VISUAL LOSS IN CANCER

Advancing glaucomatous optic neuropathy or chemotherapy-related optic nerve toxicity?

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CASE PRESENTATION

A 62-year-old male shipyard worker was diagnosed with mesothelioma in February 2007. He was started on intra venous (IV) cisplatin (150mg) and IV pemetrexed (1000mg), and received six cycles of these drugs about six weeks apart from 12 April 2007 to 9 August 2007.

Past medical history included Hodgkin's lymphoma (treated with chemotherapy 15 years before with full recovery), asthma, non-insulin-dependent diabetes and hiatus hernia. He is a non-smoker with a family history of oesophageal carcinoma and brain tumor. Repeat medications include clopidogrel (75mg), esomeprazole (20mg), levothyroxin (500mg), atorvastatin (10mg) and fluoxetine (20mg).

He was diagnosed with chronic primary open angle glaucoma (POAG) four months prior to receiving treatment for his mesothelioma. On presentation on 20 October 2006 in the eye clinic, intraocular pressures (IOP) were quite elevated – right eye (RE) = 54mmHg and left eye (LE) = 28mmHg. Baseline biomicroscopic optic nerve head evaluation showed bilaterally glaucomatous cupping with optic nerve heads with a cup to disc ratio (C/D) of 0.7 with associated bilateral early superior defects on Humphrey's 24-2 central threshold visual field perimetry. He had open angles on gonioscopy.

Initial treatment included acetazolamide tablets 250mg, latanoprost 0.005% eyedrops and a combination of timolol 0.5% with dorzolamide eyedrops. The IOP was eventually controlled only on topical treatment at a level of 18mmHg. He was again seen in the eye clinic in March 2007, when his glaucoma seemed well controlled and no alterations were made in his treatment.

He presented three months later on 27 June 2007 (patient was still on his cycle of chemotherapy) complaining of decreased vision in the right eye and visual acuity of 6/24 in the right eye. IOP was RE = 22mmHg and LE = 15mmHg, claiming compliance to his topical treatment. Threshold visual field perimetry revealed in the RE a marked reduction in sensitivity with the mean deviation (MD) dropping to -31.19 DB (legally blind) from -5.40 DB, whereas the LE appeared to be unchanged. His C/D ratios were now RE = 0.9 and LE = 0.7 An effort for further reduction in IOP was planned by changing timolol and dorzolamide eyedrops for a different combination of timolol and brimonidine eyedrops. Latanoprost was continued unaltered.

He was seen again two months later, when his visual acuity in RE had irreversibly decreased to only perception to light (PL) and LE was 6/6. IOP was still RE = 22mmHg, so dorzolamide as a separate preparation was added to his ongoing topical treatment.

DISCUSSION

Glaucoma is a group of optic neuropathies characterised by progressive visual loss associated with specific structural changes on the optic nerve head and visual fields defects. Although of multifactorial aetiology, IOP seems to play an important part in progression and a reduction of IOP, either medically or surgically, remains the mainstay of treatment in all different forms of the disease. It is in the vast majority of cases asymptomatic until late in the course of the condition. Structural optic nerve head changes can be detected sometimes even years before functional visual loss occurs (as detected by different types of visual field evaluation).

Our patient, although presenting with an advanced structural glaucomatous optic neuropathy and very high baseline IOPs (RE in particular), developed a sudden onset and rapid progression of visual loss which is not as common in chronic simple glaucoma, where gradual visual loss over months and years, spreading from the periphery of the visual field towards fixation, is the norm especially when IOP is satisfactorily controlled. The progression of the condition despite adequate (>50%) reduction of IOP on treatment suggests an alternative pathology, possibly optic nerve neurotoxicity.

Cisplatin or cis diamminedichloroplatinum (DDP) is used in chemotherapeutic regimens for many solid tumours including head, neck cancer, bladder tumours and lung cancers. Cisplatin has well-established, frequently observed side effects: nephrotoxicity, nausea and vomiting, ototoxicity, peripheral neuropathy and myelosuppression. Several instances of ophthalmic toxicity have been reported in association with intravenous administration of this drug, namely:

1. A 67-year-old man with squamous cell carcinoma of the left tonsillar fossa was treated with induction chemotherapy through the left lingual artery, the regimen consisted of cisplatin and 5-fluorodeoxyuridine as continuous infusion. The patient developed some transient mental status changes and then left eye blindness. Ophthalmologic examination was compatible with retrobulbar neuritis.[1]

2. A case of acute blindness in the left eye of a patient after treatment with cisplatin for lung cancer. Both the clinical findings and the absence of either ocular or retrobulbar metastasis suggested that the condition was related to chemotoxicity.[2]

The mechanism of neurologic injury secondary to cisplatin has yet to be established completely. However, when 15 rats were treated with cisplatin doses comparable to those used in humans, heavily-treated animals developed axonal

degeneration in the visual system, spinal cord and peripheral nerves.[3] Neuropathologic examination of the optic disc and retrolaminar optic nerve revealed focally enlarged axons, filled with maloriented neurofilaments and degenerating organelles.

The course of the toxicity is unpredictable. Several patients had complete resolution from two days to eight months after stopping the cisplatin. Some had partial improvement. Others had a permanent or progressive deficit.

CONCLUSION

In our patient, it can be suggested that optic nerve toxicity as a result of chemotherapy could be the main cause of his rapid visual loss, with glaucoma being an important yet secondary contributing factor. It may be that the toxic effects of chemotherapy on eyes already compromised by glaucoma optic nerve axons accelerated their death resulting in rapid irreversible visual loss. Why the left eye did not follow the same devastating course (fortunately for the patient) remains to be answered.

REFERENCES

1. Urba S, Forastiere AA. Retrobulbar neuritis in a patient treated with intraarterial cisplatin for head and neck cancer. Cancer 1988;62(10):2094-7

2. Gonzalez F, Menendez D, Gomez-Ulla F. Monocular visual loss in a patient undergoing cisplatin chemotherapy. Int Ophthalmol 2001;24(6):301-4

3. Chang LW. Principles of Neurotoxicology. Informa Healthcare; 1994. p51

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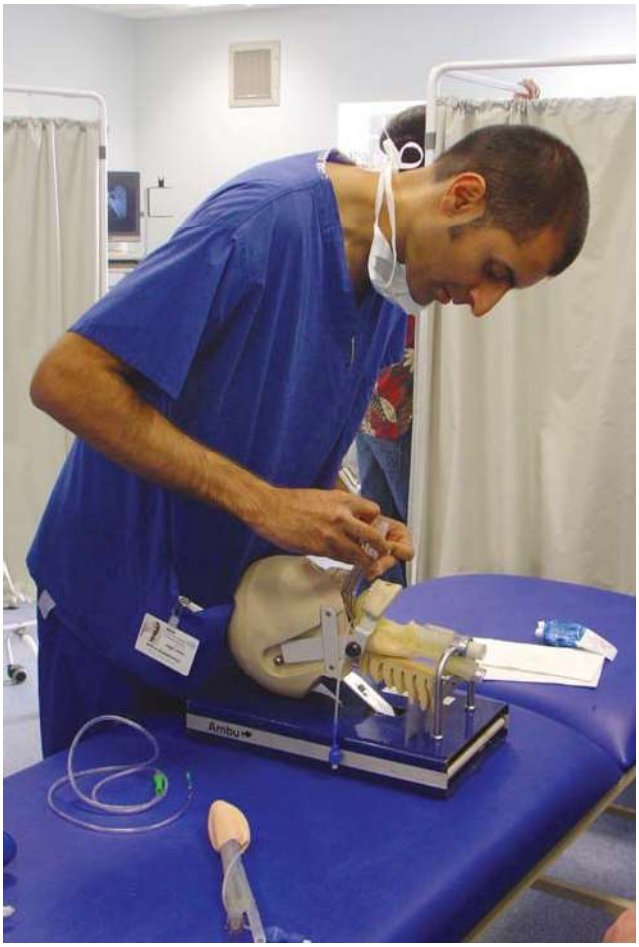

Tom Oldham, consultant anaesthetist at the Royal Lancaster Infirmary (RLI), recently held one of a series of 'Airway Skills' courses in the Education Centre, RLI, organised by Laraine Sullivan, Clinical Skills Educator. For further details of this and other courses contact:

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