Interferon α 2b treatment for residual ocular surface squamous neoplasia unresponsive to excision, cryotherapy and mitomycin-C

ABSTRACT

Three patients had residual or recurrent tumour following excision of large ocular surface squamous neoplasia (OSSN) lesions, which did not resolve despite the use of adjunctive cryotherapy and topical mitomycin-C therapy. The residual tumour was treated with topical or subconjunctival injectable interferon α 2b. All three eyes had complete resolution of the OSSN lesions after an average of 6 weeks (range 4–8 weeks) of treatment with interferon α 2b. No regrowth was seen during the follow-up period of 22.7 ± 32.3 months (range 5–60 months). No adverse reactions or complaints were reported during and following interferon use, and previous symptoms from mitomycin-C treatment resolved completely. In these patients subconjunctival or topical interferon was an effective and safe treatment for residual OSSN. Longer follow up is required to confirm the long-term efficacy in prevention of recurrences.

Key words: carcinoma in situ, fluorouracil, interferon type II, mitomycin-c.

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) is the term commonly used now to describe all non-invasive and invasive squamous neoplastic lesions of the conjunctiva and cornea.

Traditionally, OSSN has been treated by surgical excision and cryotherapy. However, complete excision is difficult, and recurrence rates are high.1,2 Multiple excisions can lead to severe limbal, conjunctival and corneal scarring, resulting in low visual acuity, dry eye and limbal stem cell deficiency.1 Complications of cryotherapy include conjunctival chemosis, frozen globe, cataract, uveitis, scleral and corneal thinning and phthisis bulbi.3,4 As a result, other treatment modalities have been investigated for OSSN. Mitomycin-C (MMC) and 5-fluorouracil have been used successfully,5 and some recent reports have showed interferon α 2b (IFNα2b) to be effective as a single therapeutic agent for primary, as well as recurrent OSSN.1,4

CASE REPORT

Three patients who had undergone surgical excision, multiple cryotherapy sessions and at least 1 month of topical MMC (0.02%) treatment for OSSN, were seen at our tertiary eye care hospital between 1994 and 2004, with large residual or recurrent OSSN lesions. One patient was a man and two were women, and their age range was 52–81 years (average 69.3 years). In all the cases, a residual lesion had persisted, despite these multiple treatments, prompting IFNα2b treatment to be initiated. The complications of previous treatments are listed in Table 1. One patient received subconjunctival IFNα2b injections (Schering Plough, Kenilworth, NJ, USA) of 3 million units/mL, given every 3 days for seven doses.1 Topical IFNα2b drops were prescribed for the other two patients in a concentration of 1 million units/mL and given one drop four times daily. The topical drops were prepared by the Sydney Eye Hospital's pharmacy by dilution of the injectable recombinant IFNα2b with preservative free balanced salt solution as described elsewhere.1,6

All the patients demonstrated an impressive therapeutic effect of IFNα2b as a single agent for residual OSSN, with no adverse reactions (Table 1 and Fig. 1). The lesions resolved completely and no recurrences were seen during an average follow up of 22.7 ± 32.3 months (range 5–60 months). Patient no. 3 had severe ocular surface scarring from repeated excision and cryotherapy treatment of recurrences, resulting in a visual acuity of light perception. She did not have any adverse effects from IFN, and no further recurrences were seen up to the time of her death from lung cancer 60 months later.

DISCUSSION

Interferon α is a cytokine with pleiotropic cellular functions, including antiviral, antiproliferative, immunomodulatory, and antiangiogenic activities. In addition, IFNα therapy is being clinically evaluated for the treatment of some malignancies, including malignant melanoma, renal cell carcinoma and myeloproliferative disorders.6

Even though the exact molecular mechanism of IFNα in not known, it has been shown to inhibit directly the growth of human neuroendocrine and hepatocellular carcinoma tumour cells by specifically delaying progression through S phase and into G(2)/M.6

Topical medical treatment for ocular surface lesions has some advantages. It is focused directly on the diseased tissue, and treats the entire ocular surface, possibly decreasing the risk of recurrences. It does not damage limbal stem cells or cause any cicatricial damage, and avoids a surgical procedure4

Mitomycin-C and 5-fluorouracil eyedrops have been used successfully for treatment of OSSN, especially for recurrences following surgical excision.1 However, they should be used with caution for invasive types of OSSN, where the recurrence rates are reported to be significant.4,5 They may cause complications including dry eye, superficial punctate epitheliopathy, punctal stenosis, corneal and a scleral melt, and cataract.6 Two of our patients (cases 1 and 2) suffered a significant adverse reaction to MMC including a
Topical application of IFN has been shown to produce no discernible conjunctival or corneal abnormalities on clinical, histopathological, or ultrastructural evaluations of rabbit eyes. 

Topical IFNα2b had none of these toxic effects in our cases, and very few side-effects have been reported in previous series. However, it is known that subconjunctival and perilesional application of INF can cause systemic side-effects including myalgias and transient fevers.

In summary, IFNα2b as treatment of residual and incompletely excised OSSN may reduce the surgical morbidity, especially when multiple surgical excisions and cryotherapy sessions are necessary. This treatment should also be considered as the initial therapy for such lesions, thereby avoiding the complications seen with other treatment modalities.

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REFERENCES


Complicated hyphaema: think sickle

ABSTRACT

Two cases of complicated hyphaema associated with sickle cell trait are presented. The pathophysiology, diagnosis and management of raised intraocular pressure in sickle cell trait are discussed.

Key words: glaucoma, hyphaema, trauma, sickle cell.

INTRODUCTION

We present two cases of persistent hyphaema and raised intraocular pressure (IOP) following minor trauma, both associated with sickle cell trait. Although this is a recognized relationship, it is not commonly encountered in Australia. These cases illustrate the need to consider the haemoglobinopathies and their management in our increasingly multicultural society.

CASE REPORTS

Case 1

An 11-year-old boy of South American ethnicity presented with a left hyphaema due to a bottle cap injury. Past ocular, medical and family history was unremarkable. Presenting left visual acuity (VA) was 6/15 and IOP was 15 mmHg. Examination of the anterior segment revealed a 50% thickness corneal laceration. The anterior chamber (AC) was deep with 4+ red blood cells (RBC) and a 2-mm red blood cell (RBC) in the AC. Again, HbEPG revealed 50% Hb S. An AC washout cleared the hyphaema and his IOP readings normalized.

Postoperatively, the IOP remained less than 14 mmHg.

At the time of surgery, examination under anaesthetic (including indentation of peripheral retina) of both eyes was performed to exclude an underlying inflammatory process and blood was taken to test for coagulopathies and haemoglobinopathies. RBC count and morphology, platelet counts and clotting times were normal. However, haemoglobin electrophoresis (HbEPG) revealed 50% Hb S, consistent with a diagnosis of sickle cell trait.

Case 2

A 40-year-old man of Arabic descent presented with a 1-mm hyphaema sustained by a soccer ball injury. He too had no significant medical, ocular or family history. Presenting right VA was 6/6 and IOP 36 mmHg. The rest of his ocular examination was normal. The IOP fluctuated from 15 mmHg to 46 mmHg over the subsequent 3 weeks despite topical timolol, iopidine, latanoprost and oral acetazolamide. The hyphaema did not reduce below 0.5 mm, with 4+ RBC in the AC. Again, HbEPG revealed 50% Hb S. An AC washout cleared the hyphaema and his IOP readings normalized.

DISCUSSION

Sickle cell disease refers to a group of autosomal recessive genetic disorders characterized by the haemoglobin variant, Hb S. Individuals with sickle cell anaemia are homozygous for the beta globin variant gene. Those with sickle cell trait possess one copy of the Hb S variant and one copy of the normal beta globin (Hb A) gene. Compound heterozygous states also exist in which there is one copy of the Hb S variant and one copy of a different beta globin gene variant such as Hb C or Hb beta-thalassaemia.

Sickle cell trait is protective against malaria. It is estimated that one in 12 African Americans, one in four West Africans, one in 50 Asians and one in 100 Northern Greeks have sickle cell trait (http://www.webhealth.co.uk). In some countries the rapid Sickle-dex screen is available, but in Australia an HbEPG is required for diagnosis. It is important to note that, as with our cases, routine full blood examinations and clotting times will be normal.

Sickle cell trait is generally regarded as a carrier, rather than a disease, state. However, situations producing hypoxia, acidosis and dehydration can occasionally result in sickling and its vaso-occlusive sequelae. These include splenic infarction due to altitude hypoxia or exercise, idiopathic sudden death and exercise-induced rhabdomyolysis, heat stroke or renal failure. In the setting of traumatic