

# Conjunctival keratoacanthoma

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**ABSTRACT.** Keratoacanthoma is a rapidly growing skin neoplasia that may stabilize or regress spontaneously. We describe here a case of conjunctival keratoacanthoma and comment about the clinical signs and symptoms and pathological findings.

**Key words:** conjunctival keratoacanthoma - conjunctival tumor - histopathology (conjunctival keratoacanthoma) - immunohistochemistry (conjunctival keratoacanthoma).

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Keratoacanthoma is a skin neoplasia characterized by rapid growth (6 to 8 weeks) which may stabilize and eventually regress within approximately 6 months. The histopathological alterations, although quite characteristic, may occasionally be difficult to differentiate from those of spinocellular carcinoma.

In 1889, Hutchinson described conjunctival keratoacanthoma as a 'crateriform ulcer of the face' and considered it to be a form of 'acute epithelial cancer'. MacCormac & Scarff (1936) reported the characteristic rapid growth of the tumor, followed by spontaneous regression.

Keratoacanthoma is relatively common on the skin and may rarely involve the mucosae. Only 8 cases of conjunctival keratoacanthoma have been reported in the literature (Table 1). We report here a case of conjunctival keratoacanthoma and comment on the clinical and patho-anatomic findings obtained.

## Case Report

BAB, a 28-year old mulatto housewife, sought the University Hospital of the Faculty of Medicine of Botucatu, UNESP, complaining of a foreign body sensation, hyperemia and the appearance of a nodule in the left eye 30 days before. The lesion appeared suddenly and grew rapidly (Fig. 1).

Biomicroscopic examination revealed the presence of a nodular, perilimbal,

nasal lesion approximately 0.7 cm in diameter, surrounded with dilated and tortuous vessels. The lesion had raised borders and a depressed crater-like center whose central area was filled with pearly white material. Dellen was present on the cornea adjacent to the tumor. The lesion did not adhere to the underlying sclera.

The clinical diagnosis was conjunctival spinocellular carcinoma and the lesion was removed with a safety margin.

Histopathological examination revealed a cutaneous neoplasia characterized by well circumscribed solid proliferation of squamous cells, with a central 'crater' filled with keratin lamellae (Fig. 2). At the base of the tumor there was an intense inflammatory infiltrate of a lichenoid lympho-histiocytic pattern, as well as areas with neutrophil and eosinophil microabscesses surrounding blocks

of squamous cells localized in the subepithelial region (Fig. 3).

Immunohistochemical study of the neoplasia showed positivity to a carcinoembryonic antigen (CEA) and cytokeratins, mainly in the central part of the lesion and in the corneal pearls. Protein S-100 was negative in the neoplastic cells. In situ hybridization studies, using biotinylated probes as described elsewhere (Beckmann et al. 1985), were performed in order to investigate the possibility of human papilloma virus (HPV) being involved in the pathogenesis of keratoacanthoma. All sub-types of HPV, namely HPV 6, 11, 16, 18, 30 and 31 were not present in the nuclei of the keratoacanthoma.

One year after surgery the patient shows no signs of recurrence.

## Discussion

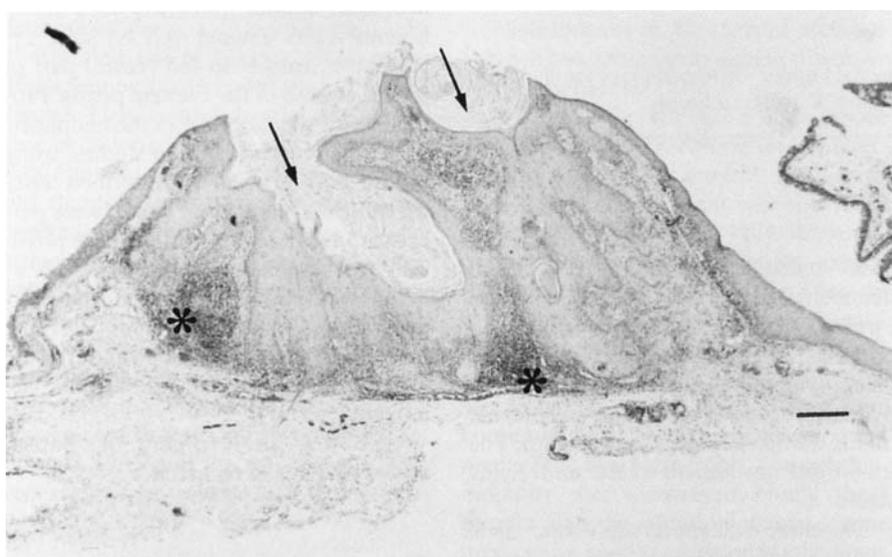
Keratoacanthoma characteristically occurs on the skin and is rare in the mucosae. The first case of conjunctival keratoacanthoma was reported by Freeman et al. (1961). Seven additional cases have been reported since, and the present patient is the 9th (Table 1).

The age range of higher incidence of skin keratoacanthoma is 58 to 92 years (Blessing et al. 1994). In contrast, con-

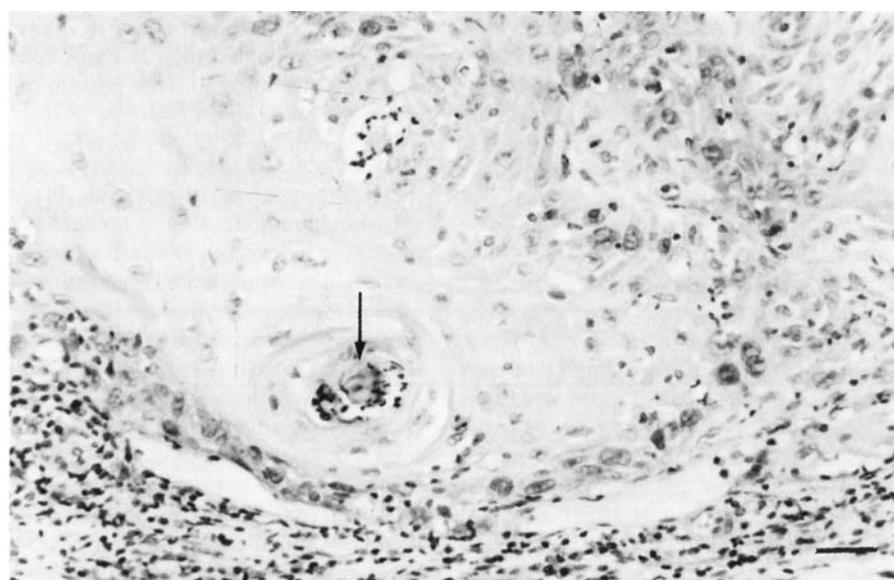
**Table 1.** Review of the conjunctival keratoacanthoma cases.

Authors	Age (years)	Sex	Race	Eye	Anatomic place
Freeman et al. (1961)	55	Male	White	right	Temporal limbus
Bellamy et al. (1963)	28	Male	White	left	Nasal limbus
Bellomio (1970)	41	Male	-	left	Nasal limbus
Roth (1978)	26	Female	White	right	Temporal limbus
	37	Male	White	left	Temporal limbus
Hamed et al. (1988)	49	Male	White	right	Temporal limbus
	40	Male	White	right	Temporal limbus
Grossniklaus et al. (1990)	65	Male	-	left	Temporal limbus
Munro et al. (1993)	42	Male	-	left	Temporal limbus
Schellini et al. (1996)	28	Female	Mulatto	left	Nasal limbus

**Fig. 1.** Conjunctival keratoacanthoma of left eye shows nodular, elevated, white conjunctival mass located at the perilimbic nasal and surrounded by dilated blood vessels.



**Fig. 2.** Section of conjunctival tumor showing proliferation of the stratified squamous epithelium with central 'crater' filled with keratin lamellae (arrow). Intense inflammatory infiltrate at the base of tumor (\*). (hematoxylin and eosin). Bar represents 200  $\mu$ m.



**Fig. 3.** Higher power view of aspect of specimen shows eosinophilic glassy-appearing cytoplasm with extracellular keratin deposition (arrow). Inflammatory cells surrounding squamous cells in stroma (hematoxylin and eosin). Bar represents 50  $\mu$ m.

junctival keratoacanthoma occurs in younger individuals aged 26 to 65 years (Table 1). Males predominate, with only 2 women having been reported thus far, i.e., the case reported by Roth (1978) and the present one. The predominance of males may be linked to the type of activity carried out by males, with greater chance of exposure to etiological factors. The condition predominates among white individuals and is rare among dark-skinned persons (Julie et al. 1984; Schwartz 1994).

As characteristically observed in keratoacanthomas, the conjunctival lesion grew rapidly in all cases described (2 to 8 weeks). Important complaints caused by conjunctival keratoacanthoma are a sensation of foreign body, hyperemia, ocular secretion and the appearance of a conjunctival nodule. In all conjunctival keratoacanthoma cases reported, the presence of dilated and tortuous perilesional vessels as well as corneal Dellen was frequent.

In all patients, keratoacanthoma occurred on the bulbar conjunctiva. In the skin, the lesion is considered to originate from hair follicles. However, in the bulbar conjunctiva, where there are no hair follicles, the tumor is assumed to originate from ectopic sebaceous glands (Guiducci & Hyman 1962). Conjunctival keratoacanthoma preferentially occurs in the limbic region, a place of transition from the corneal to the conjunctival epithelium, as also observed for spinocellular carcinoma. The lesion is more frequent in the temporal limbus, but in the present case it occurred in the nasal limbus (Table 1).

Some investigators have related the presence of keratoacanthoma to external aggressions such as exposure to the sun, radiation, carcinogenic chemicals, traumatic injury, viral infection, genetic and immunological factors (Estribi et al. 1984). Among all of these factors, viral infection has been the one most intensely studied. Over the last few years, several studies have been conducted to detect the presence of papillomavirus (HPV) in skin keratoacanthomas (Pfister et al. 1986; Gassenmaier et al. 1986; Magee et al. 1989; Höpfl et al. 1992), with positive results obtained in some cases. The rapid growth and spontaneous evolution are compatible with a viral etiology, but we didn't find HPV in our case.

Characteristically, skin keratoacanthomas present three evolutionary stages: 1) proliferative: nodule of rapid growth; 2) mature: hemispherically shaped tumor with a crater-like center; 3) involuted: necrotic tumor with a hypopigmented

central scar (Schwartz 1994). By analogy with skin lesions, the present patient was probably in the mature stage when she was diagnosed. Thus, although described as typical of conjunctival keratoacanthoma, the crater-like shape may be absent, as was the case for the patients reported by Freeman et al. (1961), Bellamy et al. (1963) and Munro et al. (1993). The 'crater' is filled with a pearly white substance. Roth (1978) curetted one of his patients twice and observed that the material was keratinous and filled the lesion again.

Histologically, the typical lesion consists of well circumscribed solid proliferation of squamous cells producing a central crater that is gradually filled with keratin. There is an intense lichenoid inflammatory infiltrate. During this phase the neoplasia has a tumoral aspect and may be deeply infiltrative. The deep part contains neutrophil and eosinophil microabscesses that are 'brought' to the surface. Eosinophils are common both in keratoacanthoma and in spinocellular carcinoma. Plasmocytes are present in the carcinoma but not in the keratoacanthoma.

The cytological alterations of the keratoacanthoma vary, but there frequently is a marked cytological atypia accompanied by numerous mitoses, including atypical ones. Perineural invasion of keratinocytes is a frequent alteration in keratoacanthoma. Thus, cytological atypia and perineural invasion are not criteria for the differentiation of spinocellular carcinoma from keratoacanthoma.

Immunohistochemical studies have demonstrated that there are no significant differences in CEA or keratin expression between keratoacanthoma and spinocellular carcinoma (Mas & Rodellas 1989; Jordan et al. 1991).

The following findings also favor the presence of keratoacanthoma in the histopathological differential diagnosis: keratin-filled crater, dome-like aspect, and eosinophil infiltrate. Findings that are more compatible with the presence of spinocellular carcinoma are: marked anaplasia and pleomorphism, atypia, numerous and/or abnormal mitoses, and desmoplastic stroma (Julie et al. 1984).

Although keratoacanthoma has the potential for spontaneous regression, surgical removal is justified by the chance of malignant transformation and by the concern about unesthetic scars. An excisional biopsy is indicated for the following reasons: there is no evidence that all keratoacanthomas regress spontaneously, aggressive keratoacanthomas may be destructive, and there is a risk of local

recurrence that will be more aggressive, as well as the risk of malignant transformation into a spinocellular carcinoma (Blessing et al. 1994; Boyton et al. 1986).

Of all conjunctival keratoacanthomas described, only one recurred one month after exeresis. Patho-anatomical examination showed tumoral involvement in the deep margin of the surgical resection. The recurring tumor invaded the anterior chamber and the authors opted for enucleation (Grossniklaus et al. 1990). Thus, even though conjunctival keratoacanthoma is a benign lesion, it may be of an aggressive nature. Surgical removal of suspected keratoacanthoma lesions, especially conjunctival ones, with a safety margin permits histological confirmation of the clinical diagnosis. Furthermore, surgery may prevent harmful consequences for the patient since the differential diagnosis from spinocellular carcinoma is not always possible even after histopathological analysis.

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