Scholars Journal of Medical Case Reports (SJMCR) **ISSN 2347-6559 (Online)**
Abbreviated Key Title: Sch. J. Med. Case Rep. **ISSN 2347-9507 (Print)**

A United of Scholars Academic and Scientific Society, India

The Association of a Perilimbic Injection of Anti-VEGF and Mitomycin C in the Treatment of Conjunctival Squamous Cell Carcinoma

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Article History
Received: 03.02.2018
Accepted: 11.02.2018
Published:20.02.2018

DOI:
10.36347/sjmcr.2018.v06i02.006

Abstract: Conjunctival Squamous Cell Carcinoma (Conjunctival SCC) and corneal intraepithelial neoplasia comprise what are called Ocular Surface Squamous Cell Neoplasias. .Conjunctival SCC is often asymptomatic at first, but it can present with the presence of a growth, red eye, pain, itching, burning, tearing, sensitivity to light, double vision, and decreased vision. Treatment of Conjunctival SCC is usually surgical excision followed by cryotherapy. Radiation treatment, topical Mitomycin C, and removal of the contents of the orbit, or exenteration, are other methods of treatment. We report this case to demonstrate the efficacy of an injection of perilimbic anti-VEGF (bevacizumab) combined with topical chemotherapy (mitomycin C) in the treatment of invasif SCC.
Keywords: Conjunctival Squamous Cell Carcinoma, Treatement, Anti-VEGF.

INTRODUCTION

Conjunctival squamous cell carcinoma (SCC) is a rare tumor, the incidence of which is evaluated from 1 to 1.9 / 100,000 [1] and typically affects caucasians in more than 90% of cases [2]. Immunosuppression (HIV, immunosuppressive therapy) and exposure to ultraviolet radiation are risk factors for this pathology [3].

It mainly concerns the perilimbic area of the conjunctiva at the level of the interpalpebral region (exposed to ultraviolet radiation) [4]. Several clinical forms are classically described: nodular, gelatinous, leukoplakia surface superficial and diffuse invasive.

Treatment options for SCC involve excision, adjuvant cryotherapy, and topical chemotherapy (interferon, mitomycin, 5-fluoracil, or cyclosporine) [5-6].

The aim of this observation is to demonstrate the efficacy of an injection of perilimbic anti-VEGF (bevacizumab) combined with topical chemotherapy (mitomycin C) in the treatment of invasif SCC.

CASE REPORT

It is about a 69 year's old aged patient, farmer by profession, monophtalmic (eye lost due to trauma in childhood). The onset of symptomatology dates back to 06 months prior to admission by the presence of a nasal conjunctival mass, gradually increasing in volume, associated with signs of ocular irritation such as tingling and foreign body sensation on the functional eye. The ophthalmologic examination finds a visual acuity at 8/10, P2. The conjunctival analysis revealed a tumoral thickening of the conjunctiva with cessation of the penetration of light and erasure of the normally visible anatomical structures. This thickening is adherent to the deep plane, namely the sclera and invading the limbus and the cornea. The rest of the ophthalmologic examination is normal (Figure 1).

An Ultrasound Biomicroscopy (UBM) was performed and confirmed the clinical data (Figure 2).

Therapeutic management consisted of surgical excision with 04 mm margins on healthy tissue, cryo-application of the tumor bed, reconstruction after changing instruments and injection of 0.1 ml of bevacizumab (25 mg / mL) in perilimbic at 1 hour quadrant of the tumor lesion.

The patient was given a 0.04% Mitomycin C eye drops to be used for 4 cycles spaced by 15 days, at a rate of 1 drop 4 times a day for one week.

The piece of surgical excision addressed to the anatomopathologist has found a malignant tumor proliferation with keratosic cells. Tumor cells are large, cytoplasms are polyhedral, nuclei are voluminous with anisocaryosis, bulky nucleoli and increased mitotic activity. The tumor was infiltrating.

Close monitoring of the patient was initiated at 1 month and then every 3 months in which, in addition to the clinical examination, a UBM is performed

During treatment with mitomycin C, the patient experienced eye irritation suppressed by artificial tears Currently, after 02 years, no recurrence has been objectified clinically or at the UBM (Figure-3-4).

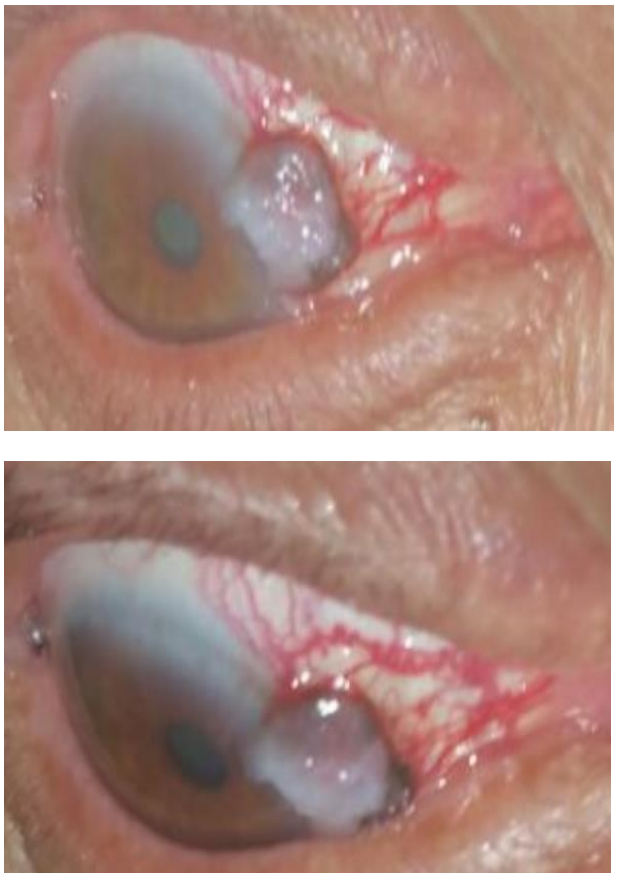


Fig-1: clinical aspect of the tumor process

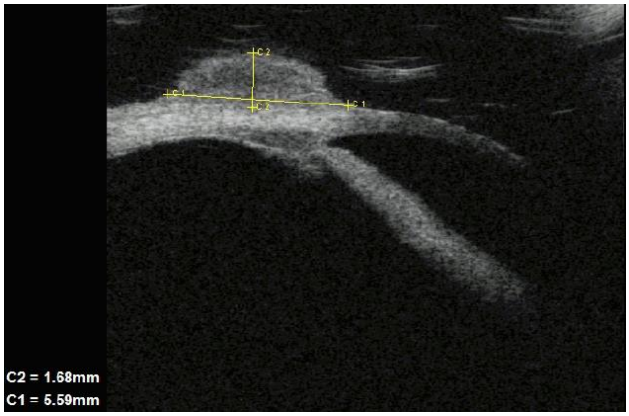


Fig-2: Nasal limbic lesional process, measuring 5.59 * 1.68 mm reaching the sclera without separation.

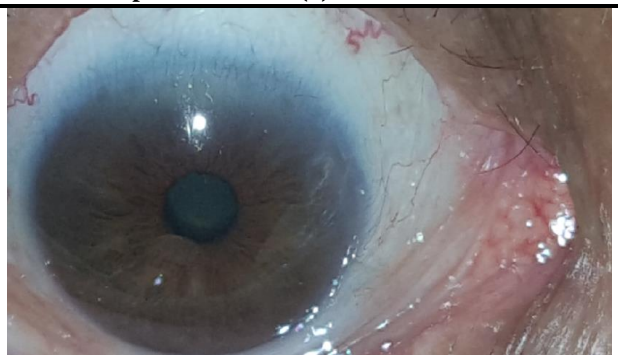
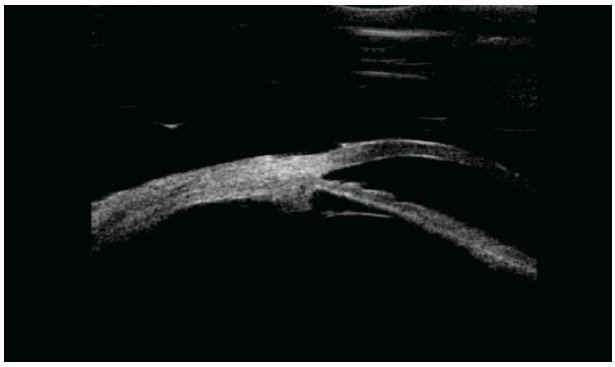
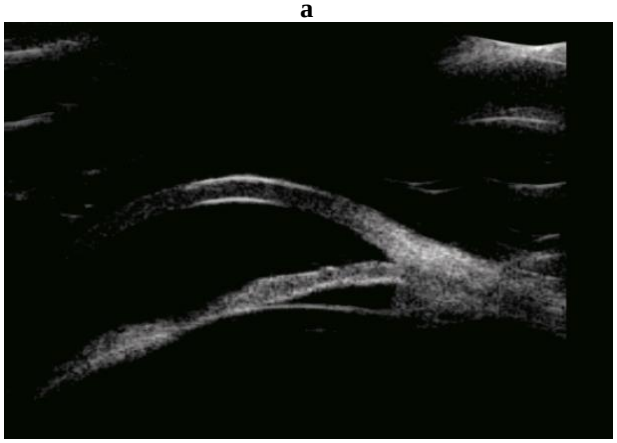


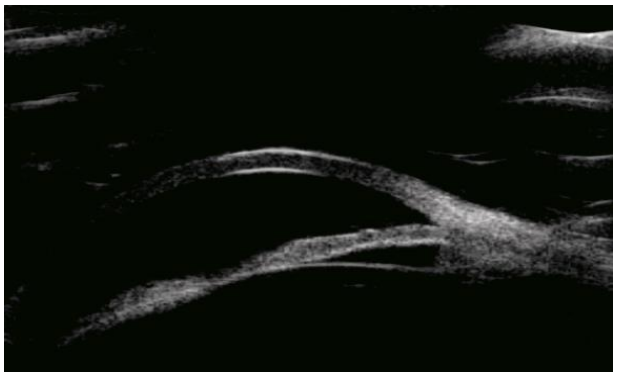
Fig-3: Clinical appearance after 18 months of treatment



a



b



c

Fig-4: The UBM control after treatment, a: 6 months/ b: 12months/ c: 18 months

DISCUSSION

Conjunctival carcinoma is included in the general clinical term of OSSN, along with the more specific histopathologic terms of CIN and SCC [7, 8]. Overall, OSSN includes a spectrum of malignancy that ranges from mild epithelial dysplastic changes (CIN) to more severe invasive carcinoma, invading through the basement membrane into the substantia propria (SCC).

Conjunctival OSSN classically occurs in older white males, particularly those exposed to years of solar radiation in activities such as golfing, fishing, boating, construction, and farming

Meta-analysis demonstrated strong association with human immunodeficiency virus (HIV) (OR, 6.2) and human papillomavirus (HPV) (OR, 2.6) [9].

Ocular surface squamous neoplasia usually presents as a unilateral vascularized gelatinous limbal mass, located in the sunexposed interpalpebral fissure medially or laterally. Other occasional features include overlying leukoplakia, tortuous dilated feeder vessels, and foamy infiltration of the adjacent corneal epithelium [10].

The clinical classification is based on tumor size (≤5 mm versus >5 mm), tumor invasiveness (in situ, substantia propria, adjacent structures, orbit, bone, sinuses, and brain). The pathology classification is based on histopathologic grade of differentiation. Our case was classified T3 NO MO G1, according to AJCC 8th Edition of Conjunctival Carcinoma (OSNN).

Although for early-stage SCC different treatment modalities including IFN α-2b, mitomycin C, and 5-fluorouracil exist, for advanced SCC the surgical treatment, including orbital exenteration remains the main option. Recurrences after surgical treatment of SCC are frequent [11-12].

However, depending on the study, the rate of recurrence differs between 5 and 56%, with variable follow-up times.

In our case, given that the patient is monophthalmic, we opted for a conservative treatment despite the tumor is invasive. It is considered that the association of an injection of Bevacizumab in perilimbic at a distance from the tumor bed contributes to reducing the risk of recurrence.

Bevacizumab is a vascular endothelial growth factor inhibitor and has been used as an effective adjuvant therapy for many types of advanced and recurrent tumors.

CONCLUSION

In summary, intraoperative perilimbic injection of bevacizumab can be an effective and safe adjuvant therapy for treatment of conjonctival squamous cell carcinoma.

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