

Sarcomatoid Squamous Cell Carcinoma of the Conjunctiva: A Rare Entity and A Brief Review of Literature

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ABSTRACT

Sarcomatoid variant of squamous cell carcinoma has been known to involve numerous tissues like an aerodigestive tract, skin. A reddish mass of the left bulbar conjunctiva, with intraocular extension on ultra-bio-microscopy (UBM) was present. Histopathologic examination showed the characteristic spindle-shaped cells in continuity with the overlying epithelium with positive immunostains for cytokeratin, epithelial membrane antigen and vimentin. The presence of such an entity in the conjunctiva is rare and here we report such a case, this being the 37th case to be documented in literature. We also give a brief review of literature.

Keywords: Sarcomatoid Squamous Cell Carcinoma, Spindle Cell Carcinoma, OSSN, Ocular Surface Tumor, Enucleation

Introduction

Ocular surface squamous cell neoplasia is the most common carcinoma of the ocular surface. The spindle cell (sarcomatoid variant) of squamous cell carcinoma of the conjunctiva is a rare variant of squamous cell carcinoma which is more aggressive; typically, they are vimentin-positive and weak staining for cytokeratin and EMA. An epithelial origin with dedifferentiation to a spindle cell morphology is the most accepted hypothesis. The cells shift from a squamoid to spindled appearance due to dysfunctional intercellular adhesion complex, causing more infiltration^[1]. The tumour, due to its aggressive nature, has a higher likelihood of intraocular extension. It needs to be identified and properly removed. Here we describe the 37th such case ever documented and a brief review of the literature.

Case Description

A 40-year-old male presented with a complaint of a pinkish mass in his left eye for three months. The lesion started as a small swelling in the superomedial part of the bulbar conjunctiva and gradually increased in size over three months to encroach the medial aspect of the left eye. He had no history of trauma, smoking or any other addiction or any mass anywhere else in the body. He had no history of any systemic illness.

On general examination, he was well built, and there was no evidence of any systemic illness. On local ophthalmological examination, he had a visual acuity of

6/9 in both eyes, and intraocular pressure was 16mm Hg. Anterior and posterior segment examination of the right eye was within normal limits. On viewing his left eye, his left eyelids were edematous. Local examination showed a gelatinous, reddish mass which was soft and lobulated on palpation. It extended from medial canthus medially and engulfed medial half of cornea from 6 o'clock to 1 o'clock. (Figure 1). Superiorly and inferiorly, it extended up to the fornices. A prominent tortuous vessel which ran diagonally from above downwards towards the cornea fed the tumour mass. Slit-lamp examination of the anterior segment was within normal limit except for senile cataractous changes. Posterior segment examination was within normal limits. Extraocular movements were full and within normal limits.

An ultrasound bio-microscopy showed corneal and anterior segment involvement with sparing of the ciliary body. A contrast-enhanced computed tomography (CECT) scan ruled out an orbital extension.

Based on the clinical findings and history, a diagnosis of left eye ocular surface squamous cell neoplasia was made. The patient underwent USG of the cervical nodes and abdomen to rule out any systemic spread of the disease, which came out to be negative. As per AJCC 8th edition, the clinical stage of tumour was T3N0M0.

The patient underwent extended enucleation followed by cryotherapy of the margins of conjunctiva followed by a primary silicone implant placement. The enucleated

specimen was sent for histopathological examination, which showed a tumour measuring 12 mm at the limbus. The tumour cells were spindle-shaped and infiltrated the corneal stroma, sclera, and trabecular meshwork. Focal squamoid differentiation was seen (Fig 2 A-C). On IHC these were positive for pancytokeratin (AE1/AE3),

epithelial membrane antigen, p63 and vimentin (Figure 3 A&B). Immunostains were negative for S-100, desmin, SMA, CD 34 and HMB-45. Thus, a diagnosis of spindle cell variant of squamous cell carcinoma was reached. The patient has been on follow up for three months, and there has been no evidence of any recurrence to date.

Table 1: Review of cases of sarcomatoid squamous cell carcinoma of the conjunctiva.

S. No	Study	Age at presentation /gender	Clinical Presentation	Treatment	Histopathology features	IHC	Outcome
1.	Cohen et al., 1980 [5]	Case 1 – 28 y /M	Inferotemporal subconjunctival mass	Conjunctival Excisional biopsy	Continuity of tumor with surface epithelium no surface atypia (misdiagnosed as chronic inflammation and malignant fibrous histiocytoma)	Not available	Recurrence and resections (2 times). Exenteration – no recurrence and metastasis in 9 months follow up.
		Case 2 – 30 y / M	Vascular mass in nasal limbus	Excisional biopsy	Stromal infiltration by atypical spindle cells continuous with surface epithelium	Not available	Not available
2.	Huntington et al 1990(retrospective study of 6 cases registered in AFIP) Intraocular extension present in all 6 cases EMA present in all 6 cases [7]	Case 1 – 30 y / F	Not known	Exenteration	Stromal tissue infiltrated by chronic inflammatory cells, spindle shaped tumor cells present. 4 out of 6 cases showed continuity with overlying surface epithelium.	Polyclonal anti keratin + Anti – EMA + AE1/3 – PKK1 -	Not studied
		Case 2 – 72 y/M	Phthisical eye with Limbal papilloma (past history of recurrent keratitis and underwent multiple ocular surgeries)	Enucleation		Polyclonal anti keratin + Anti – EMA - AE1/3 + PKK1 +	
		Case 3 – 55 y /M	Phthisical eye with multiple conjunctival nodules and unspecified ocular inflammation for 40 years			Polyclonal anti keratin + Anti – EMA + AE1/3 – PKK1 +	
		Case 4 -85y/ M	Large, Solitary, sessile limbal mass overlying cornea			Polyclonal anti keratin + Anti – EMA- AE1/3 - PKK1 -	
		Case 5 – 80y/ F	Single nodule of bulbar conjunctiva	Exenteration		Polyclonal anti keratin - Anti – EMA - AE1/3 – PKK1 -	
		Case 6 -	Single nodule of bulbar conjunctiva	Excisional biopsy	Polyclonal anti keratin - Anti – EMA - AE1/3 – PKK1 -		
3.	Schubert et al., 1995[8]	31y/ F	2.5 mm bulbar conjunctival mass	Excisional biopsy	Spindle shaped cells continuous with surface epithelium. with presence of chronic inflammation	Cytokeratin + EMA antigen positive	No recurrence in 5-year lamellar resection of sclera at original site of nodule with cryotherapy
4.	Seregard et al., 1995[9]	70 y/M	Pterygium	Excisional biopsy	Spindle cells infiltrating stroma diffusely with few cells continuous with surface epithelium above	Vimentin + Monoclonal antibodies for MFN 116+ AE1/3 -	Recurrence (2 times) Received EBRT Metastasis to lung and ribs Died in 14 months after initial treatment
5.	Slushker et al., 1997[10]	101 Y/ F	Large mass arising from conjunctiva	Enucleation	Spindle shaped cells with pleomorphism	EMA + Cytokeratin + Vimentin - S100 - HMB 45 –	Not reported
6.	Shields et al., 2007[11]	51 Y/ M	Pterygium	Excision	Spindle cells subepithelial and CD 68 positive multinucleated giant cells	Vimentin + S100 - HMB 45 – AE1/AE 3 -	Recurrence in 1 month – full thickness eye wall resection with scleral graft No tumor recurrence in 6 months

S. No	Study	Age at presentation /gender	Clinical Presentation	Treatment	Histopathology features	IHC	Outcome
7.	H.M.Akatan et al., 2010[12]	72y/ M	Recurrent lesion at site of previously excised mass and diagnosed as spindle cell carcinoma	Excision	misdiagnosed as recurrent squamous cell carcinoma (review of slides and report from exenterated tissue) showed poorly differentiated, pleomorphic squamous cells and continuous with overlying epithelium	Positive for cytokeratin	Reported 2 years later with recurrence for which anterior exenteration was done Bilateral lung metastasis 3 years after exenteration
8.	Coban et al., 2016[14]	85 y/M	Pedunculated mass without ulceration for 3 months	Excisional biopsy	Carcinoma in situ – spindle or epithelioid cells arranged in herds and bundles with presence inflammatory cells	Vimentin + Pancytokeratin + EMA + SMA + CD 99, p63, Calponin + ve Caldesmon and MyoD1 negative	Lost to follow up
9.	Patel et al., 2016 [15]	55 y / M	Pedunculated mass of conjunctiva without ulceration for 4 months	Enucleation	Dysplasia of stroma with spindle cells arranged in fascicles	AE 1 + Cytokeratin 5/6 + Vimentin + S – 100 and HMB 45 negative	Not reported



Fig. 1: Clinical picture of the patient showing vascularized fleshy mass in the superomedial aspect of left bulbar conjunctiva with a feeder vessel.

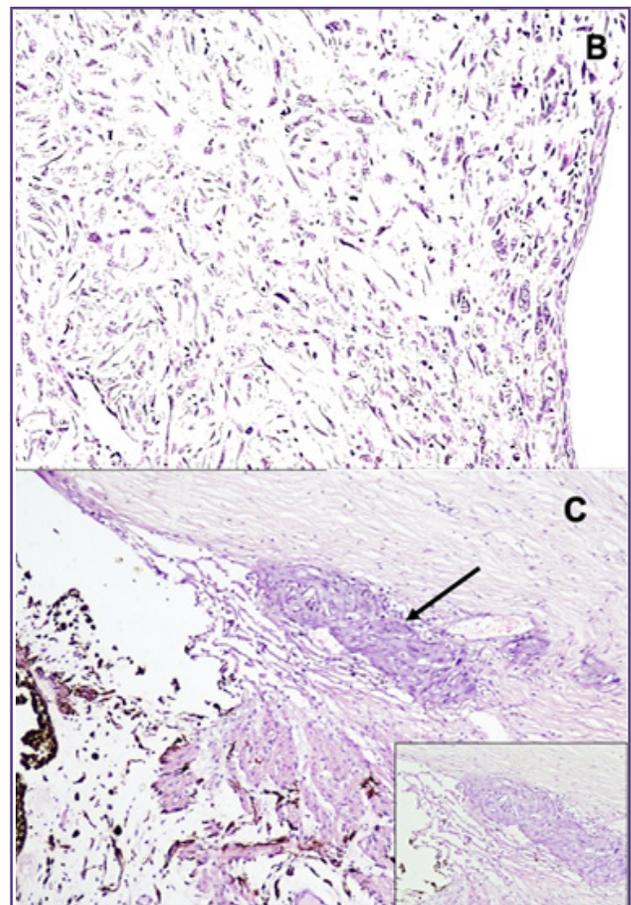
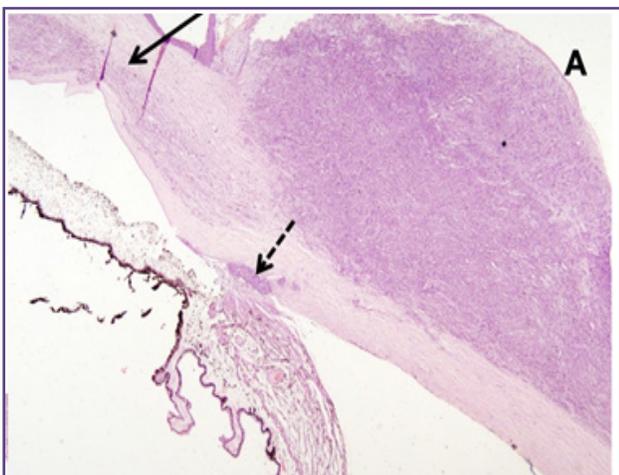


Fig. 2: A- Low power view shows tumor cells in the stroma, scleral infiltration(arrow) and trabecular meshwork infiltration(dashed arrow) is seen (H &E x100), B- High power view to show pleomorphic spindle shaped tumor cells below the epithelium(H&E x200), C- Tumor cells infiltrating the Trabecular meshwork (H&E x100, inset shows squamoid appearance of tumor cells (H&E x 200).

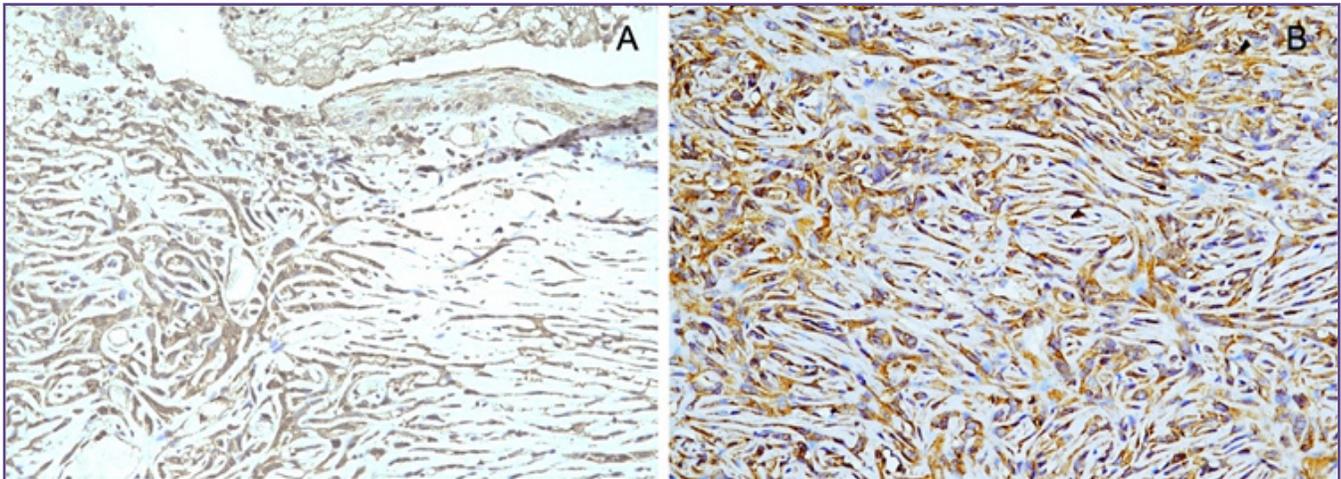


Fig. 3: A- Tumor cells in the subepithelium showing Epithelial membrane positivity(Avidin Biotin x 200), B- Cytoplasmic Vimentin positivity is seen in the tumor cells (Avidin Biotin x 200).

Discussion

Squamous cell carcinoma is the most common malignant tumour of the conjunctiva^[2]. It was first described in 1860 by von Graefe^[3]. Over the period of time, multiple studies have been conducted, which has led to the classification of the disease in many ways. Spindle cell squamous cell carcinoma is a rare and a poorly differentiated variant of squamous cell carcinoma and has been reported to occur in numerous sites like an aerodigestive tract, skin. It is also known as spindle cell carcinoma^[3-11]. Other terms which have been used to describe the same include polypoid carcinoma, pleomorphic carcinoma, carcinosarcoma or pseudosarcoma^[4].

Sarcomatoid or spindle cell carcinoma of the conjunctiva, however, is a very uncommon entity. It arises from squamous cell carcinoma with dedifferentiation to sarcomatoid variant; thus, it comprises two components – epithelial component and mesenchymal component, and so is a biphasic tumour^[6]. The squamous component may be scant or not seen on light microscopy. In such cases, immunohistochemical evidence of squamous origin is necessary for diagnosis. The sarcomatous component is vimentin-positive with weak staining for cytokeratin/EMA. p63 and p40 are both useful markers with comparable sensitivity for epithelial differentiation in such cases, however p40 has greater specificity^[12]. Histological feature to guide Immunohistochemistry (IHC) for sarcomatoid squamous cell carcinoma is the presence of spindle cell tumour, which may have continuity with surface epithelium.

On the literature review, the first case of spindle cell carcinoma of the conjunctiva was reported nearly 50 years back by Wise AC in 1967^[7]. Over the past 50 years, a total

of 26 cases of spindle cell carcinoma of conjunctiva have been reported. Table 1 gives details of reported cases and outcomes. Other than these cases, in 1997, Cervantes et al. had published a study on clinicopathological features of 287 cases of squamous cell carcinoma of the conjunctiva, of which only 2 were spindle cell carcinoma^[16]. Ni C and Guo BK studied clinicopathological features of 8 patients and classified spindle cell carcinoma as fibrosarcomatous, rhabdomyosarcomatous and fibrohistiocytomatous^[17].

Review of literature suggests sarcomatoid squamous cell carcinoma to be a locally aggressive carcinoma with a risk of recurrence and metastasis if not resected adequately and promptly. Intraocular invasion is common^[13]. Invasion of the trabecular meshwork has been described in 2/26 conjunctival SCC by Mckelvie et al. None of the 2 cases were, however, sarcomatoid SCC^[18].

Conclusion

Because of its variable and benign appearance, clinician may take a conservative approach initially. It is also challenging for pathologists to give a definitive diagnosis based on histopathological features alone, and it may be misdiagnosed for chronic inflammation or sarcoma. Immunohistochemistry plays a key role in the diagnosis of spindle cell carcinoma where it is positive for cytokeratins, epithelial membrane antigen suggesting epithelial origin with a sarcomatous component. Absence of S-100 and HMB 45 positivity further rules out sarcomatous tumours of neural origin and amelanotic melanoma.

Conflicts of Interest

None

Sources of Funding

None

Acknowledgement

None

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, patient has given his consent for the images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal the identity of the patient.

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Financial or other Competing Interests: None.

Date of Submission : 18/04/2021

Date of Final Revision : 03/06/2021

Date of Acceptance : 05/06/2021

Date of Publication : 30/06/2021