Intralesional bleomycin for the treatment of periocular capillary hemangiomas

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Periocular infantile capillary hemangiomas do not always respond well to conventional treatment modalities such as systemic or intralesional corticosteroids, radiotherapy or debulking surgery. The authors describe the use of intralesional bleomycin injections (IBIs) to treat potentially amblyogenic lesions in two cases where other modalities have failed. In both cases monthly IBIs successfully cleared the visual axis of the affected eye before the age of 1 year thus preventing permanent sensory deprivation amblyopia. A total of five and nine injections, respectively, were used and no significant side effects were noted. IBI appears to be a useful alternative in the treatment of periocular capillary hemangiomas refractory to more conventional modalities.

Key words: Bleomycin, periocular hemangiomas, treatment

Infantile periocular capillary hemangiomas have a reported incidence of 5.6% (range 0–11.8%). Sensory deprivation, astigmatism, and anisometropia contribute to the risk of developing amblyopia which is as high as 64%. By the time spontaneous involution occurs, amblyopia may be less amenable to treatment and earlier intervention is therefore often required. Conventional treatment options include oral and intralesional corticosteroids, external beam radiation, laser therapy, interferon alpha-2b and surgical excision. The use of beta-blockers has also been described recently.

We present two cases illustrating the successful use of intralesional bleomycin injection (IBI) where conventional treatment modalities have failed.

Case Reports

Institutional review board approval (IRB0005239) was obtained as well as written consent from the mothers of both patients to use photographs of their children for publication.

Case 1

A 3-month-old girl was referred to our tertiary eye clinic with a large capillary hemangioma covering her forehead, nose and the left side of her face [Fig. 1]. She could only open the left eyelids to a vertical fissure height of 1 mm but was able to fix and follow with both eyes. Ocular examination was normal.

Oral prednisone (2 mg/kg) and intralesional corticosteroid injections both failed to clear the visual axis while surgery and radiotherapy were considered inappropriate due to their unacceptable risk profile.

The successful off-label use of IBI prompted us to use a test dose for her left upper lid and, 1 month later, the left palpebral fissure had noticeably increased in size. The visible tumor was subsequently treated with monthly IBI using a dose of 0.5 mg/kg bleomycin diluted in a volume of normal saline equivalent to the estimated volume of the lesion. Treatment was discontinued after nine injections over 10 months since the final result was very satisfactory [Fig. 2].

Case 2

A 10-week-old girl was referred to our clinic with a right periocular capillary hemangioma after earlier debulking surgery had not cleared the visual axis. Examination revealed a normal left eye as well as normal anterior and posterior segments on the right with complete mechanical ptosis due to the hemangioma [Fig. 3]. Given the failure of surgical intervention, monthly IBI treatments of 0.5 mg/kg diluted in normal saline were commenced and no adverse effects related to the treatment were noted.

After five IBIs, the right marginal reflex distance matched that on the left [Fig. 4] and the patient was orthophoric with no evidence of amblyopia.

No deterioration has been noted in either patient up to 12 months after the discontinuation of treatment.

Discussion

Bleomycin was first isolated in 1966 by Umezawa from a soil fungus, Streptomyces verticillus. The main mechanism of action of bleomycin is DNA cleavage via oxidative damage caused by free radicals which form when its metal binding core is oxidized. Bleomycin also induces apoptosis in rapidly growing cells and has a sclerosing effect on the vascular endothelium which makes it useful in the proliferating phase of vascular neoplasms. Additional mechanisms include blocking the cell cycle at G2, degrading cellular RNA and the induction of tumor necrosis factor.

Many investigators have reported the successful use of IBI in treating hemangiomas and lymphangiomas in various anatomic locations. One conservative estimate indicates that 56.2% of lesions treated with IBI will undergo 70–100% regression although other reports indicate a significantly higher success rate. Basal cell carcinoma, Kaposi sarcoma, keratoacanthoma and skin metastases of malignant melanoma have also responded well to IBIs.

Based on previous publications, we used the following technique and dosages:
Figure 1: Capillary hemangioma covering the left forehead, periorcular area, nose, cheek, and upper lip as well as medial right upper lid at presentation

Figure 2: Ten months later, after nine injections of intralesional bleomycin, the left visual axis is completely cleared and all treated areas show marked improvement

Figure 3: Two months after debulking surgery, a small notch, representing inadequate clearance of the visual axis, is visible in the right upper lid

Figure 4: After five intralesional bleomycin injections, the right visual axis has been cleared completely and regression of the remaining tumor has commenced

- General anesthesia for all injections.[5]
- Dose: 0.5 mg/kg (recommended range: 0.2 to 0.9 mg/kg per injection if aged under 1 year).[1]
- Volume: the dose in milligrams calculated above is then diluted in a volume of normal saline roughly equivalent to the volume of the lesion,[5] for example, if the lesion measures 1 x 2 x 2 cm = 4 cm³, then the calculated dose is diluted in 4 ml normal saline.
- A multipuncture technique is used with a 23-gauge needle, entering through normal skin and advancing into the lesion.[5,6]
- Local pressure is applied for 10 min.[6]
- Oral analgesics are prescribed post-injection.[6]
- Review and retreatment are done every 4 weeks as needed.[6]

Pulmonary fibrosis is the most important dose-dependent complication of systemic bleomycin therapy but has not been reported after IBIs. In one study, no spill-over of bleomycin into the bloodstream could be demonstrated after IBIs which could imply that the risk of developing pulmonary fibrosis after IBIs is small.[9] Reactions that commonly occur immediately after IBIs include erythema, swelling, and pain. Bleeding, ulceration, cellulitis, eschar formation, hypopigmentation, transient alopecia and flu-like symptoms may also occur. Lymphangitis, flagellate hyperpigmentation, and Raynaud's phenomenon have been reported but are rare.[9] The side-effect profile of IBIs therefore compares favorably with that of conventional treatment modalities.

Based on our experience, we would like to suggest that IBIs also warrant consideration in the treatment of children with eyelid hemangiomas where conventional modalities have been unsuccessful or where treatment with beta-blockers may be contraindicated. This could represent a significant step forward in the management of a condition that can prove very difficult to treat.

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