- 5 Sloper JJ, Headon MP, Powell TP. Effects of enucleation at different ages on the sizes of neurons in the lateral geniculate nucleus of infant and adult monkeys. Brain Res 1987:428:259–65.
- 6 Yücel YH, Kalichman MW, Mizisin AP, et al. Histomorphometric analysis of optic nerve changes in experimental glaucoma. J Glaucoma 1999;8:38–45.

### Strabismus

Anatomical diagnosis

### J L Demer

# Important even in strabismus surgery

n the 21st century, it is uncommon for modern general and specialty surgeons to operate without preoperative imaging studies to clarify the anatomy of the surgical site.1 A frequent exception to this rule has been ophthalmology, since direct visual inspection of the beautifully transparent eye permits ophthalmologists to see anatomical detail at exquisite resolution with no more than the array of optical instruments routinely maintained in our offices. Nevertheless, the paper by Ela-Dalman and colleagues, in this issue of BJO (p 682), illustrates the importance of application of modern magnetic resonance imaging (MRI) to the preoperative evaluation of complex strabismus.

Ela-Dalman and colleagues describe two patients in whom complicated endoscopic sinus surgery invaded the orbit and resulted in severe iatrogenic trauma to the medial rectus muscle. Clinical recognition that these patients developed a large exotropia with severe limitation of adduction did not uniquely narrow the differential diagnosis of the strabismus; possibilities included multiple entities requiring differing management. Endoscopic injury to the orbit can avulse or deeply transect extraocular muscles so severely that no recovery would be possible.<sup>2</sup> In this event, there is nothing to be gained by delaying definitive treatment, and resorting promptly to nasal transposition of the vertical rectus muscles to mitigate the adduction defect would more expeditiously confer functional benefit. Invasion of the orbit by endoscopic sinus surgical instruments may contuse the nerve to innervating an extraocular muscle. Contusion to a motor nerve or to its intramuscular branches is likely to result in a transient weakness, with a good possibility of

spontaneous recovery without surgery. On the other hand, nerve avulsion (iatrogenic motor neurectomy) is unlikely to be associated with realistic hope of functional recovery, and should be treated in the same manner as deep myotomy or substantial myectomy. Finally, invasion of the orbit by an endoscopic cutter can entrap connective tissues or other structures to restrict duction, a situation in which prompt surgical release may be optimal management. None of the foregoing pathogenetic mechanisms can be ascertained by external examination, particularly of an ecchymotic, oedematous orbit in an uncomfortable patient.

7 Harwerth RS, Crawford MU, Frishman U, et al.

8 Yücel YH, Zhang Q, Weinreb RN, et al. Atrophy

of relay neurons in magno- and parvocellular

layers in the lateral geniculate nucleus in experimental glaucoma. *Invest Ophthalmol Vis Sci* 2001;**42**:3216–22.

Visual field defects and neural losses from experimental glaucoma. *Progr Ret Eye Res* 2002;**21**:91–125.

Advances in the technology of MRI of the orbit have taught us much in recent years.3 The use of surface coils to improve signal to noise ratio and permit smaller fields of view has improved resolution.4 Recognition of the importance of control of movement artefacts has motivated use of fixation targets during scanning that minimise ocular motion and permit multipositional imaging for demonstration of residual contractility of extraocular muscles based on changes in their cross sectional area related to gaze effort.<sup>4</sup> Rapid sequence contrast techniques can distinguish contusion within the motor nerve arborisation of extraocular muscles. Using excellent technique, the individual motor nerves can nearly always be demonstrated to medial rectus, inferior rectus, and lateral rectus muscles,5 the most common targets of iatrogenic trauma during endoscopic sinus surgery.

We owe it to our patients to appreciate the progress in clinical anatomy, and to apply relevant and appropriate imaging techniques in our presurgical evaluations

- 9 Headon MP, Sloper JJ, Hiorns RW, et al. Effects of monocular closure at different ages on deprived and undeprived cells in the primate lateral geniculate nucleus. Brain Res 1985;350:57–78.
- 10 Yücel YH, Gupta N, Zhang Q, et al. Memantine protects neurons from shrinkage in the lateral geniculate nucleus in experimental glaucoma. Arch Ophthalmol 2006;124:217–25.

The paper by Ela-Dalman and colleagues emphasises the importance of "sagittal" orbital imaging. In this regard, it is crucial to be precise about anatomical terminology. Sagittal images, defined relative to the head as a whole, will typically parallel the plane of normal medial rectus and superior oblique muscle bellies.6 Such true craniotopic sagittal images would have been optimal for the study by Ela-Dalman and colleagues. It appears in their study, however, that direct sagittal images were not acquired, but were obtained by reformatting of sets of coronal images. The major disadvantage to this reformatting technique is that the resolution of the reformatted images is reduced approaching the plane thickness of the original image set. Thus, with 2 mm thick coronal images, reformatting will provide resolution closer to 2000 µm than to the original in-plane images of  $312\,\mu m$  in this series. Although the reformatted images were adequate to make the clinical distinctions required by Ela-Dalman and colleagues, the reduced resolution might be insufficient in other clinical situations. Modern MRI scanners are capable of acquiring oblique image planes of arbitrary orientation without reformatting. Thus, it is worthwhile to instruct the radiologists and MRI technicians directly to acquire images in the planes that are clinically relevant. This optimises resolution, and maximises the odds that relevant anatomical features will be demonstrated.

"Quasi-sagittal" image planes are defined as parallel to the long axis of each orbit.<sup>6</sup> These can be obtained only by scanning each orbit separately, and are optimal for the vertical rectus muscles whose paths parallel the quasi-sagittal planes. In the case of the two patients described by Ela-Dalman and colleagues, quasi-sagittal image planes would not have been as well suited to demonstrate trauma to the medial rectus muscle as would true cranial sagittal image planes.

The foregoing anatomical complexity argues that ophthalmologists direct the strategy for orbital imaging in complex strabismus. Before ordering an MRI scan of the orbit in such a situation, it would be prudent for the referring ophthalmologist to consider all possible muscle pathologies that might be playing a part, and specifically request MRI planes and gaze directions that would be informative in narrowing the differential diagnosis and in guiding treatment. Ophthalmologists cannot rely on radiologists or MRI technicians to understand the nuances of extraocular muscle anatomy and function well enough to direct the imaging strategy in complex situations such as these.

Just as new imaging modalities such as optical coherence tomography are revolutionising our understanding and management of retinal disease,<sup>7</sup> modern imaging modalities are revolutionising our understanding of extraocular muscle structure, function, and innervation. Ophthalmologists, and particularly strabismus and orbital surgeons, should review the new findings from orbital magnetic resonance imaging and correlate an immunohistochemistry, since even the fundamental anatomy of the orbit has changed considerably from

### Pterygium

## Pterygium A S Solomon

what most have learned as residents,<sup>8</sup> challenging concepts such as "oblique muscle dysfunction."<sup>9 10</sup> We owe it to our patients to appreciate the progress in clinical anatomy, and to apply relevant and appropriate imaging techniques in our presurgical evaluations.

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#### REFERENCES

 Demer JL, Ortube MC, Engle EC, et al. High resolution magnetic resonance imaging demonstrates abnormalities of motor nerves and extraocular muscles in neuropathic strabismus. J AAPOS 2006; (in press).

ygiom

### Can we provide medical and not surgical cure?

**P**terygium is a common frequently occurring ocular surface lesion characterised by inflammation, angiogenesis, and cellular proliferation, which result in tissue remodelling.

In this issue of *BJO* (p 769), Wong and colleagues present the finding of a new gene that was changed in primary pterygium.

It is the gene for insulin-like growth factor binding protein-3, (IGFBP3), which modulates the effects of insulinlike growth factor on cells. IGFB3 was significantly decreased in pterygium samples compared with normal conjunctiva. Decreased levels of IGFB3 protein have been strongly correlated with the presence of cancer.<sup>1</sup> It might be that the low level of IGFP3 is related to loss of control of the cell proliferation process, which explains the continued growth of pterygium. Solomon and colleagues<sup>2</sup> found in their work an insulin-like growth factor binding protein-2 (IGFBP2) overexpression in pterygium body fibroblasts. This is strong evidence to support the transformed phenotype of these cells and may explain the continual process of growth of fibrovascular tissue. The above findings elucidate two of many factors that are implied in the appearance and the development of pterygium.

#### An overall view of the growth process of pterygium reveals a multiplicity of factors that are correlated and interrelated

We have to remember that the increased incidence of pterygium is in people and populations that are exposed to excessive solar radiation. It is the ultraviolet light (UV) that plays the critical part in the pathogenesis of this disease. UV radiation starts a chain of events at the intracellular and extracellular level that involve DNA, RNA, and extracellular matrix composition. Di Girolamo and colleagues<sup>3</sup> showed in their work that UVB radiation stimulated the induction of matrix matalloproteinase (MMP)-1 expression in human ocular surface epithelial cells,

- 2 Thacker NM, Velez FG, Demer JL, et al. Strabismic complications following endoscopic sinus surgery: diagnosis and surgical management. J AAPOS 2004;8:488–94.
- 3 Demer JL. Pivotal role of orbital connective tissues in binocular alignment and strabismus. The Friedenwald lecture. *Invest Ophthalmol Vis Sci* 2004;45:729–38.
- 4 Demer JL. A 12 year, prospective study of extraocular muscle imaging in complex strabismus. J AAPOS 2003;6:337–47.
- 5 Demer JL, Clark RA, Engle EC. Magnetic resonance imaging evidence for widespread orbital dysinnervation in congenital fibrosis of extraocular muscles due to mutations in KIF21A. Invest Ophthalmol Vis Sci 2005;46:530–9.
- 6 Demer JL, Miller JM. Orbital imaging in strabismus surgery. In: Rosenbaum AL, Santiago AP, eds. Clinical strabismus management: principles and techniques. Philadelphia: WB Saunders, 1999:84–98
- 7 Yannuzzi LA, Ober MD, Slakter JS, et al. Ophthalmic fundus imaging: today and beyond. Am J Ophthalmol 2004;137:511–24.
- 8 Demer JL. The orbital pulley system: a revolution in concepts of orbital anatomy. Ann NY Acad Sci 2002;956:17–32.
- Demer JL. Clarity of words and thoughts about strabismus. Am J Ophthalmol 2001;132:757–59.
- 10 Tan KP, Sargent MA, J PK, et al. Ócular overelevation in adduction in craniosynostosis: is it the result of excyclorotation of the extraocular muscles? J AAPOS 2006;9:550–7.

which is mediated through the ERK1/2 MAPK dependent pathway.

Nolan and colleagues<sup>4</sup> found that UVB radiation creates overexpression of heparin binding epidermal growth factor (HB-EGF) in pterygial tissue. HB-EGF is a potent mitogen and may be considered a major driving force in the development of pterygium. Di Giorolamo and colleagues<sup>5</sup> correlated the two above findings in another study. They found that epidermal growth factor receptor signalling is partially responsible for the increased MMP-1 expression in ocular cells after UVB radiation. Tsai and colleagues6 present a very important aspect of the pathology of pterygium-oxidative DNA damage. UV radiation is noxious to the conjunctiva tissue either by direct phototoxic effect or indirectly by formation of radical oxygen species (ROS). One of the markers of oxidative stress is 8hydroxydeoxyguanosine (8-OHdG). It is the result of UV damage to DNA. An overexpression of 8-OhdG in pterygia was found in this study, a fact that correlates the UV with the oxidative damage to the conjunctiva and the creation of pterygium. The same evidence was found by Kau and colleagues.<sup>7</sup>

Pterygium involves in its development a vascular proliferative process. Marcovici and colleagues<sup>8</sup> found that VEGF and von-Willebrand factor (vWF) are overexpressed in pterygium tissue. This is evidence of the angiogenesis that is found during the development of pterygium.