

ORIGINAL ARTICLE

Conjunctival Leiomyosarcoma: A Report of Two Cases

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ABSTRACT

Purpose: Leiomyosarcoma is a common soft tissue tumor in the body. However, ocular leiomyosarcoma is rather uncommon. Herein, we describe the clinical and histopathological features of two cases of conjunctival leiomyosarcoma. There have only been three previously documented cases of conjunctival leiomyosarcoma.

Results: A 34-year-old male presented with a 2-year history of a whitish mass in the right eye. He underwent an incisional biopsy of the mass, which supported the diagnosis of leiomyosarcoma on histopathological examination. Computed tomography showed orbital extension of the mass, following which he underwent an eyelid sparing orbital exenteration of the right side. The second case was that of a 39-year-old male, who had a history of a whitish limbal mass, which had been previously excised elsewhere. The pre-operative clinical photographs and histopathology slides of the excised mass were reviewed. A histopathological diagnosis of conjunctival leiomyosarcoma was established and due to base positivity, he was treated with plaque radiotherapy. Both the cases showed no tumor recurrence or systemic metastasis at one-year follow-up.

Conclusion: Primary conjunctival leiomyosarcoma is uncommon. Appropriate treatment of the tumor is associated with good prognosis.

Keywords: Conjunctiva, eye, leiomyosarcoma, sarcoma, tumor

INTRODUCTION

Leiomyosarcoma is the most common soft tissue sarcoma representing 24% of soft tissue sarcomas, arising from the mesenchymal cells with smooth muscle differentiation.¹ They are most commonly found in the soft tissue (48%), skin (14%), uterus (7%), gastrointestinal tract (7%) and the retroperitoneum (7%).¹ Leiomyosarcoma is a rare tumor of the eye and adnexa and can be primary, secondary, or metastatic.

There have been rare case reports of leiomyosarcoma of the conjunctiva, uvea, and orbit.^{2–7} Ocular and/orbital leiomyosarcoma can arise as a primary tumor from the vascular or sympathetic smooth

muscle, occur secondary to radiation therapy, metastasize from distant sites, or extend from paranasal sinuses.^{2,3,6} Herein, we describe the clinical and histopathological features of two cases of conjunctival leiomyosarcoma.

A systematic Medline search was performed on PubMed using the keywords: *leiomyosarcoma*, *conjunctiva*, *conjunctival*, *ocular*, and *eye*. There was no restriction on date of publication. Although this review primary relied on articles written in English, non-English-language articles that had abstracts translated into English were also reviewed. However, only three documented cases of conjunctival leiomyosarcoma were found, all of which are discussed in this article.

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CASE REPORTS

Case 1

A 34-year-old male presented with a history of fleshy white mass in his right eye (OD) for 2 years, which had been gradually increasing in size. On examination, the visual acuity in both eyes was 20/20 N6. The anterior and posterior segment examinations of the left eye were within normal limits. Examination of the right eye revealed an elevated fleshy white, vascular mass over the bulbar conjunctiva, extending from the superior fornix to the inferior fornix, sweeping across 6 clock hours of the limbus (Figure 1A). Inferiorly, a whitish mass was seen in the cornea, with an associated shallow anterior chamber. On performing an ultrasound biomicroscopy, the mass was seen extending into the deeper layers of corneal stroma with no definite evidence of intraocular extension. A computed tomography (CT) scan of the orbit revealed a hyperdense lesion extending from the ocular surface medially to the anterior orbit (Figure 1B). A working diagnosis of conjunctival squamous cell carcinoma with orbital extension was made and an incision biopsy was performed. A diagnosis of conjunctival

leiomyosarcoma was established on histopathological examination. Subsequently, the patient underwent orbital exenteration due to extensive conjunctival involvement and orbital extension.

On gross examination of the exenteration specimen, the clinical findings were confirmed. On histopathological examination, sheets of spindle-shaped and ovoid cells interspersed with hyalinized stroma were noted. These cells were pleomorphic and showed vesicular nuclei, prominent nucleoli and a rim of fibrillary cytoplasm (Figure 1C). The cornea was found to have full thickness stromal invasion by tumour cells, nearly obliterating the anterior chamber inferiorly. Descemet's membrane, however, was intact with no evidence of intraocular tumor extension (Figure 1F). The exenterated specimen's margins were clear of tumor cells.

On immunohistochemistry, the tumour cells displayed strong cytoplasmic positivity for smooth muscle actin (SMA) and Vimentin and were negative for pancytokeratin and desmin. Ki-67 staining showed high replicative activity with an average index of 20%. Based on these features, a diagnosis of conjunctival leiomyosarcoma with orbital extension was confirmed.

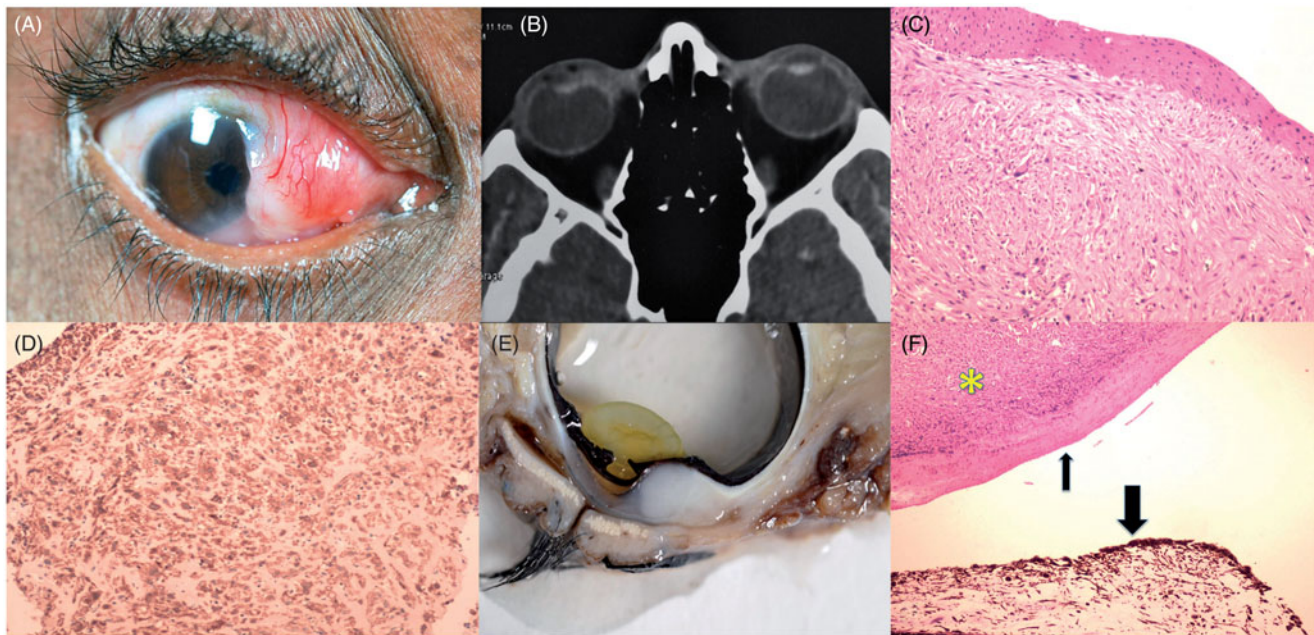


FIGURE 1. A photograph of the right eye shows a fleshy, white, vascular mass over the conjunctiva, sweeping across 6 clock hours of the limbus. Inferiorly, the whitish mass is seen involving the cornea, and apparently extending into the anterior chamber (A). On the right, a CT scan showing an ill-defined hypo-isodense lesion extending from the globe medially into the orbit (B). (C) A photomicrograph shows the stratified squamous epithelium above and spindle and ovoid tumour cells seen as narrow cords with hyalinized stroma below. These cells show vesicular nuclei with nucleoli, a rim of fibrillary cytoplasm (Hematoxylin Eosin stain, 10× magnification). Immunohistochemistry studies showing that the spindle cells exhibit strong cytoplasmic activity for smooth muscle actin (SMA) (D). (E) shows a cut section of the exenterated specimen showing the tumour was involving the full thickness of the cornea, nearly obliterating the anterior chamber inferiorly but no obvious tumour seen extending intraocularly. This finding is corroborated histopathologically: note the tumour cells within the cornea (asterisk), the intact Descemet's membrane (thin arrow) and the pigmented iris tissue (thick arrow) (F). Haematoxylin & Eosin stain, 10× magnification.

A thorough systemic evaluation showed no evidence of systemic metastasis. At 1-year follow-up, the patient was doing well, with no evidence of tumor recurrence or systemic metastasis.

Case 2

A 39-year-old male presented with a history of whitish mass in the left eye for 4 months and had undergone an excision biopsy of the same elsewhere. On examination, visual acuity in both eyes was 20/20 N6. Anterior and posterior segment examination of both eyes was normal except for conjunctival scarring temporally in his left eye (OS). There was no evidence of residual tumor in the left eye. The pre-operative clinical photographs and histopathology slides of the excised mass were reviewed. The photographs showed an elevated whitish mass extending 2 clock hours from 2 to 4o' clock on the temporal limbus (Figure 2A).

On histopathology, a cellular tumor composed of spindle-shaped cells arranged in sheets and fascicles was noted. The tumor cells demonstrated moderate cytoplasm and atypical elongated nuclei with coarse chromatin. Bizarre nuclei were seen along with few multinucleated cells. Atypical mitosis was also present. The stroma was fibrotic and showed some inflammatory cells. Tumor cells extended to the base of lesion. On immunohistochemistry, the tumor cells were immunoreactive for SMA and Vimentin; and negative for cytokeratin (CK), desmin, MyoD1, Myogenin, S-100 and CD34. Ki-67 Index was noted to be positive in 25% of the tumor cells. A histopathological diagnosis of conjunctival leiomyosarcoma was established. Owing to tumor base positivity on histopathology, ruthenium plaque radiotherapy with an apex dose of 8000 cGy at 2-mm depth was performed (Eckert & Ziegler BEBIG GmbH, Berlin, Germany).

At 14 months' follow-up, the patient was doing well, with no evidence of tumor recurrence or systemic metastasis.

DISCUSSION

Leiomyosarcoma is a malignant neoplasm composed of cells showing smooth muscle differentiation. Conjunctival leiomyosarcoma is an extremely rare disease with only 3 previously reported cases.^{4,7,8} Large series that have reported the spectrum and frequency of conjunctival tumors have not recorded a single case of conjunctival leiomyosarcoma, owing to the rarity of the disease.^{9,10} In the absence of native smooth muscle tissue, conjunctival leiomyosarcoma has been postulated to arise from the vascular smooth muscles or primitive mesenchymal cells of soft tissue.⁴

Wolff-Rouendaal reported a 20-year-old woman who presented with a history of xeroderma pigmentosum and a limbal tumor that was initially believed to be leiomyoma on biopsy.¹¹ The tumor, however, recurred rapidly and required orbital exenteration. Although leiomyosarcoma was suspected, it was never confirmed histomorphologically as review of the original slides was no longer possible. White et al. reported leiomyosarcoma arising from the conjunctiva in a 66-year-old man.¹⁰ The patient initially underwent excision biopsy of the conjunctival lesion, which was diagnosed as squamous cell carcinoma with stromal invasion.

Subsequently, the patient had tumor recurrence involving the conjunctiva and cornea, 26 years after primary excision. He underwent penetrating keratoplasty along with excision of the conjunctival lesion, which showed a malignant spindle cell neoplasm. In view of incomplete resection indicated by positive tumor margins, the patient underwent

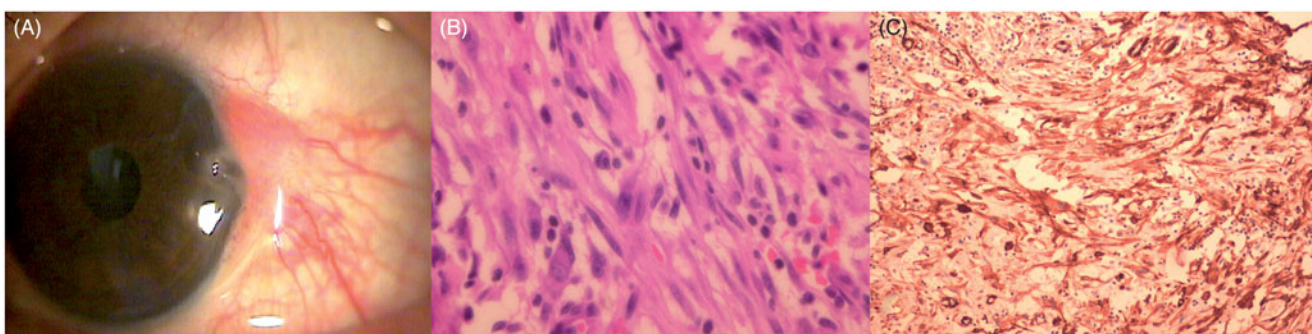


FIGURE 2. Slit lamp photograph of the left eye showing a fleshy white mass extending 3 clock hours from 1 o'clock on the temporal limbus. Note the presence of intrinsic vascularity and feeder vessels (A). Photomicrograph showing spindle-shaped tumour cells arranged in sheets and fascicles. The tumour cells demonstrated moderate cytoplasm and atypical elongated nuclei with coarse chromatin (B) (Haematoxylin-Eosin stain, 40× magnification). The tumour cells showed a strongly positive immunoreactivity for smooth muscle actin (SMA) (C).

TABLE 1. Conjunctival leiomyosarcoma: review of literature.

Author/year of publication	Age (years)/gender	Affected eye/duration of symptoms (months)	Orbital extension of conjunctival tumor	Treatment	SMA/MSA	Vimentin	Follow-up (months)	Final outcome at last follow-up
White <i>et al.</i> (1991) ¹⁰	66/M	OS/>48	No	Orbital exenteration	+	+	24	Alive and well
Guerriero <i>et al.</i> (2011) ⁴	56/F	OS/4	Yes	Orbital exenteration	+	+	NA	Metastasis and death
Kenawy <i>et al.</i> (2012) ⁶	37/F	OS/2	No	Wide excision biopsy	+	+	12	Alive and well
Current study (Case 1)	39/M	OD/24	Yes	Orbital exenteration	+	+	9	Alive and well
Current study (Case 2)	39/M	OS/12	No	Wide excision biopsy + plaque radiotherapy	+	+	9	Alive and well

M = male; F = female; OS = left eye; OD = right eye; SMA = smooth muscle actin; MSA = muscle specific actin; NA = not available.

subtotal exenteration. The biopsy revealed a pleomorphic spindle cell neoplasm involving the conjunctiva and cornea. Based on microscopic, immunoperoxidase staining profile, and electron microscopic findings, the diagnosis of leiomyosarcoma involving the conjunctiva and cornea was established. Over a follow up of 2 years, there was no evidence of tumor recurrence.

Kenawy *et al.* also reported a case of conjunctival leiomyosarcoma in a 37-year-old female, which was managed by excision biopsy with wide surgical margins. Over a follow-up of 12 months, patient had no tumor recurrence.⁷

Guerriero *et al.* reported another case in 56-year-old Caucasian female with a rapidly progressive conjunctival mass of 4 months' history arising from the inferior fornix.⁴ The mass was seen extending into the orbit with locoregional lymph node metastasis at presentation. The patient underwent orbital exenteration which confirmed the diagnosis of conjunctival leiomyosarcoma. Despite extensive conjunctival disease and locoregional metastasis at presentation, no intraocular tumor extension was noted. The features of 3 three cases as well as the 2 presented here have been tabulated in Table 1.

Diagnosis

The diagnosis of conjunctival leiomyosarcoma can be established only histologically with immunohistochemical studies and possibly electron microscopy. On microscopy this tumor usually exhibits spindle cells, arranged in fascicles with central, cigar-shaped nuclei; distinct from myofibrosarcoma, which shows myoid differentiation with bland or pleomorphic stellate to spindled cells with eosinophilic cytoplasm and tapered nuclei in a collagenous stroma.¹² Immunohistochemical staining for anti-smooth muscle actin helps to confirm the diagnosis. Guerriero *et al.* have described the electron microscopic features of conjunctival leiomyosarcoma.⁴ The tumor cells show irregular and often grooved nuclei

with prominent nucleoli, moderate amount of cytoplasmic thin filaments with focal densities, immature cell junctions and discontinuous basal lamina material along the cell surface.⁴ Although not always necessary, electron microscopy may help to clinch the diagnosis in cases of doubt.

Treatment

The management of this rare clinical entity is based on lessons drawn from systemic disease. Even a few mitoses in leiomyosarcomas carry a poor prognosis.⁵ Surgical resection of the tumor forms the primary treatment modality. Radiotherapy may be used for as adjuvant therapy where complete resection is not possible, such as when limited by vital structures. Chemotherapy is reserved for palliation in metastatic disease. Although 3 of the 5 cases (3 case reports and 2 from our series) required orbital exenteration, the case reported by Kenawy *et al.* as well the second case presented here show that for conjunctival leiomyosarcoma, complete tumor excision with clear margins can be attempted for disease control.⁷ However, extensive disease may necessitate an orbital exenteration. Plaque radiotherapy may be used as adjuvant treatment in presence of positive surgical margin after primary excision as was the case in our patient.

CONCLUSION

Conjunctival leiomyosarcoma is an infrequently encountered tumor, which requires a high degree of clinical suspicion in its diagnosis and an aggressive management strategy given its clinical course and rare occurrence.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of

the article. Dr. Swathi Kaliki has had full access to all the data in the study and takes responsibility for the integrity and accuracy of the data.

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