

## CASE REPORT

# Squamous carcinoma of the conjunctiva

MIHAELA CRISTIANA COROI<sup>1)</sup>, ELENA ROȘCA<sup>2)</sup>, GABRIELA MUȚIU<sup>3)</sup>,  
T. COROI<sup>4)</sup>

<sup>1)</sup>Department of Ophthalmology

<sup>2)</sup>Department of Pathology

<sup>3)</sup>Department of Histology

Faculty of Medicine and Pharmacy, University of Oradea

<sup>4)</sup>"Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca

### Abstract

We present the case of a 63-year-old patient who was hospitalized for pain and loss of vision in the right eye (RE). Clinical examination reveals a conjunctival tumor of 1.5/1 cm infiltrating the cornea and sclera. Biopsy and histopathological examination showed the existence of a spinocellular carcinoma.

**Keywords:** conjunctiva, spinocellular carcinoma, immunohistochemistry (AE1/3, CK7, CK20, EGFR, VIM).

### Introduction

Conjunctival epithelial carcinomas are rare tumors, most commonly located in the corneal limbus where there is transitional-type epithelium. Among known risk factors, prolonged exposure to sunlight is the most important [1]. Histologic examination establishes the diagnosis and evaluates the depth of invasion and the histological grading – important elements for prognosis.

Malignant tumors of the conjunctiva are rare. Carcinomas of the conjunctiva are the most frequent malignant tumors of the ocular surface [2]. The highest incidence is in men between 50–75-year-old. The incidence is 0.13–1.9 per 100 000 inhabitants [3]. Conjunctival carcinoma may develop on lesions such as leukoplakia, intraepithelial carcinoma (Bowen's disease), and chronic trauma of a papilloma with dysplasia. Other incriminated factors are vitamin A deficiency, chronic infections as trachoma, HPV, chronic irritations with dust or other factors [4].

Any lesion of the conjunctiva requires a differential diagnosis between benign and malignant diseases; every clinical aspect should always be completed with histopathologic examination [5].

Spinocellular carcinomas that develop on the epibulbar conjunctiva, in the palpebral fissure, tend to invade the corneal limbus and the corneal stroma [6]. Spinocellular carcinomas are 10 times more frequent than the basal-cell carcinomas.

Gross anatomy of the conjunctival carcinomas may present various aspects:

- papillomatous degenerated aspect with a diameter of 2–3 mm;
- sessile tumor, irregular surface, polylobated, friable, sometimes hemorrhagic, ulcerated;
- basocellular carcinomas that are always flat.

The microscopic examination shows the classic appearance of the spinocellular carcinomas. In a fibrous

connective stroma there are islets of carcinomatous cells of squamous type, with different degrees of differentiation: well, moderate and low. Carcinomatous cells are large, highly eosinophilic, and have anisokaric nuclei. The presence of intracytoplasmatic keratinisation or keratotic pearls indicates the degree of differentiation. Low-differentiated forms show a more aggressive evolution compared to the well-differentiated forms. Basocellular carcinomas, with a lower incidence in the conjunctiva, are flat tumors composed of islets of basaloid cells (small cells with reduced cytoplasm, tachychromatic basophilic nuclei with anisocytosis and less anisokaria). Immunohistochemical techniques are useful for the differential diagnosis between carcinomas, sarcomas and between different types of carcinomas. The presence of Ki67 cellular proliferation factor is of prognostic importance. The evolution of the conjunctival carcinoma is progressive and may invade the sclera, the eyeball, regional lymph nodes, and may spread to the lungs or brain. The usual treatment is surgical resection followed by cryotherapy and, if necessary, enucleation. Squamous neoplasia of the conjunctiva depends upon the local, regional and general extension of the malignancy. Frequent relapses impose long-term follow-up. In general, the management is based on surgical resection and cryotherapy. The high rate of recurrence is due to a failed surgical clearance. Some authors administered chemotherapy with or without Mitomycin C [7] or 5-Fluorouracyl, but with severe side effects for the ocular surface. Studies were performed using interferon alfa-2b in topic administration, with high efficiency and with no side effects for the ocular surface [8].

Good results were also obtained by Barzetto IA *et al.* [9] when using dynamic phototherapy, less aggressive for the surrounding tissues. A new therapeutic method is represented by the surgical removal and proton therapy [10] for recurrent or invasive carcinomas.

## ☐ Patient, Methods and Results

The patient was admitted in the Ophthalmology Clinic of the Emergency County Hospital of Oradea, in 2008. He was complaining of eye-pain and loss of vision in the right eye. There are no ophthalmologic antecedents except an appendectomy and a right shoulder dislocation.

In the clinical examination of the right eye (RE), the anterior pole examination revealed a conjunctival tumor located temporally, invading the cornea at the limbus, vascularized, 1.5 cm in diameter, adherent to the sclera (Figure 1).



**Figure 1 – Gross aspect of the tumor: ulcerated and infiltrative aspect with eyeball invasion.**

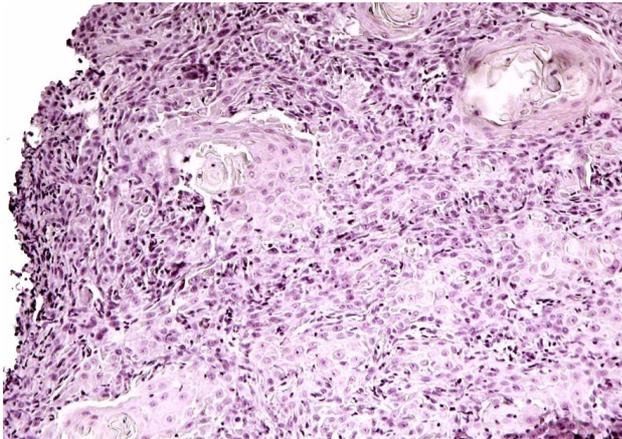
The cornea was thinned in the invaded area. The iris and the pupil revealed a posterior synechia. The intraocular pressure of the RE was 38 mmHg. The dilated fundus examination revealed a dark fundus. In the left eye (LE) examination, the anterior pole

examination revealed the opacification of the crystalline and the dilated fundus examination revealed retinian angiosclerosis. The CT examination did not reveal any tumor extension. There was a slight thickening of the sclera. Laboratory data were within the normal range except the erythrocyte sedimentation rate (ESR): 8 mm at 1 hour, 20 mm at 2 hours. After local instillations with mydriatics, the pupil dilated irregularly with numerous posterior synechia. After local and general antibiotic and anti-inflammatory treatment a biopsy was performed.

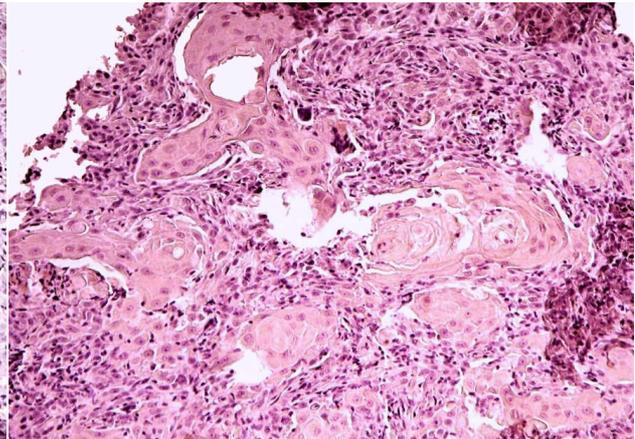
Histopathologic examination of the conjunctival tissue biopsy showed a rich fibroblastic chorion with small islets of tumor squamous cells with keratotic pearls. The diagnosis was well-differentiated squamous carcinoma of spinocellular type (Figures 2 and 3).

Immunohistochemical examination revealed the positivity for AE1/3 (anti-cytokeratin monoclonal antibodies) (Figure 4), EGFR (epidermal growth factor receptor) (Figure 5) and the negativity for CK7 (cytokeratin 7) (Figure 6), CK20 (cytokeratin 20) and Vimentin (Figure 7), confirming once again the squamous spinocellular carcinoma.

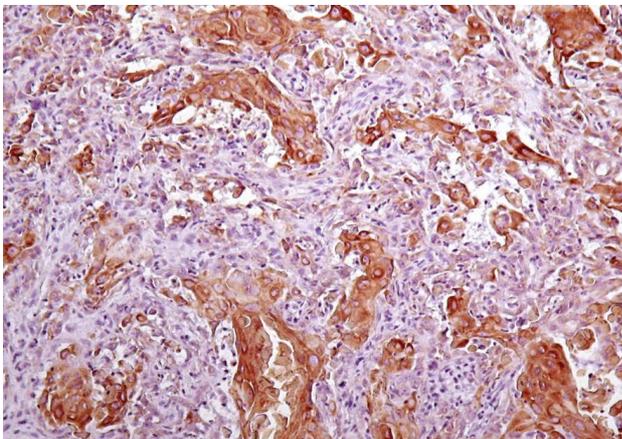
An enucleation was performed. The histopathologic examination of the surgical sample confirmed the previous diagnosis.



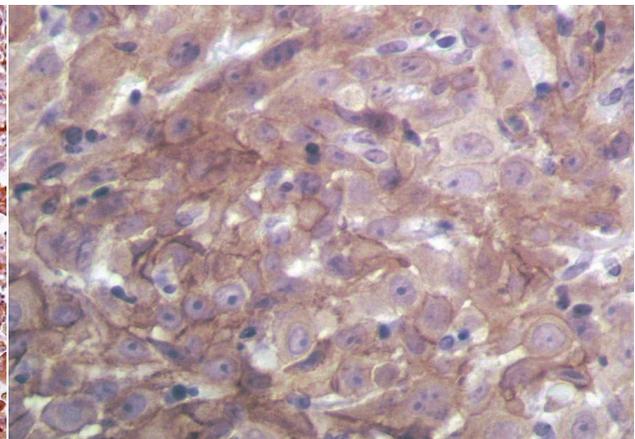
**Figure 2 – Carcinomatous cell islets of squamous type with keratotic pearls and intracytoplasmic keratinisation (HE stain, ob.  $\times 10$ ).**



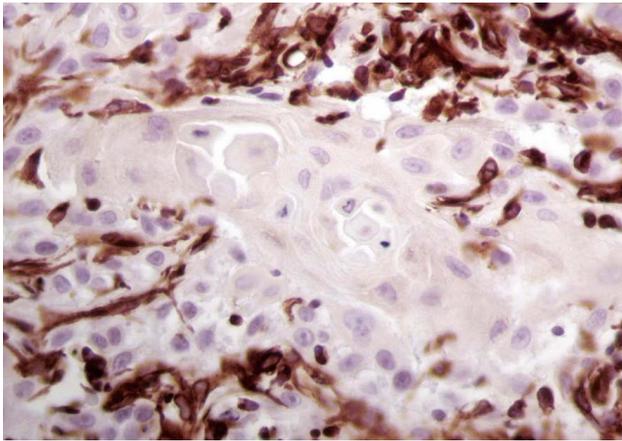
**Figure 3 – Carcinomatous cell islets of squamous type with keratotic pearls (HE stain, ob.  $\times 10$ ).**



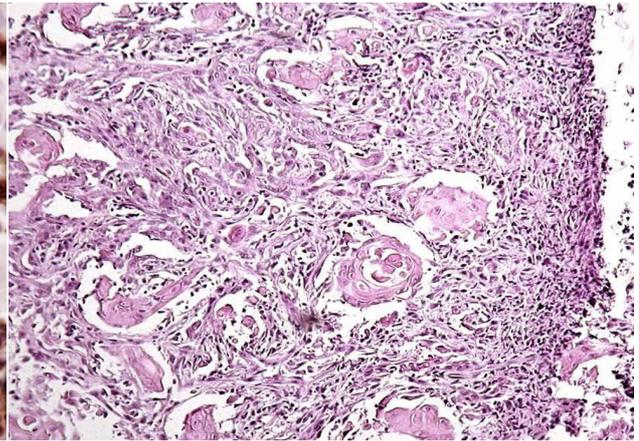
**Figure 4 – Pancytokeratin-positive carcinomatous cells (IHC, ob.  $\times 10$ ).**



**Figure 5 – EGFR positivity of malignant cells (for differentiation from basal-cell carcinoma) (IHC, ob.  $\times 40$ ).**



**Figure 6** – *Vimentin-negative carcinomatous cells and positive stroma (IHC, ob.  $\times 40$ ).*



**Figure 7** – *Carcinomatous cells negative for CK7 (IHC, ob.  $\times 10$ ).*

### Discussion

Immunostaining enhances the accuracy of the histopathologic diagnosis in the case of malignant tumors. Positivity for pan-cytokeratin directs the diagnosis towards the carcinomatous origin of the tumor. In our case, the immunomarking for vimentin is negative in epithelial cells and positive in stromal structures. The absence of immunostaining for CK7 and CK20 is a clue in favor of the squamous origin of the malignant tumor. The differentiation from other types of carcinoma (basal-cell carcinoma) is made by the membrane positivity for EGFR. The postoperative course was uneventful. A year after enucleation, the orbit showed a normal clinical aspect. Our case had only one therapeutic option – enucleation. The neoplastic lesion invaded the corneal limbus as shown in Figures 3 and 4. Moreover, a secondary glaucoma was developing. We considered that the enucleation, although a maiming intervention, hardly accepted by the patient, was the only therapeutic option able to improve the vital prognosis. In case of exeresis, oncologic security margins would have been difficult to achieve, with risk for recurrence and prolonged illness for the patient. In current medical practice, the diagnosis of carcinoma, either conjunctival or any other, is made using usual staining techniques (Hematoxylin–Eosin, Van Gieson, reticulin). At the present, immunohistochemistry implies supplementary costs and is used exceptionally for the differential diagnosis and for the diagnosis of low differentiated types.

### Conclusions

Conjunctival carcinomas, although rare, have a high potential for recurrence and, if not operated in the early stages, might lead to enucleation or exenteration.

### Corresponding author

Mihaela Cristiana Coroi, Associate Professor, MD, PhD, Department of Ophthalmology, Faculty of Medicine and Pharmacy, University of Oradea, 23 Republicii Street, Ap. 5, 410032 Oradea, Romania; e-mail: optictlar@gmail.com

Early diagnosis is followed by surgery and adjuvant treatments as cryotherapy, local chemotherapy or radiotherapy. The aim is to avoid the loss of the eyeball. Increased awareness of the population to the risk factors, especially the protection from the ultraviolet radiation, is a desideratum, besides the education for early presentation in case of the slightest sign of disease.

### References

- [1] ACIS D, DONNIO A, AYÉBOUA L, RICHER R, GUYOMARCH J, WARTER A, MERLE H, *Conjunctival squamous cell carcinoma. Four cases reported in the French West Indies*, J Fr Ophtalmol, 31(5):533.e1–5.
- [2] GROSSNIKLAUS HE, GREEN WR, LUCKENBACH M, CHAN CC, *Conjunctival lesions in adults. A clinical and histopathologic review*, Cornea, 1987, 6(2):78–116.
- [3] LEE GA, HIRST LW, *Ocular surface squamous neoplasia*, Surv Ophthalmol, 1995, 39(6):429–450.
- [4] TULVATANA W, TIRAKUNWICHCHA S, *Multifocal squamous cell carcinoma of the conjunctiva with intraocular penetration in a patient with AIDS*, Cornea, 2006, 25(6):745–747.
- [5] ERIE JC, CAMPBELL RJ, LEISEGANG TJ, *Conjunctival and corneal intraepithelial and invasive neoplasia*, Ophthalmology, 1986, 93(2):176–183.
- [6] SHIELDS CL, SHIELDS JA, *Tumors of the conjunctiva and cornea*, Surv Ophthalmol, 2004, 49(1):3–24.
- [7] GUTHOFF R, LIEB WE, STRÖBEL P, ZETTL A, *Exenteration of invasive conjunctival squamous cell carcinoma*, Br J Ophthalmol, 2004, 88(8):1093–1094.
- [8] HUERVA V, MANGUES I, *Treatment of conjunctival squamous neoplasias with interferon alpha 2b*, J Fr Ophtalmol, 2008, 31(3):317–325.
- [9] BARZETTO IA, LEE TC, ABRANSON DH, *Treatment of conjunctival squamous cell carcinoma with photodynamic therapy*, Am J Ophthalmol, 2004, 138(2):183–189.
- [10] CAUJOLLE JP, MASCHI C, CHAUVEL P, HERAULT J, GASTAUD P, *Surgery and additional protontherapy for treatment of invasive and recurrent squamous cell carcinomas: technique and preliminary results*, J Fr Ophtalmol, 2009, 32(10):707–714.