not fit into the normal clinical pattern. An expanding tumour within the eyelid is soon noticed and a number of pleomorphic adenomas are

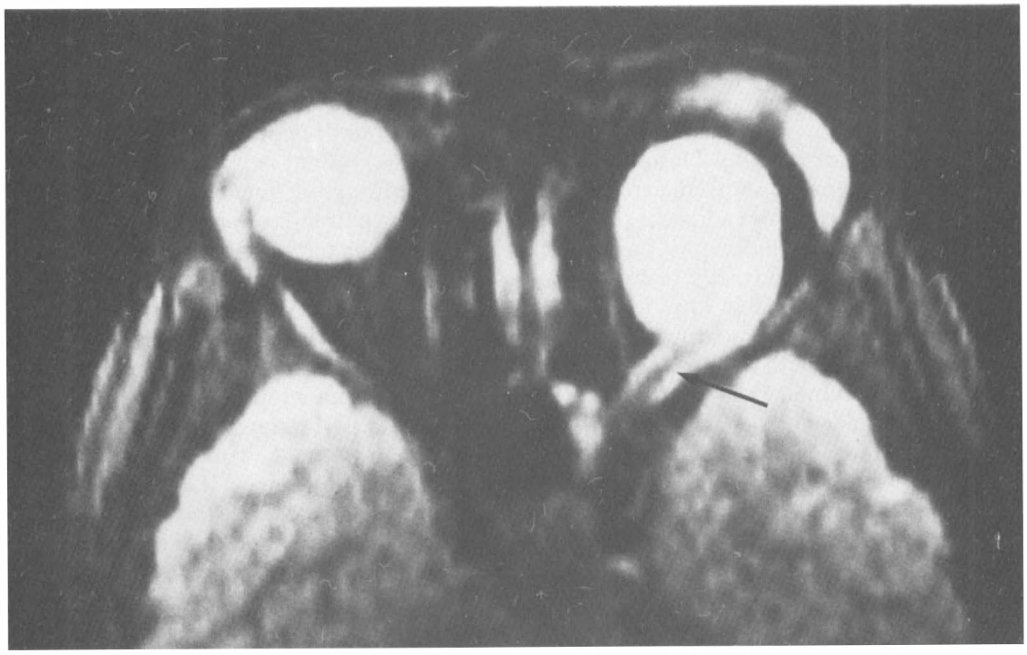

Fig. 1. *NMR image of optic nerve glioma with perineural spread (arrowed) typically seen in neurofibromatosis. Note the fusiform dilatation of the nerve.*

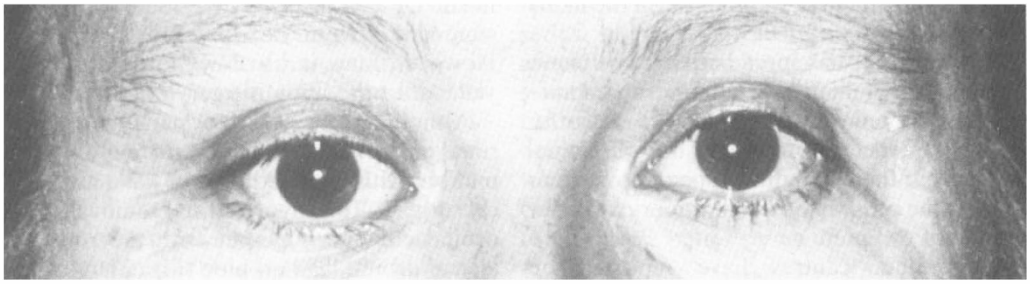

Fig. 2. *Patient with pleomorphic adenoma in the right lacrimal gland. The right eye is displaced downwards and forward, note the fullness of the upper eyelid.*

either inadvertantly biopsied or subtotally removed.

The importance of distinguishing these two groups prior to surgical intervention cannot be over emphasised. Pleomorphic adenomas should be excised without biopsy whereas carcinomas should be biopsied before deciding which type of treatment is most appropriate.

Pleomorphic Adenoma

Godfredson[8] was the first to demonstrate that recurrences were uncommon after complete removal of a pleomorphic adenoma. Henderson[9] reported a similar experience. Font and Gammell[10] concluded from the AFIP series that the incidence of recurrence within five years was 32 per cent if the tumour was biopsied before excision but only 3 per cent if excision was total without prior biopsy. Eventually these lesions undergo malignant transformation, a particular risk after biopsy or incomplete excision. Using an actuarial method to analyse their series, Font and Gammell forecast that after 30 years 30 per cent of treated pleomorphic adenomas would have undergone malignant change. The forecast referred to a group of patients with a 30 per cent recurrence of the original pleomorphic adenoma after 15 years, a reflection of the large proportion of patients who must have been poorly managed initially.

A lateral orbitotomy is the only surgical approach that will expose adequately the whole of the lacrimal gland so that a pleomorphic adenoma can be removed totally without breaching its capsule.[11] This cannot be done with an anterior or a transcranial approach. It is most important that the plane of dissection is always outside the 'false capsule' formed by compressed normal tissue, for tumour cells often extend into the capsule of the adenoma.[12] Removal of the normal portion of the gland ensures that should the disease be multifocal, there is no chance of continued growth of a small but unrecognised tumour that might only become apparent after a lengthy interval. Full evaluation of this series of patients with benign mixed cell tumours will have to wait another ten or twenty years, for recurrence of this type of lesion has been reported many years after the initial surgery. It is, however, very encouraging that there has been no recurrence in any of the 40 patients whose lacrimal gland was totally removed at least five years ago.

Malignant Tumours

The outlook for patients with primary carcinoma of the lacrimal gland is usually very poor. Once the diagnosis has been established histologically, after a trans-septal biopsy, the ophthalmologist must try to determine the extent of the malignant tissue. High resolution CT and NMR pictures will usually show any involvement of the surrounding bone. However, three patients in this series who underwent radical surgery were found to have invasion of the dura of the middle and anterior cranial fossae despite extensive radiological investigations which were normal. In addition adenoid cystic carcinoma often spreads perineurally and can extend into the cavernous sinus along the lacrimal nerve without any detectable abnormality in NMR and CT scans. In evaluating these patients a most careful neurological assessment must be made

before consulting the radiologist on the likely extent of the tumour.

If the tumour has spread outside the orbit, treatment is palliative. Radiotherapy sometimes combined with local resection may offer the best prospect of prolonging life and reducing pain. If the carcinoma appears to be confined to the orbit then radical surgery can offer a hope of complete cure.

Two other centres have reported on patients with lacrimal gland carcinomas. Forrest[13] recorded 20 cases of adenoid cystic carcinoma, all of whom were treated by exenteration often with removal of adjacent bone. Fourteen patients died of tumour, 11 within ten years of initial treatment and the remainder at intervals up to 14 years after the initial diagnosis. Only two patients were free of disease at two and four years. Henderson reported on 11 patients with adequate follow-up. Nine died within eight years and seven months after an average survival of three years and seven months. A further patient died of other causes although recurrent tumour was present in the orbit. Only one patient was still alive, with recurrent tumour, at the time of the report. In the series from our clinic, patients with inoperable tumour survived an average of 3.2 years.

Adenocarcinomas have an equally poor prognosis. Forrest reported on ten patients in his series. Seven died within one year of the initial surgery and a further patient died after four years. The remaining two patients survived with continued growth of tumour for 12 months and four years after the initial diagnosis. Of four patients described by Henderson, three were dead within 18 months. However, one is alive without tumour 19 years after the initial surgery.

Although the outlook for patients with lacrimal gland carcinoma is extremely poor a number with localised disease have had radical surgery. This involves total removal of the orbital contents together with the roof and lateral orbital wall en bloc (Fig. 3). The surgery is best done by a team of surgeons used to performing radical surgery of the face and skull. A large skin flap can be rotated to cover the exenterated orbit or a free skin graft anastamosed to one of the regional arteries. Preliminary results are encouraging, for two patients with adenoid cystic carcinoma and one with adenocarcinoma have survived beyond ten years without recurrence. More time must elapse before the efficacy of this treatment can be fully evaluated.

Vascular Abnormalities

Vascular abnormalities are the commonest space occupying lesions encountered in the orbit. There are three common types, capillary haemangioma, cavernous haemangioma, and the group of venous abnormalities.

Capillary Haemangiomas

These occur in infants and in this series all commenced during the first three months of life. They consist of areas of endothelial cell proliferation with numerous small capillary sized channels. In the orbit they typically occur in the upper eyelid and are usually asso-

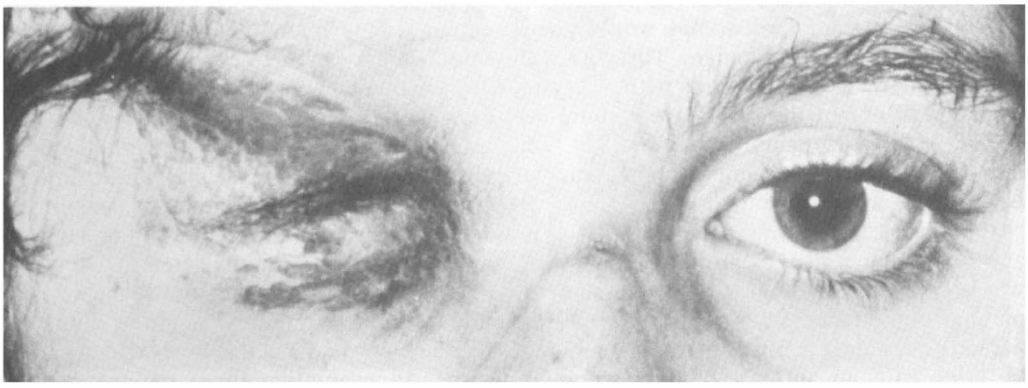

Fig. 3. *Nine year old boy after radical removal of adenoid cystic carcinoma.*

ciated with a 'strawberry mark' in the overlying skin or conjunctiva. The skin lesion is diagnostic (Fig. 4). Most lesions grow for a few months and remain static and involute when the child is five or six years old. In some patients the mass can be quite extensive producing displacement of the globe or severe mechanical ptosis; in this situation normal visual development may be threatened.

The management of capillary haemangiomas is controversial. The general consensus is that in the absence of any threat to visual development the lesion should be watched and treated conservatively, for they invariably disappear by the age of six years. Intervention is justified when the mass is interfering with vision either by producing an acquired astigmatism or in cases of severe ptosis, deprivation amblyopia. Local resection can be very effective in reducing the bulk of the mass but the haemangioma often does not have an easily defined capsule and blood loss, particularly when the surgeon is inexperienced, can be severe and difficult to control. Small doses of radiotherapy will certainly reduce the size of the tumour but clinicians are generally reluctant to apply this type of treatment to an infant with a benign lesion. Currently, the most popular method of treatment is to give steroids systemically or locally to inhibit the endothelial proliferation. In this series, injections of 40 mg of Triamcinalone around the haemangioma on separate occasions has proved very effective in most cases. Occasionally the mass continues to enlarge despite all efforts to halt its growth. Surgical treatment should be deferred until the child is older for major plastic surgery may be needed to produce a better cosmetic result.

Cavernous Haemangioma

Cavernous haemangiomas commonly occur in middle-aged adults. In this series the mean age of the group was 45.6 years with the youngest patient aged 24 years. They are well encapsulated, slow growing masses usually occurring within the muscle cone, and cause a slowly progressive proptosis. The CT appearances are typical (Fig. 5). The tumour has a sponge-like consistency with numerous dilated cavernous-like blood filled spaces lined by flattened endothelium. A connective tissue stroma lies between these spaces which may contain small foci of inflammatory cells and areas of capillary proliferation under the smooth fibrous capsule. Despite its vascular origin the tumour has a very poor blood supply. If the mass is close to the globe then the optic disc may be swollen with associated retinal and choroidal striae. Occasionally the

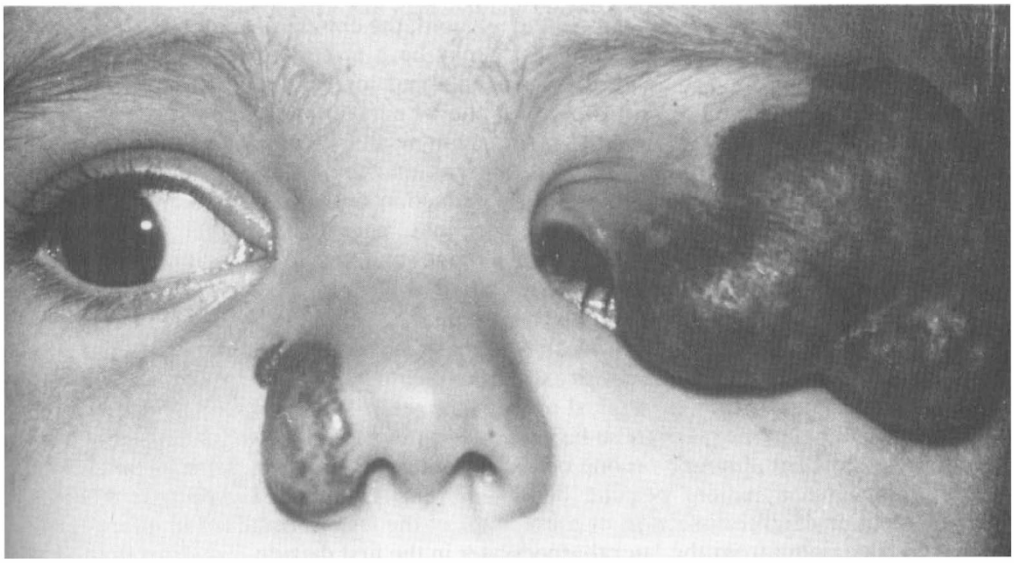

Fig. 4. *Child with capillary haemangioma of left orbit and nose.*

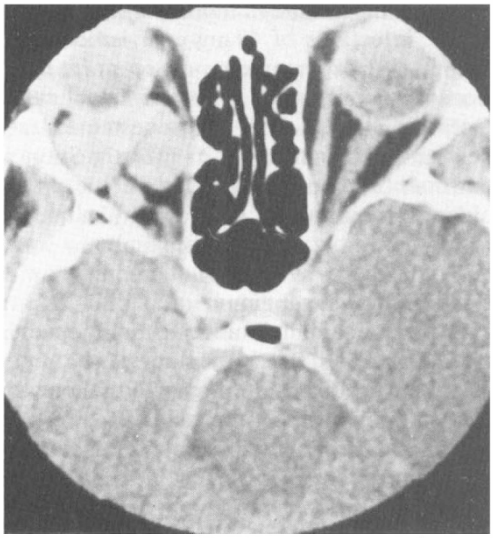

Fig. 5. *CT scan showing multiple well encapsulated cavernous haemangiomas in right orbit.*

tumour may occur in the apex of the orbit and cause optic nerve compression with optic atrophy.

Cavernous haemangiomas gradually enlarge and should be removed to prevent damage to the orbital structures, unless the patient is very elderly or in poor general health. The best approach to the intraconal space is through a lateral orbitotomy. The mass can usually be freed from the orbital contents without great difficulty and dissection can be helped by passing a traction suture through the mass. This will improve manipulation of the tumour and by allowing blood to escape from the cavernous spaces, reduce its size. Dissection must be meticulous and the mass never avulsed from the orbital contents. In many cases, particularly where the tumour is large, the oculomotor nerves may be incorporated in its posterior surface. They must be dissected free using fine microsurgical instruments and an operating microscope with axial illumination. Using this type of surgical procedure the results of removal of these lesions is uniformly excellent although on one occasion in this series a patient became blind despite the most careful dissection of a cavernous haemangioma from the lateral aspect of the optic nerve. Postoperative fluorescein angiograms showed an infarct of the choroid, almost certainly due to interference with the lateral ciliary trunk which divides to form the lateral short posterior ciliary arteries.

Venous Abnormalities

The most common vascular abnormality seen at the Orbital Clinic is the venous anomaly. These are either a primary congenital enlargement of the orbital veins, or secondary enlargement, caused by arterial blood entering the veins. The latter is much less common but can be easily differentiated on clinical and radiological grounds from the congenital type of venous anomaly.

Arterialisation of the orbital veins is usually caused by an A–V shunt in the region of the cavernous sinus, either a carotico-cavernous fistula or a dural shunt. Occasionally the shunt may be within the orbit and involves the ophthalmic or lacrimal artery and adjacent veins. The rise in pressure in the orbital veins causes them to dilate so that the whole of the venous system together with the extraocular muscles enlarge and produce proptosis. This proptosis is often bilateral but may be ipsilateral or contralateral depending on the nature of the shunt and the very variable anatomy of the veins in the region of the cavernous sinus. Patients with a carotico-cavernous fistula are usually easy to diagnose for in addition to proptosis the intraocular pressure is raised, the episcleral veins enlarged and there may be a lateral rectus palsy caused by an enlarged inferior petrosal sinus pressing on the VI nerve. These signs of venous engorgement may be complicated in some patients by signs of intraocular ischaemia caused by a reduction in the pulse pressure in the central retinal artery. Peripheral retinal haemorrhages and neovascularisation may result.

Primary Venous Anomalies

These were the most common lesions encountered in the orbit in this series: 111 patients were recently reviewed. The average age of the patients was 13 years with an age range from birth to 64 years, females predominated in a ratio of nearly 2:1. Approximately a quarter of the lesions occurred in infancy, a quarter in the first decade, a quarter in the second decade and a quarter thereafter. The clinical

presentation of these patients fell into four main groups:

(1) Intermittent proptosis without any visible lesions 26 per cent.
(2) Visible lesions subconjunctivally and in the lids 15 per cent.
(3) Mixed, i.e. visible lesions with proptosis 53 per cent (Fig. 6).
(4) Acute orbital haemorrhage 6 per cent.

The natural history of these lesions is one of progressive enlargement probably due to recurrent episodes of thrombosis and haemorrhage within the mass of abnormal vessels. The position of the abnormal veins within the orbit can be demonstrated either by orbital venography or with CT or NMR. Ninety per cent occurred in the medial half of the orbit with a majority involving the upper inner quadrant; phleboliths were demonstrated within the mass in 20 per cent of patients (Fig. 7). Vascular abnormalities on the hard and soft palate were seen in 10 per cent of patients.

Whilst clinicians recognise this common orbital lesion, its nomenclature still excites considerable debate. Two terms are used, lymphangioma and orbital varices.[14] The first was applied by Ira Jones[15] in 1959 when he reviewed 62 patients recorded in the literature up to that date. Subsequent workers, notably Iliff and Green[16] have also thought that these lesions arise from lymphatic channels within the orbit, basing their argument on the presence of endothelial lined channels with associated lymphoid aggregates, the enlargement of the lesion with upper respiratory tract infections and the presence of cyst-like lesions filled with clear fluid within the orbit.

There are several arguments against this thesis. The position of these lesions corresponds with the normal venous anatomy. Normal lymphatic channels have never been demonstrated within the human orbit. The presence of lymphoid aggregates adjacent to the abnormal vessels does not prove they are lymphatics for similar lymphoid aggregates can be seen within the orbit adjacent to typical veins. It is true that these lesions will enlarge with an upper respiratory tract infection but they will also enlarge for several hours after a patient has cried. The enlargement is probably due to venous congestion in the nose, nasopharynx and orbit rather than enlargement of lymphoid tissue within the orbit and Waldeyers' ring in the nasopharynx. A recent paper by Rootman[17] has attempted to reconcile these views and he thinks that they should be regarded as a spectrum of vascular hamartoma. The controversy continues. We are currently undertaking a full review of our patients together with light and electron microscopy of excised specimens and will make a further contribution to the debate.

Whatever the likely nature of these lesions their management gives little cause for controversy. Most surgeons find them technically difficult to excise because the enlarged ectatic

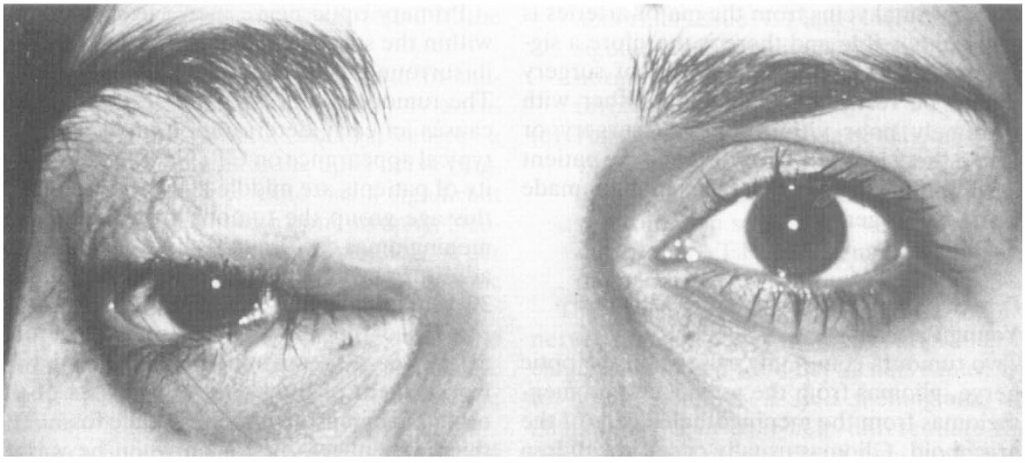

Fig. 6. *Twenty-two year old female with orbital varices involving the caruncle and nasal aspect of the right eyelids.*

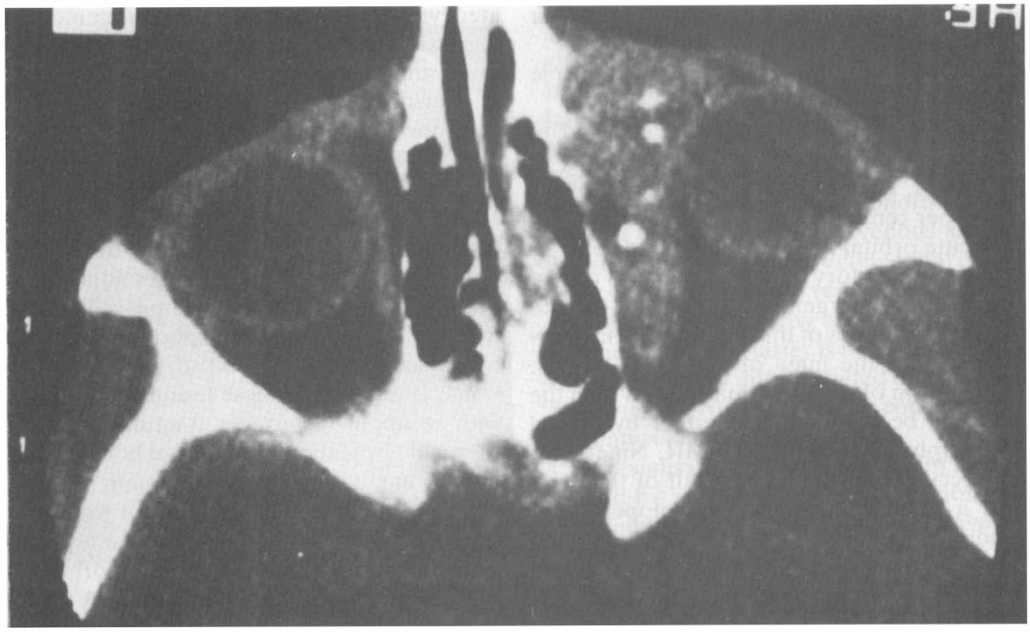

Fig. 7. *Axial CT scan showing abnormal vein in medial part of the right orbit. Note the phleboliths within the vascular mass.*

vessels are friable and bleed easily. If vision is good, surgical excision of these lesions should be confined to the anterior orbit. This will usually provide an improvement in the patient's appearance, however they should be warned that recurrences are common. Severe proptosis can be relieved by removal of extensive varices within the inner surgical space through a lateral orbitotomy, but dissection of the abnormal veins from the major arteries is often impossible and there is therefore a significant risk to vision. This type of surgery should be restricted to patients either with extremely poor vision prior to surgery or where there is severe proptosis and the patient is willing to accept that vision may be made worse by surgery.

Primary Tumours of the Optic Nerve in Young Patients

Two tumours commonly arise from the optic nerve, gliomas from the astrocytes and meningiomas from the meningothelial cells of the arachnoid. Gliomas usually occur in children and are relatively indolent lesions. Meningiomas occur in middle age but they can arise in children and young adults and in these age groups behave in a very aggressive manner, extending up the optic canal to invade the chiasm and middle fossa. Early diagnosis and excision are essential if the tumour is to be completely removed. The differentiation of meningioma from glioma can be very difficult clinically and radiologically.

Primary optic nerve meningiomas expand within the space between the optic nerve and its surrounding thick and tough dural sheath.[18] The tumour compresses the optic nerve and causes an early deterioration in vision and a typical appearance on CT (Fig. 8). The majority of patients are middle aged and female. In this age group the tumour grows slowly but meningiomas can occur in children and young adults. Four patients in this series were under 30 years when first seen. Three had a local removal of the meningioma. In each case after a few years the meningioma recurred with involvement of the bones of the apex of the orbit and extension into the middle fossa. The third patient was first seen when he was 13 years old and thought to have an optic nerve

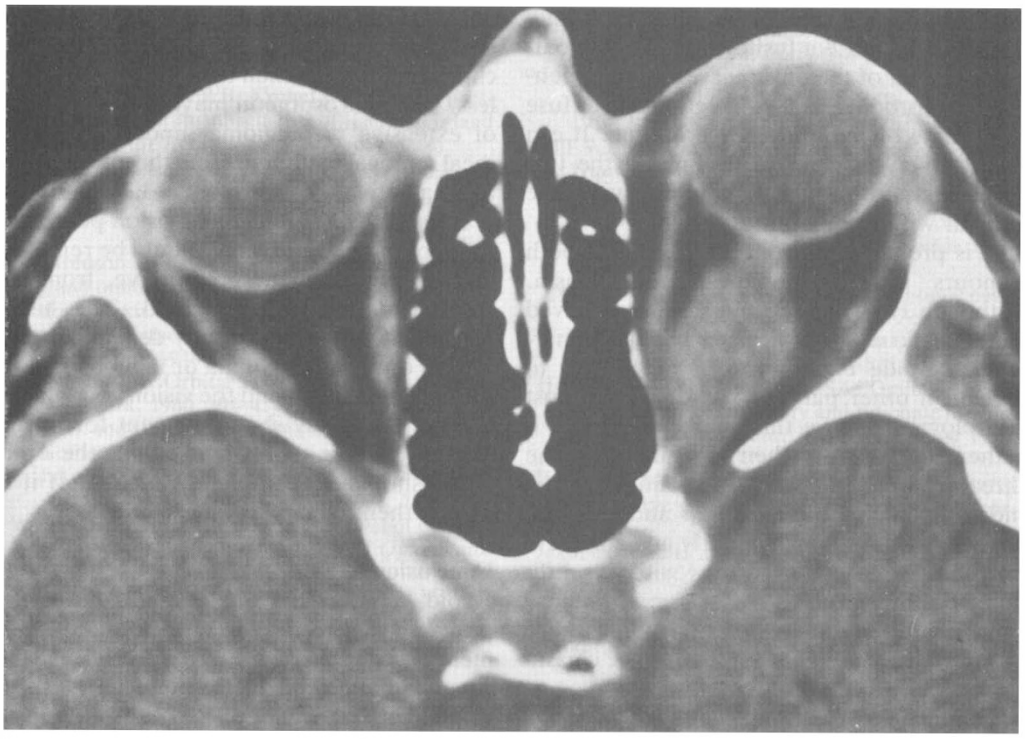

Fig. 8. *Axial CT scan of primary optic nerve meningioma, note the diffuse irregular outline of the tumour.*

glioma. Surgical intervention was not advised and he was subsequently lost to follow-up. He returned in 1986 aged 24 with increasing proptosis. CT scans showed tramline calcification within the orbit typical of optic nerve meningioma. Transcranial surgery was performed and extensive meningioma was found in the orbit and middle fossa.

Optic nerve gliomas usually occur in children, and are invariably grade 1 astrocytomas. The tumour usually causes a fusiform enlargement of the optic nerve (Fig. 1). In most cases the child has a significant impairment of vision with optic atrophy. Neurofibromatosis occurs in approximately 60 per cent of patients and enlargement of the optic canal in 90 per cent.

A major clinical problem is to determine the posterior extent of a glioma[20] within the optic nerve. Three factors hinder the clinician:

(a) Arachnoid hyperplasia remote from the glioma can enlarge the optic nerve and canal. This makes the tumour appear more extensive than it really is.
(b) The glioma may extend into the chiasm without enlargement. In these circumstances a histopathologist may have difficulty in detecting the boundaries of abnormal tissue. CT and NMR can detect significant enlargement of the chiasm but normal studies do not exclude its involvement.
(c) Astrocytes are the connective tissue of the visual system. The tumour can therefore involve the chiasm without interfering with function so that the visual field and directional VEPs may remain normal on the contralateral side.

The clinician dealing with a primary optic nerve tumour, in a young patient, which is clinically confined to the optic nerve must try to decide whether it is a meningioma or glioma. CT scans can help differentiate the two lesions but at best this is only possible in 80 per cent of patients[21] and there is always a

considerable element of uncertainty. Typically gliomas cause a fusiform or 'Dutch loaf' enlargement of the optic nerve whereas meningiomas produce a more irregular and diffuse thickening of the optic nerve outline. It can also be very difficult to distinguish the two from material obtained by biopsying the tumour within the orbit.[22]

It is probable that in young patients both tumours pose a threat to the chiasm. Although Hoyt and Bagdassarian[19] believed that they do not grow and behave like hamartomas, Grade 1 astrocytomas are known to spread in other parts of the CNS and most pathologists believe that they can extend, if rather slowly, from their original site. The threat from a meningioma in a young person is more certain and more rapid and the best chance of total removal is early and complete excision. A method of dealing with this difficult situation would be to excise all primary optic nerve tumours in young patients where vision is significantly damaged and the chiasm intact.

Patients under 40 years who present to the clinician with a primary optic nerve tumour should therefore be fully investigated with CT, NMR, field examination and directional VEPs. If all these tests indicate that the chiasm is intact then patients can be divided into two groups (Fig. 9):

(1) *Patients with good vision.* If CT or NMR scans show an appearance typical of primary optic nerve meningioma then the patient should be referred for neurosurgical exploration. The remainder should be observed to see if there is any change in vision or CT.

(2) *Patients with poor vision.* All patients with vision of 6/18 or worse should be referred for neurosurgical exploration.

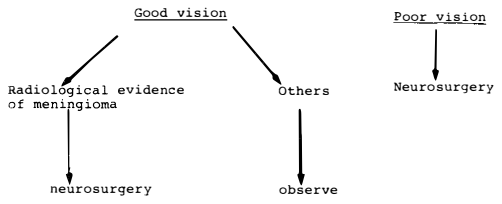

Fig. 9. *Flow chart for the management of young patients with primary optic nerve tumours when the chiasm is clinically intact.*

Transfrontal exploration will show whether the chiasm is macroscopically involved. If the chiasm is involved then further surgery is useless. The neurosurgeon may, in the presence of extensive meningioma, undertake piecemeal removal of tumour from the middle fossa as a palliative measure.

If the chiasm is intact and vision poor then the roof of the optic canal should be removed and the whole of the optic nerve, from the chiasm to the globe, excised. The histopathologist can subsequently decide whether it is an optic nerve glioma or meningioma. If the chiasm is intact and the vision good then a substantial biopsy should be sent for frozen section. If it is meningioma then the optic nerve should be completely excised. If it is glioma then removal is unwarranted.

Conclusions

Rapid advances have been made during the past 20 years in the investigation and treatment of orbital disease. It is likely that the pace of change will accelerate with advances in molecular biology and new imaging systems. Patients with orbital disease will still provide the clinician with numerous complex and challenging problems.

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