Serious corneal complication of 5-fluorouracil

Marie Hickey-Dwyer, P K Wishart

The success of filtering surgery in eyes with a poor prognosis can be improved by 5-fluorouracil (5-FU). 5-FU is known to be potentially toxic to corneal epithelium and epithelial defects have been reported. It has been suggested that the doses of 5-FU originally recommended were excessive and that with lower doses corneal problems may be less common.

Case report
This case reports an adverse effect of 5-FU occurring in the left eye of an 81-year-old man who underwent a fornix based trabeculectomy to lower raised intraocular pressure uncontrolled by medical treatment. The patient had a 15 year history of open angle glaucoma, and the left eye had previously undergone an extracapsular cataract extraction (corneal section) with implantation of a posterior chamber lens. Before surgery both eyes had mild idiopathic band keratopathy (Fig 1) for several years, with intact overlying epithelium. The patient was diabetic and preoperatively he was receiving topical timolol and pilocarpine in the left eye. At surgery 0.2 ml (5 mg) of undiluted 5-FU was injected subconjunctivally in the inferior fornix with a further 5 mg of undiluted 5-FU the following day. At his first outpatient review 9 days following surgery a central corneal epithelial defect was noted and no further 5-FU was given (Fig 2).

The epithelial defect failed to heal despite topical treatment associated with padding. Because of discomfort due to the epithelial defect, a bandage contact lens was inserted into the eye 4 months later. This made the eye comfortable but no healing of the ulcer occurred. He subsequently presented with reduced visual acuity in the eye, associated with intense pain. Examination revealed the presence of a deep ulcer with a corneal abscess and hypopyon (Fig 3).

On intensive treatment with topical cefuroxime and gentamicin the infection was
Surgical complications of S-fluorouracil

Comment
5-FU is an antimetabolite which interferes with normal cell mitosis. It interferes with the S phase and the G2 phase of the cell cycle which correspond, respectively, with the synthesis of DNA and cellular components required for mitosis. As corneal epithelial cells are constantly undergoing replication they are particularly susceptible to its toxic effects.

Reduction of dosage has been suggested as a method of reducing complications including potential toxicity to corneal epithelium. However in this case minimal dosage resulted in toxicity to the cornea.

Diabetes mellitus is associated with impaired healing of corneal epithelium owing to the increased thickness of the basal lamina resulting in impaired organisation of epithelial cells and anchorage to underlying stromal collagen.

This case demonstrates that in patients with compromised corneas even judicious use of very small doses of 5-FU may result in serious corneal complications. We feel that band keratopathy is a contraindication to subconjunctival injections of 5-FU and the possible delay in healing of epithelial defects in patients with diabetes means that in such cases it should be used with extreme caution and stopped immediately if epithelial defects appear.