

78-Treatment of Conjunctival malignancies with topical chemotherapy

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Squamous cell carcinoma and malignant melanoma are the two most common malignant tumors of the conjunctiva. Prime treatment modalities for these lesions include local excision with subsequent radiation therapy. However, recurrence of these tumors is still high, even in cases with clear surgical margins. Moreover, recurrences may be multiple, and their appearance greatly increases the risk of both local and distant metastases.

It is with these factors in mind that Edoardo Midena, MD, of Padova, Italy, sought to investigate the efficacy of 5-Fluorouracil (5-FU) and Mitomycin-C (MMC) drops for the treatment of epithelial and melanocytic conjunctival malignancies. He presented his results at the AAO meeting in San Francisco.

Both 5-FU (1%) and MMC (0.04%) were used topically in this study. These dosages were chosen based on the literature. Both drops were given QID for a 4 week period.

Because 5-FU is a pyrimidine analogue which has been used to treat many epithelial cancers, it was selected to treat conjunctival squamous cell carcinoma. 5-FU has the advantages of being low-cost, and easily handled by medical personnel.

MMC, on the other hand, is a chelating agent, which affects the cell cycle. It was thus selected to treat melanoma, which, as a slow-growing tumor, might be more

susceptible to this mode of action. MMC suffers the disadvantages of being unstable, with several serious side effect.

Scraping cytology and/or histology were used to document the original diagnosis as well as the pattern of regression. All patients were followed at six-month intervals, for a minimum of 18 months. No patient was lost to follow-up.

5-FU alone as used to treat 8 cases of conjunctival squamous cell carcinoma; of these cases, 2 were primary, 3 were recurrent, and 3 were represented previously incompletely incised lesions.

MMC was used to treat 5 cases of conjunctival melanoma; of these cases, 1 was primary, 3 were recurrent, and 1 was incompletely excised.

Seven of 8 patients treated with 5-FU for squamous cell carcinoma had stabilization or regression of their lesions. A single patients in this group had a local recurrence, which was successfully treated with another course of 5-FU. Cytologic specimens at 3 months showed replacement of previously abnormal conjunctiva with normal conjunctival cells.

Four of 5 melanoma patients treated with MMC exhibited regression of their lesions after a single one month course of MMC. In the one case where the melanoma persisted, a second one month course of MMC successfully caused regression.

Transient toxic keratoconjunctivitis was observed in all 5-FU cases acutely, and in all MMC cases both acutely and chronically. This toxicity was easily controlled with additional topical medications in all cases. No patient discontinued therapy because of this side effect.

Surgical excision alone or in conjunction with cryotherapy is insufficient to eliminate malignant conjunctival tumors. One of the major limitations of surgery to treat this entity is that clinically “clear” margins may, in fact, be infiltrated with malignant cells. Radiotherapy, while helpful in controlling recurrences, is often fraught with serious side effects.

In conclusion, topical therapy selective for neoplastic cells, such as 5-FU and MMC, may represent a new modality in the treatment of conjunctival malignancies. In Dr. Medina's view, such therapy may have the added advantage of being efficacious over a wider area, compared to either surgery or radiotherapy.

This paper was discussed by Peter R. Laibson, MD, of the Wills Eye Hospital in Philadelphia, PA. Dr. Laibson encouraged the histopathologic examination of full-thickness conjunctival specimens to make an accurate diagnosis, as well as assign a stage and grade to each lesion before treatment. This is important because, depending of the stage and grade of the tumor, different treatment modalities may be appropriate. Without such a priori analysis, it is impossible to divide out which classes of tumor respond best to topical therapy.

Epithelial scrapings alone, commonly used in Europe but not in the US, cannot accurately assess the depth of invasion of epithelial lesions of the conjunctiva. This may be a serious drawback of the current study, and of standard European pathological methodology, according to Dr. Laibson.

“Long-term” follow-up means different things when applied to different studies. As Dr. Laibson pointed out, in the case of malignant tumors, “long-term” should really include at least 2, and preferably 5 years of follow-up. Further, larger studies from multiple centers, including true long term follow-up, will be necessary to ultimately assess the efficacy of this potential therapeutic modality.