



Laryngeal Basaloid Squamous Cell Carcinoma with a Substantial Spindle Cell Component: Case Presentation and Updated Review of Literature

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Abstract

Basaloid squamous cell carcinoma with spindle cell component is an uncommon aggressive variety of squamous cell carcinoma with only a few reported cases in literature. Histologically a combination of basaloid squamous cell carcinoma and spindle cell squamous cell carcinoma is appreciated and immunohistochemistry serves a role in differentiation from malignant neoplasms of salivary gland or neuro-endocrine origin. Prime treatment modality is combination of surgery and external beam radiotherapy. A case of basaloid squamous cell carcinoma with proliferation of bizarre mesenchymal component is being reported here with an updated literature review.

Keywords Basaloid · Epithelial mesenchymal transition · Glottis · Spindle cell

Introduction

Basaloid squamous cell carcinoma (BSCC) of the head and neck is considered to be an uncommon malignancy with an unfavorable clinical outcome. In 1986, Wain et al. reported the first head and neck case [1]. In rare instances, a biphasic histological presentation comprising of basaloid squamous cell carcinoma with spindle cell component has been reported in various sites such as hypopharynx, tonsil, larynx, nasal cavity, skin, ureter, rectum [2–9]. Muller and Barnes are credited for reporting the first two cases of BSCC with spindle component in the head and neck area [2].

Regarding treatment, there is slight disagreement between individual reported cases. Some cases were management by neo-adjuvant radiotherapy followed by surgery while surgical excision was considered as first line of treatment in other reports with adjuvant chemo- or radiotherapy.

Here, we report a glottic basaloid squamous cell carcinoma showing a substantial spindle cell component extending to sub-glottis and right pyriform sinus (hypopharynx) with emphasis on histological differential diagnosis and review of literature.

Case Presentation

We received a specimen of total laryngectomy of size 10×6×5 cm of a 59 years old male patient (South Indian, linguistically malayali) with bilateral neck dissection. On incisional biopsy a diagnosis of moderately differentiated squamous cell carcinoma was given. He had presented with a chief complaint of difficulty in breathing and swallowing in June 2017. Patient had noticed a change in his voice since last 2 years. The patient had a history of daily alcohol intake for 33 years and 61.25 pack-year smoking.

On gross examination laryngeal lumen showed an indurated exophytic and polypoid to ulceroproliferative growth involving mainly the right vocal cord with transglottic extension of size 5.5×3.5 cm. The specimen was cut open by a longitudinal split on the posterior aspect. The tumor appeared solid white on sectioning with infiltrative borders (Fig. 1). The maximum thickness was 2.5 cm and lesion was seen extending to left side of larynx and right pyriform sinus. Histological sections

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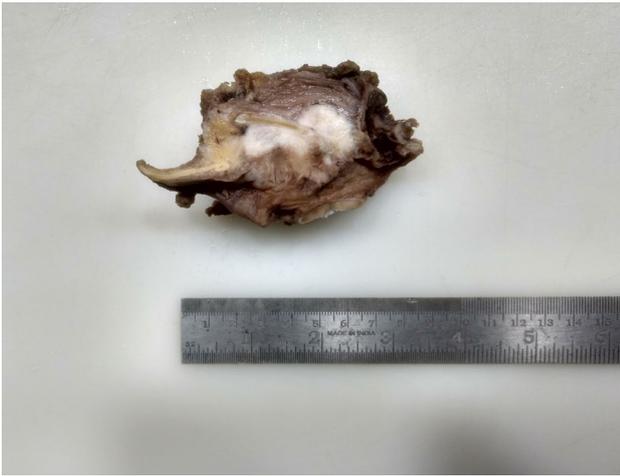


Fig. 1 Gross picture of the laryngectomy specimen

showed an invasive epithelial neoplasm composed of tumor cells invading the underlying connective tissue in islands, nests and sheets (Fig. 2). The tumor cells showed variegated appearance from mainly basaloid (50%) to keratinizing squamoid (15%) at areas to highly pleomorphic spindle shaped at other areas (35%, mainly in the deeper parts of tumor). In basaloid region, the nuclei of tumor cells were hyperchromatic with scanty cytoplasm and showed peripheral palisading, comedo necrosis, small cyst like spaces and stromal desmoplasia. While other areas showed transition from basaloid and squamous tumor cells to highly pleomorphic bizarre appearing spindle cells with increased atypical mitotic figures. The squamous component showed features of moderately differentiated squamous cell carcinoma. Some islands show keratin pearl formation. There were no lympho-vascular emboli or perineural invasion. All the resected margins, thyroid gland, tracheostomata and pre-epiglottic fat were free of tumor. Right pyriform sinus, thyroid cartilage and cricoid cartilage were involved by the tumor. Multiple ipsilateral lymph nodes [1 (R) level IIB, 2 (R) level III and 1 para tracheal nodes] showed metastatic deposits with size of largest metastatic deposit being 1.9 cm. No extra-nodal extension was seen.

A panel of immunohistochemical markers was done (Fig. 3). Details of primary antibodies used and findings of both the epithelial and the sarcomatous component are listed in Table 1. A final diagnosis of transglottic basaloid squamous cell carcinoma with a substantial spindle cell component was made. The tumor was staged as pT4a N2b (AJCC 8th edition). Adjuvant external beam radiotherapy (60 Gy for 30 days) was given. Eight months after the completion of radiotherapy, the patient is disease free. The patient is being followed up.

Discussion

A search in Pubmed database was done with key words ‘basaloid’, ‘head and neck’, ‘sarcomatoid’ and ‘spindle’. The cases were retrieved and reviewed. A detailed clinicopathological data is presented in Table 2. As already mentioned, other than head and neck region such a unique histopathological presentation has been reported in various sites including ureter and rectum [8, 9]. Tumors with histological diagnosis other than basaloid squamous cell carcinoma with spindle component or spindle cell carcinoma with prominent basaloid squamous cell component were excluded. Tumors of non head and neck region are also not listed. For all the cases including ours mean age of occurrence was 67.18 years. Males were affected far more commonly than females (M:F—4.5:1). An association was noted between smoking and alcohol use and tumor with basaloid squamous cell and spindle cell component. Deleterious habits were not mentioned in three cases while, in other two cases of the nasal cavity there was no history of tobacco or alcohol use.

In the present case, close histological differential diagnosis included mainly adenoid cystic carcinoma (ACC) and small cell neuroendocrine carcinoma. Further a possibility of association with HPV was also speculated. Primary ACC in larynx is rare and mainly arise in subglottic area followed by glottis. Histologically ACC show small angulated hyperchromatic nuclei with scant cytoplasm and arranged in cribriform solid or tubular pattern. Our case presented with an extensive growth involving glottis and sub-glottis with supra-glottic extension. Grossly the borders were infiltrative. The tumor cells were comparatively larger and oval showing prominent nucleoli at areas. There was no PNI which is ubiquitously seen in ACC. Squamous component seen in the present case is universally absent in ACC. Immunohistochemically, p63 was diffusely positive unlike ACC where p63 expression is restricted to abluminal cells. CD117 was altogether absent in the present case.

Small cell neuroendocrine carcinoma show small angulated nuclei with speckled chromatin and positivity for one of neuroendocrine markers unlike our case. A causal relationship between few BSCC cases and HPV and some cases has been documented in the upper aerodigestive tract [10]. Chernock et al. in their study found that none of 16 laryngeal/hypopharyngeal tumors were positive as depicted by ISH for HPV DNA and p16 immunohistochemistry [11]. While, in another study one laryngeal and one sinonasal BSCC (2/32 non oropharyngeal tumors) were found to be associated with HPV [12]. p16 immunostaining is used as surrogate IHC marker for detection of HPV; p16 was negative in the present case ruling out any association with HPV. Rectal case of BSCC with spindle

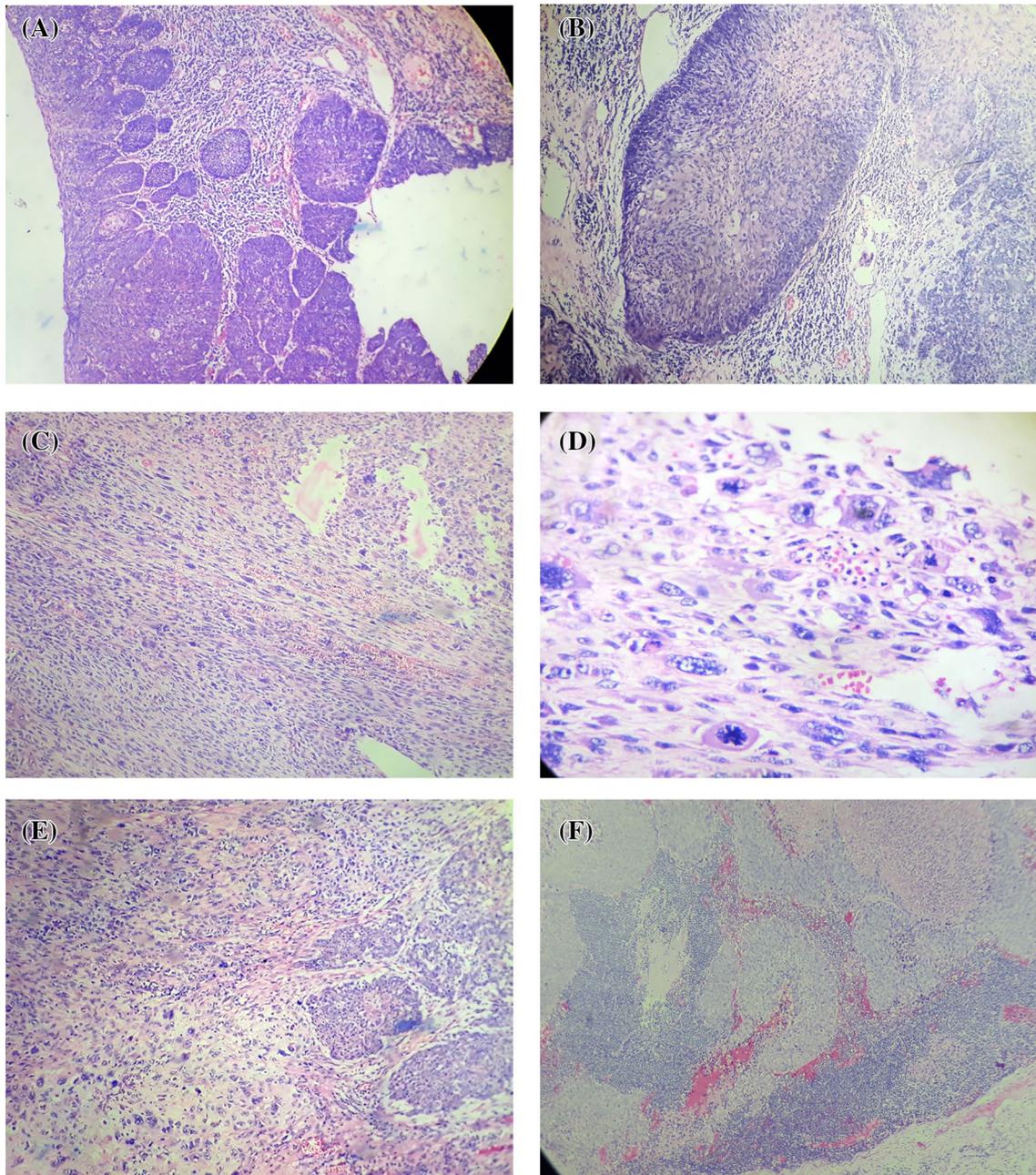


Fig. 2 **a** Photomicrograph showing the superficial portion of the tumor composed of severely dysplastic epithelium with invading basaloid tumor islands; **b** peripheral palisading and small cyst like spaces; **c** streaming fascicles of spindle cells showing marked pleomorphism; **d** increased abnormal mitotic count; **e** photomicrograph

showing transition from basaloid tumor islands to highly pleomorphic spindle cells; **f** metastatic deposit in lymph node with basaloid morphology and necrosis. Focally squamous differentiation is noted (**a–c** and **e–f**— $\times 40$; **d**— $\times 100$)

cell proliferation was also positive for p16 in both epithelial and mesenchymal tumor components. The finding was further confirmed by chromogenic in-situ hybridization (CISH) and electron microscopy [9].

Considering tumor of such a unique histopathological presentation as carcinosarcoma, the basaloid areas being the carcinomatous component, possibility of epithelial

mesenchymal transition (EMT) can be contemplated. Under the aegis of EMT, the epithelial cells gain motility and invasiveness. The cells undergo a loss in cell-to-cell adhesion and loss of cytological polarity with reorganization of cytoskeletal elements [13]. Furthermore, there is decreased or loss of expression E-cadherin and plakoglobin, and increased expression of vimentin, SMA,

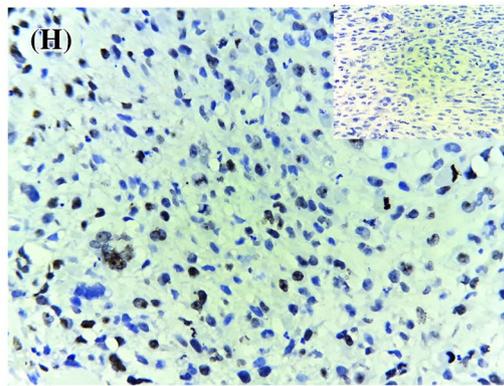
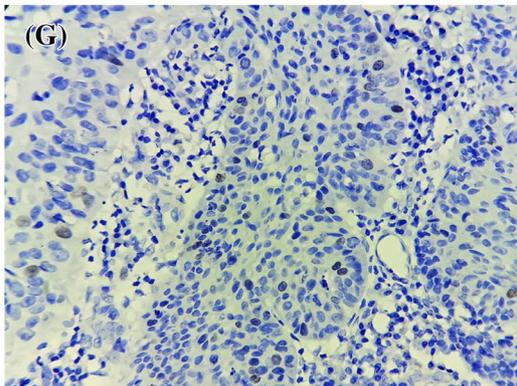
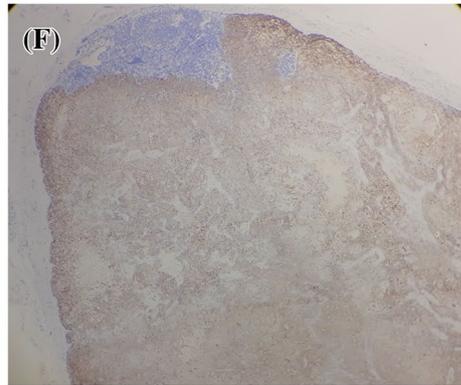
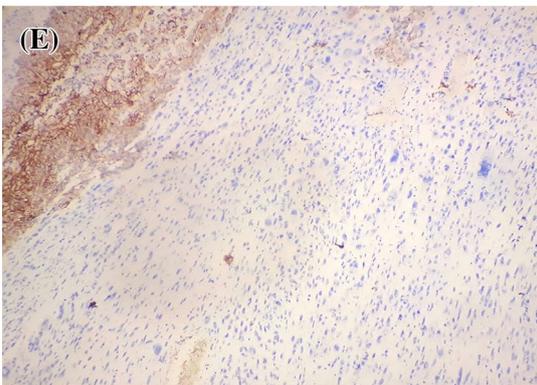
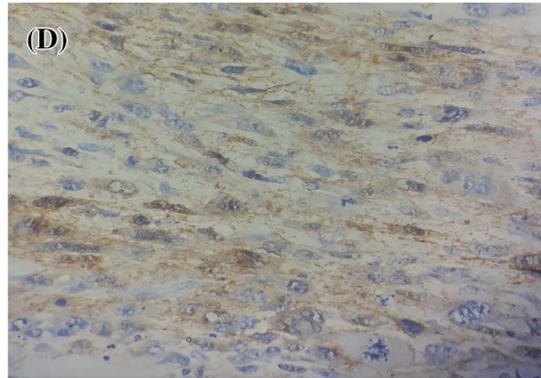
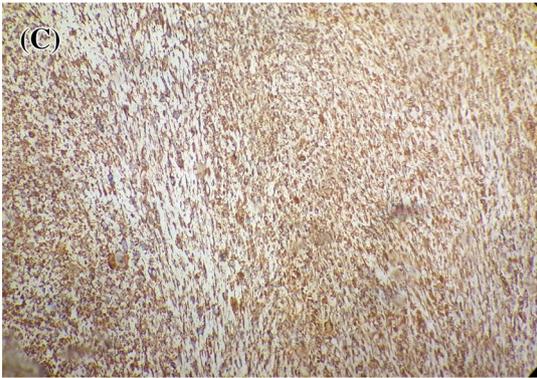
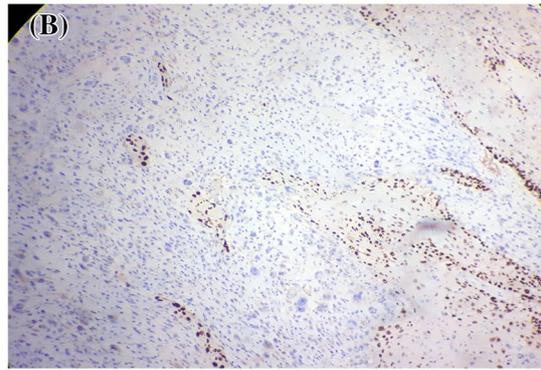
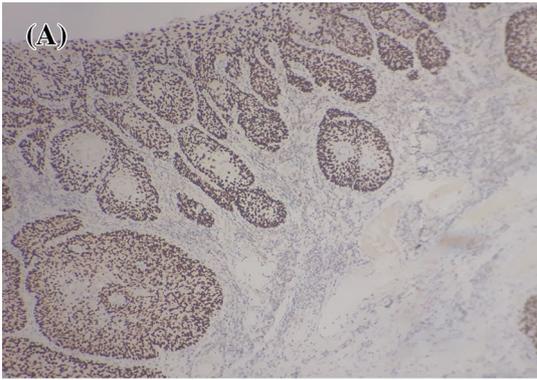


Fig. 3 Representative immunohistochemistry photomicrographs (only positive markers are shown). **a** Strong nuclear positivity of p63 in basaloid component; **b** focal strong nuclear positivity of p63 in spindle component; **c** diffuse strong expression of vimentin in sarcomatous area; **d** SMA expression in spindled cells; **e** expression of e-cadherin in epithelial component with concomitant loss of expression in spindle cells; **f** expression of e-cadherin in metastatic node; **g** Ki-67 expression in basaloid component; **h** high and low (inset) Ki-67 expression in spindle cell component (depicting tumor heterogeneity)

and fibronectin. In our presentation of a single case we also found a loss of expression of E cadherin with concomitant expression of SMA in the spindle component favouring EMT. This cascade of cellular events favors metastasis, an adverse prognostic factor. At the metastatic site, reversibility of the process (mesenchymal epithelial transition, MET) has been observed during embryonic development once the migratory cells have reached their destination [14] which is further supported by the fact that re-expression of E-cadherin occur at metastatic nodes [15, 16]. Bukholm et al. opined that re-expression of adhesion molecules at metastatic site may play an important role for tumor cells to adhere in the remote organs [15]. Re-expression of E cadherin was observed in the metastatic node in our case reiterating the role of EMT and MET (Fig. 3e, f).

Ki-67, a non histone protein, is associated with cell proliferation and has been regarded as a marker for high risk of recurrence and poor survival particularly in breast cancer [17]. We found that the Ki-67 score was 15% in the basaloid component and was higher in the spindle cell component (28%). Thus, the tumor cells having a higher Ki-67 proliferation rate may be expected to be more sensitive to radiation. Although in none of the previously reported cases of BSCC with spindle cell component, Ki-67 proliferative marker was used, prognosis may be correlated to administration of adjuvant or neoadjuvant external beam therapy. Neo adjuvant therapy followed by surgery was considered for one patient. For another patient with hypopharyngeal mass, surgery alone was the prime treatment modality and in that patient the tumor recurred within 1 year and the patient succumbed to death. It is thus prudent to regard such tumors as locally aggressive and combined surgery with adjuvant therapy should be given with a close follow-up. Further, most of the patients did not have a long term follow up period which can actually predict the exact clinical outcome.

In conclusion, we present another case of BSCC with proliferation of spindle cells which can be regarded as a locally aggressive variety of squamous cell carcinoma. Auxiliary diagnostic aids such as immunohistochemistry can help in exclusion of other closely appearing tumor on

Table 1 Table showing details of panel of antibodies used for immunohistochemistry and their expression in both the epithelial component and the sarcomatous component

Antigens	Clone	Epithelial component	Sarcomatous component
Pan CK	AE1/AE3	Diffuse cytoplasmic positivity	Focal cytoplasmic positivity
p63	DAK-p63	Diffuse nuclear positivity	Focal nuclear positivity
Ki67	MIB-1	15%	28%
Vimentin	V9	Negative	Diffuse cytoplasmic positivity
Desmin	D33	Negative	Negative
SMA	EP188	Negative	Positive
P16 (INK4)	G175-405	Negative	Negative
Chromogranin	DAK-A3	Negative	Negative
e-cadherin	NCH-38	Positive	Negative
CD117(dilution 1:400–1:600)	c-kit	Negative	Negative

Table 2 Table showing details of previously reported cases of biphasic tumors of head and neck with basaloid and spindle cell components

	Location	Age/sex	Symptom	Habit	H/P diagnosis	Treatment	Follow up
Muller et al. (1995)	True vocal cord with subglottic extension	59/M	Difficulty in breathing	–	BSCC with a spindle cell component	Surgery with 58 Gy external beam radiotherapy	Disease free 6 months
Muller et al. (1995)	Tonsil	79/M	Dysphagia	–	BSCC with a spindle cell component	Surgery with external beam cobalt radiotherapy (total 66 Gy)	Disease free after 7 years
Wieneke et al. (1999)	Left nasal cavity	69/M	Blurred vision	None	BSCC with fascicles of pleomorphic spindle cells	Surgery alone	Recurred within 1 year (dead)
Wieneke et al. (1999)	Left nasal cavity	41/F	Obstruction	None	BSCC with fascicles of pleomorphic spindle cells	Surgery for primary disease, radiation therapy for recurrent disease	Multiple at 2, 3, 4, 5 year [alive]
Kimura et al. (2005)	Left pyriform sinus	82/M	Sensation of foreign object with mild pain	Yes (smoking and alcohol)	BSCC with an extensive spindle cell component	Surgery alone	6 months (disease free)
Altrabulsi et al. (2006)	Right nasal cavity	73/M	Severe dyspnea and swelling of right face	Yes (smoking and alcohol)	Spindle basaloid squamous carcinoma	58-Gy external beam radiation followed by partial maxillectomy	14 months (disease free)
Altrabulsi et al. (2006)	Post cricoid region	69/M	Dysphagia	Yes (smoking and alcohol)	Spindle basaloid squamous carcinoma	66 Gy external beam radiation (50 Gy for regional lymph nodes) followed by total laryngectomy	Disease free 10 months after completion of therapy
Altrabulsi et al. (2006)	Right pyriform sinus	59/M	Dysphagia and odynophagia	Yes (smoking and alcohol)	Spindle basaloid squamous carcinoma	Refused therapy	Alive 8 months after diagnosis
Lavialle-Guillotreau et al. (2011)	Right pyriform sinus	61/M	Dysphonia and dysphagia	Yes (smoking and alcohol)	Basaloid squamous carcinoma with a spindle cell component and osseous metaplasia	Chemotherapy; after 3 months RT (66 Gy; 30 Gy to regional nodes) followed by bilateral neck nodes dissection	Disease free 1 year after therapy
Wollina et al. (2017)	Skin of Supraclavicular area	88/F	Symptom less growth	–	Basaloid carcinosarcoma	Delayed Mohs surgery	–
Present case	Left vocal cord	59/M	Dyspnea and dysphagia	Yes (smoking and alcohol)	Basaloid squamous carcinoma with a spindle cell component	Surgery with adjuvant RT (60 Gy)	Being followed up for last 8 months (disease free)

histopathology. Our case demonstrated higher proliferative rate in spindle cell component as compared to basaloid area. Thus, adjuvant or neo-adjuvant external beam therapy treatment with radical surgical procedure seems mandatory for a disease free survival.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Statement The manuscript is based on the total laryngectomy specimen received in our department with no additional psychological, physical and financial burden for the patient.

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