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# The clinical presentation and treatment of an invasive conjunctival squamous spindle cell carcinoma

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## Abstract:

Ocular surface squamous neoplasia represents neoplastic epithelial abnormalities of conjunctiva and cornea, ranging from squamous dysplasia to invasive squamous cell carcinoma and is both sight- and life-threatening. Squamous spindle cell carcinoma (SSCC) of conjunctiva is a rare variant with distinct behavior which is thought to be more locally aggressive. We describe an 83-year-old woman with a progressively enlarging huge SSCC in her right eye over the past 2 years. The tumor bulged out with local invasion into intraocular and orbital cavities. Wide excision of the tumor with frozen section control was performed. After surgery, topical 0.03% mitomycin C was given as adjuvant therapy. At 40-month follow-up, the lesion site showed no evidence of local recurrence. This case provides a valuable and complete experience of the clinical presentation for the progression and treatment of this rare disease.

## Keywords:

Conjunctival neoplasms, conjunctival spindle cell carcinoma, ocular surface squamous neoplasia, squamous cell carcinoma

## Introduction

Conjunctival squamous cell carcinoma (CSCC) is a rare ocular surface tumor of epithelial malignancy and accounts for the incidence rate ranging from 0.02 to 3.5 per 100,000 population with racial and geographical variations.<sup>[1,2]</sup> It is predominant among males and the elderly and mainly occurs in the limbus.<sup>[2]</sup> Increasing incidence and aggressiveness of CSCC have been recognized among patients in the tropical regions due to environmental factors, such as solar ultraviolet light exposure.<sup>[3]</sup>

CSCC is generally considered as a nonaggressive malignancy; however, it could be sight- and life-threatening because of its high recurrence rate and potential to invade into intraocular structures,

sclera and orbit. Some patients may even die of metastatic diseases.<sup>[2,3]</sup> Intraocular and orbital invasion had been reported in 2%–15% and in 12%–16% of squamous cell carcinoma, respectively.<sup>[1]</sup> Erie *et al.* suggested that the lesion involving the cornea might be indicative of aggressiveness of the lesion.<sup>[4]</sup>

Histological variants of CSCC are few and squamous spindle cell carcinoma (SSCC) is one of the rare but more aggressive variants that behaves distinctly different from ordinary spindle cell carcinoma (SCC).<sup>[5]</sup> Cervantes had reviewed 287 cases (286 patients) of CSCC. Typical keratinized squamous cell carcinoma of the conjunctiva accounted for 98%, and other variant lesions were identified by histology as lymphoepithelioma-like carcinoma (3 cases), SCC (2 cases) and mucoepidermoid carcinoma (1 case).<sup>[6]</sup>

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There was no much experience published previously in the treatment of the variant-type tumor. We herein described the clinical characteristics, disease process, and histopathology of a rare locally aggressive SSCC with both intraocular and orbital invasion.

### Case Report

An 83-year-old woman presented with a giant pterygium over the nasal side of right eye for many years. Since her first visit to our oculoplastic department, the lesion had grown progressively into a giant mass rising from the nasal and upper limbus in her right eye over the past 1 year [Figure 1a]. The best-corrected visual acuity was only 2/200. Surgical excision was recommended. However, the patient declined and received no further treatment due to poor family support. One year later, she came back with an overhanging huge mass [measuring size: 7 cm × 4.5 cm × 1.2 cm, Figure 1b] protruding directly from the palpebral fissure. The tumor had increased gradually and painlessly in size with oozing discharge and foul smell over the past 1 year. It concealed the entire eye and blocked vision completely. The posterior limit of the mass was not palpable or visible. SCC was identified from a small piece of biopsy by the histopathological examination.

Contrast-enhanced computed tomography (CT) scan including orbit, head, and neck disclosed a giant well-defined, homogenous, iso-dense tumor bulging out from the limbus with local invasion into intraocular and inferior nasal orbital cavities [Figure 2a]. There was no evidence of bony erosion or tumor invasion into the paranasal sinuses. Physical examination findings of primary site as well as regional preauricular and submandibular lymph nodes were compatible with results from CT scan. Systemic evaluation including chest X-ray, abdominal, and renal ultrasound examination revealed no other distal metastasis.

Removal of the tumor was performed in a two-step procedure instead of an *en bloc* excision because the large volume obscured the eye surface. After the middle stalk of the huge tumor was tied, the protruding mass was then resected [Figure 3]. The second step followed by lid-sparing anterior orbital semi-exenteration [Figure 1c].

The medial side of the lower and upper eyelids was incised from the tarsus along a tumor-free margin, ranging from 0.1 cm (medial side) to 0.3 cm (margins except medial side), to the lateral side for preservation of the anterior lamella. Insertion sites of the anterior part of the medial and superior rectus muscles, as well as the soft-tissue deep to the medial wall periosteum, were removed. The 14-mm silicon sphere implanted was covered by the inferior and lateral rectus muscles alongside the residual tenon and conjunctival tissue [Figure 2b]. The anterior lamella of the upper and lower eyelids was finally closed by tarsorrhaphy.

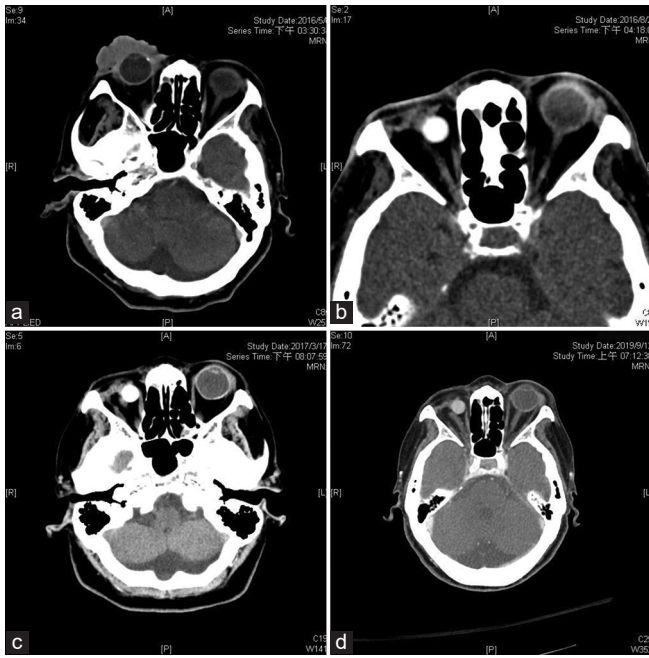
Histopathology of the specimen revealed intraocular infiltration of pleomorphic and spindle-shaped tumor cells intermixed with abundant inflammatory cells in storiform pattern. Immunohistochemical stains demonstrated positive staining for vimentin, AE1/AE3, p63, and focally SMA [Figure 4], but negative staining for S100, CD31, HMB45, ALK-1, desmin, p40, and CD21. Taken together, these findings confirmed the diagnosis of "SSCC". Lymphatic system metastasis was highly suspected according to the finding from the CT scan and physical examination. However, the patient refused lymph node biopsy. According to the 7<sup>th</sup> edition of the American Joint Committee on Cancer (AJCC) classification (AJCC 7<sup>th</sup>), the cancer stage should be pT4aNxM0 which was compatible with results from the CT scan showing the tumor invading the orbit soft tissue but without bone invasion. Although we strongly recommended the need for further management of the regional preauricular and submandibular lymph nodes, the patient refused treatment and follow-up.

Topical chemotherapy with mitomycin C (MMC) (0.03%) four times daily was used as postoperative adjuvant therapy for 4 weeks. There was no local recurrence in the orbital cavity on CT images or clinical finding during the 10- or 40-month follow-up after treatment [Figure 2c and d]. Forty months later, the patient came back to the emergency department because of acute respiratory distress. A large neck mass had compromised her airway [Figure 5a]. The enlarged submandibular and cervical lymph nodes were suspected to be SSCC metastases based on the last CT scan, although there was no pathological confirmation [Figure 5b and c]. Despite tracheostomy, she unfortunately died of respiratory failure 2 months later.

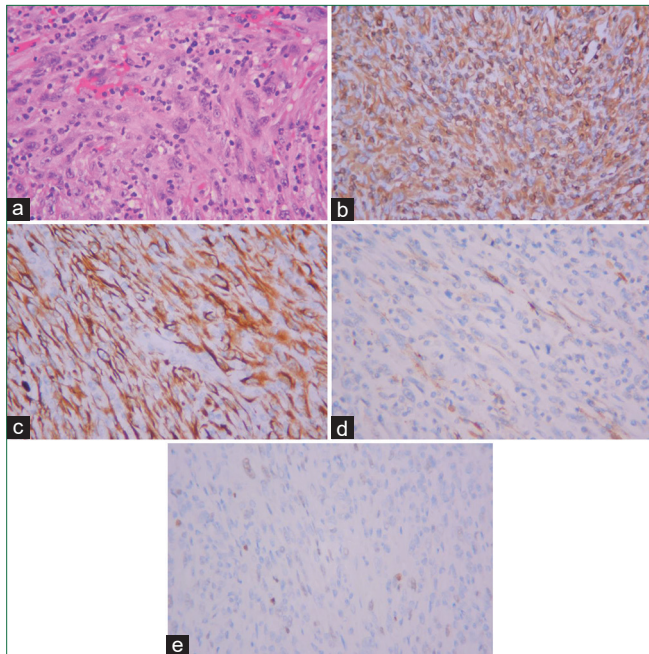


**Figure 1:** (a) A vascularized huge mass rising from the limbus of the right eye with superior-nasal conjunctiva and cornea extension was obviously presented initially. Underlying pterygium-like lesion was also noted. (b) One year later, this tumor enlarged and was hanging from the eye, obscuring almost the entire eye surface. (c) Postoperative appearance of the orbit.





**Figure 2:** The orbital computed tomography scan. (a) Preoperative image. A huge tumor in front of muscle insertions from the equator of eyeball. (b) Postoperative image at 3 months. The silicon implant with some granulation tissue. (c) Postoperative image at 10 months. (d) Postoperative image at 40 months. The computed tomography images and pathological biopsy from granulation tissue proved no evidence of recurrence



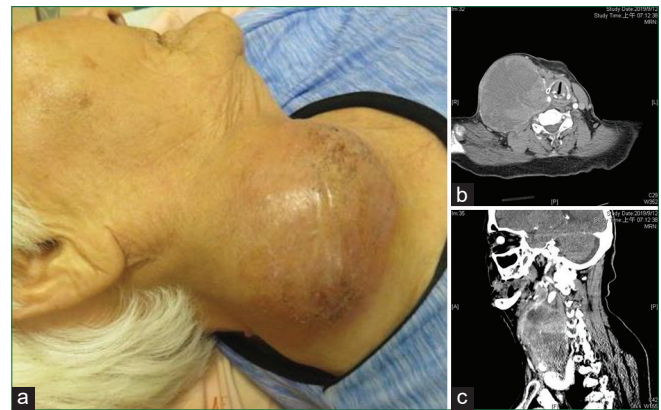
**Figure 4:** (a) The histopathologic appearance of malignant spindle-shaped cells (H and E,  $\times 400$ ). (b) Vimentin (diffuse area) stain. (c) AE1/AE3 (diffuse area) stain. (d) p63 (scattered area) stain. (e) Smooth muscle actin (focal area) stain

## Discussion

Complete surgical excision with 4-mm margin clearance without touching the tumor, known as the “no-touch technique,” combined with or without cryotherapy



**Figure 3:** The major portion and eyeball part occupied with malignancy after en-bloc tumor excision combined with lid-sparing semi-exenteration



**Figure 5:** (a) An huge mass on the right side of the neck. (b) The axial view of the head and neck computed tomography scan. An enlarged lymph node with tracheal compression. (c) The sagittal view of the head and neck computed tomography scan

remains the widely accepted treatment strategy for CSCC.<sup>[1]</sup> Radiotherapy, surgical excision in combination with absolute alcohol, Vitamin A, excimer laser, and adjuvant topical or perilesional chemotherapy are other treatment options with favorable outcomes.<sup>[7]</sup> In cases with positive margins related to inadequate surgical excision, higher recurrence and more local invasion had been demonstrated.<sup>[8]</sup> The rate of recurrences after surgical treatment of advanced SCC varies from 5% to 56% depending on different treatments.<sup>[4,9]</sup> Furthermore, a retrospective study from a German institution reported 20% of recurrences of the disease even in patients receiving orbital exenteration.<sup>[10]</sup> For patients with extensive or recurrent tumors, treatment with topical MMC, 5-fluorouracil, or interferon  $\alpha$  and interferon 2b may be employed.<sup>[7]</sup>

SSCC is thought of as a poorly differentiated and more aggressive variant of squamous cell carcinoma. Mortality from metastatic lung disease had been reported by Seregard and Kock and Alkatan *et al.*<sup>[5,11]</sup> In the present case of a rare, presumably more aggressive SSCC

accompanied with both intraocular and intraorbital invasion, MMC was used as an adjuvant therapy with lesion soaking after tumor excision during surgery and topical eye drops was administered at clinical follow-up. Topical MMC has been documented effective without significant adverse effects.

Systematic reviews and meta-analyses had reported main risk factors including solar ultraviolet radiation, smoking, human immunodeficiency virus and human papilloma virus. Vitamin A deficiency is also considered a potential risk factor but has not been investigated.<sup>[3]</sup> Our case is a farmer and her husband has long-term smoking history, both of which should be possible risk factors leading to tumor formation. Moreover, significant increase in risk of recurrent tumor or large diameter and high proliferation index of the tumor had been observed among the elderly.<sup>[12]</sup>

The patient declined surgical resection of the tumor at her first visit probably because of fear and insufficient family support. The delay in the prompt management of such malignant tumor led to extensive spread and cosmetic disfigurement. Although CSCC is of low-grade malignancy, it has high recurrence rate. The 5 and 10-year overall survival estimates were 70% and 50% respectively.<sup>[13]</sup> For recurrence after 5 years, the survival rate decreased to 11% and the metastasis rate was 14%.<sup>[14]</sup> Few mortality had been reported in the literature and most causes of death were diffuse metastases.<sup>[2,3,5,11]</sup> We found that the patient's disease progression was consistent with previously published schema: Intraocular and intraorbital invasion and lymph nodes metastasis. We speculated that some mechanisms were involved in the change of tumor malignancy, namely older age, the original tumor cell type without transformation, and spindle cell transforming from original squamous cell as disease progression.

Ocular surface squamous neoplasia is a distinct condition of the ocular surface that can be treated successfully with miscellaneous modalities. No single treatment option has been shown to superior and combination therapy may be necessary in some cases to achieve a favorable outcome. The experience in the management of SSCC is rare, especially in local invasion or metastasis. The present case provided a valuable opportunity to understand the overall natural course of the disease.

### Human subjects

This study includes human subject/tissues. Study protocol was approved by the Chang Gung Memorial Hospital Institutional Review Board, Taiwan (IRB: 201900637B0).

### Declaration of patient consent

The authors certify that they have obtained all appropriate

patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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