SPINDLE CELL CARCINOMA OF LARYNX- A DISTINCT CLINICOPATHOLOGICAL AND HISTOLOGICAL ENTITY

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Abstract

Background:
Spindle cell carcinoma is a variant of Squamous cell carcinoma with biphasic components and more aggressive behaviour. Its rarity and histopathological pattern poses a diagnostic challenge. Early diagnosis and treatment results in decrease in local and distant metastasis

Case presentations:
Case 1 is a 71 years old lady presented with Hoarseness of voice and dyspnoea for 2 years without any risk factors. Fiber optic laryngoscopy revealed smooth polyp hanging from anterior 2/3rd of left vocal cord. Micro-laryngoscopic excision revealed Spindle cell carcinoma followed by post-operative radiotherapy and is currently alive. Case 2 is a 72 year old male presented with worsening stridor for 2 years post excision of laryngeal nodule and history of smoking and Hookah use for > 20 years. He developed dysphonia after a few months with fixed hard level 3 nodes at right side. Fibre optic laryngoscopy showed a polypoid mass extending from left vocal cord into the supraglottis. Fine needle aspiration cytology of the neck swelling confirmed the diagnosis of spindle cell carcinoma. Computerized tomography chest/abdomen showed distant metastasis. Palliative radiotherapy was given but patient died after 3 months due to loco-regional failure. Case 3 is a 35 year old male presented with history of hoarseness for 3 years with no risk factors. Fibre optic laryngoscopy sowed a 1.2 cm polypoid growth on right vocal cord. Total laryngectomy was performed and histopathology showed spindle cell carcinoma. Radiotherapy was given and patient is alive without disease with regular follow ups. Smoking and alcohol are thought to be the contributing factors causing this disease. Biphasic nature of the tumour requires pathological sampling for diagnostic confirmation. Surgery combined with radiotherapy has a better survival outcome.

Conclusion:
Spindle cell Carcinoma is a rare tumour with a tendency for loco-regional recurrence. Surgery should remain the mainstay of treatment followed by Postoperative radiotherapy for a better control.

Keywords: Larynx, Spindle cell carcinoma, Radiotherapy

Introduction:
Spindle cell carcinoma (SpCC) is more aggressive and malignant form of squamous cell carcinoma, comprising 2-3% of all laryngeal cancers [1-3]. Histologically it has a biomorphic pattern composed of both epithelial and mesenchymal components. Epithelial component comprises of squamous cell (in situ or invasive) and mesenchymal with spindle cells [4]. The carcinoma has male preponderance and occurs more commonly in 6th or 7th decade of life with a 5 year survival of 65-95% [5]. The prognosis of spindle cell carcinoma is excellent depending upon stage of the tumour and regional nodal metastasis which is seen in one quarter of the cases and distant metastasis occur in 5-15 % [6]. The most common site of distant metastasis is the lung followed by soft tissues and other viscera. The rate of local recurrence is 7-26%. In most instances, the relapses occurred within 12 months of initial treatment [7].

The calamity of the disease is the difficult diagnosis and definitive management to avoid recurrence. In this case series, we have discussed the
Clinicopathological aspects of four cases of SpCC along with its management.

**Case 1:**
A 71 year old Bengali woman presented at Head and Neck clinic, xxx. The presenting complaints were hoarseness of voice and occasional difficulty in breathing for last 2 years. She had no history of smoking or any other addiction. Her flexible fibre optic laryngoscope (FOL) examination showed a large smooth surface polyp hanging from anterior two third of the left vocal cord with both cords being symmetrically mobile. Later that month, micro-laryngoscopic excision was performed and histopathology revealed spindle cell carcinoma (Figure 1). The post-operative magnetic resonance imaging (MRI) scan showed nodularity along left vocal cord without significant neck nodal disease with AJCC stage-I (T1N0M0). She received hypo fractionated radiotherapy of 55 Grey in 20 fractions (275cGy/fraction). The patient did well and went back to her country and is alive till date.

**Case 2:**
A 72 year male presented at Head and Neck Clinic with worsening hoarseness for last two years. He had been smoking cigarettes and huqa for last 20 years. He started his treatment six months earlier with excision of laryngeal nodule performed at another centre. Histology of the surgical specimen was inconclusive at that time. He developed dysphonia again after a few months for which he was brought to our institute. Clinically, he had a hard and fixed nodal swelling at level III on right side of neck. Fibre optic laryngoscopy showed a polypoid mass extending from left vocal cord into the supraglottis. Fine needle aspiration of the neck swelling was done that confirmed the diagnosis of spindle cell carcinoma. Computerized tomography neck showed nodular thickening of the left vocal cord extending up to the anterior commissure. There is evidence of supraglottic extension with involvement of ipsilateral aryepiglottic fold, resulting in obliteration of pyriform fossa, while CT-Chest/abdomen and chest x-ray confirmed the presence of extensive pulmonary, pleural and hepatic metastatic disease (Figure 2). Meanwhile patient developed dysphnea and stridor for which emergency tracheostomy was done. Palliative radiotherapy of 20 Gy in 5 fractions was given and he died after 3 months because of progressive local and distant disease.

**Case 3:**
A 35 years old male presented at radiation oncology department with complaints of hoarseness for last 3 years. There was no history of any addiction.

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Figure 1: Low power magnification (10x) showing tumour comprising interlacing bundles and fascicles (indicated by arrow).

Figure 2: Chest X-ray showing lung metastasis
reported. Fibre optic laryngoscopy showed a 1.2 cm polypoid growth on right vocal cord. Lymph nodes were not palpable. Excision biopsy done at another centre showed high grade sarcoma. CT neck also showed T3 disease because of para-glottic extension with bilateral tiny sub centimetre radiologically insignificant lymph nodes. Thus, a total laryngectomy was performed and biopsy revealed spindle cell carcinoma. On gross examination larynx contained a polypoid well circumscribed tumour measuring 1.2 cm x 1.0 cm x 0.6 cm, present on the right side involving the glottic area and extending into the sub-glottis. Histological examination revealed a tumour showing foci of squamous cell carcinoma in situ carcinoma with focal invasive component (Figure 3). Bulk of the tumour was formed by spindle cells with elongated nuclei and these cells were negative for CK5/6. But CK5/6 was positive in epithelial component.

These findings favoured carcinosarcoma (Spindle Cell Carcinoma). The tumour invades into the para-glottic space. All resection margins were free of tumour. A radiation dose of 50 Gy in 20 fractions was given to neck including primary and bilateral cervical nodes. The patient has maintained regular follow up visits and is free of disease till date.

Discussion
Spindle cell carcinoma (SpCC) is a rare and highly malignant variant of squamous cell carcinoma. It has been referred to by a number of terms such as pseudo carcinoma, pleomorphic carcinoma, collision tumours, combination tumours, composition tumour, Lane tumour, polypoid carcinoma [8]. This is explained by the fact that the true nature of the disease has remained controversial for long time. The incidence is 2-3% of all laryngeal cancers. The real cause, like most of the other carcinomas, is not known. However, the risk factors include cigarette smoking and alcohol consumption. Many cases reported history of radiation exposure but there is no definitive evidence to prove this hypothesis [9-11].

The spindle cell carcinoma more commonly involves glottis than any other sub sites in larynx. Therefore clinically patients present with complaints of hoarseness, dysphonia, dysphagia and foreign body sensations in the throat. Mostly tumours are pedunculated, exophytic or polypoid in clinical exam causing obstructive respiratory symptoms at an early stage leading to prompt diagnosis and treatment of the tumour. One quarter of patients presents with nodal metastasis and distant metastasis is seen in 5-15%. One of our patients presented not only with nodal metastasis but also with extensive lung and liver metastasis which signify the appropriate staging work-up before the start of radical treatment.

Pathological examination of the biopsy specimen leads to definitive diagnosis. The tumour has a biphasic pattern composed of both carcinomatous and sarcomatoid component. Typically, a confirmation is achieved by the observation of surface epithelial cells with underlying sarcomatoid spindled-shaped neoplastic proliferation. In case of surface ulceration or denuded epithelium the dignity remains undefined and diagnosis of spindle cell carcinoma is difficult to render. The pathogenesis of SpCC is controversial.
and its derivation as remained ambiguous till date. Although there are no large mass studies available that suggests the epithelial origin of the tumour but a few histological theories are certain in favour of it including 1) its location and occurrence are at the site of squamous epithelium 2) neoplastic mesenchymal spindle cells occurring in association with nests of benign or malignant squamous epithelium 3) there polyploid nature 4) Immunohistochemical analysis shows reactivity to epithelial antigen. However, there are many evidences that demonstrate metastasis of both sarcomatoid and epithelial component in a single lymph node or separate metastasis of individual component to various sites, suggesting that sarcomatoid spindle cells are not just a metaplastic reaction to overlying malignant epithelium rather it's an independent morphology fully capable of having its own natural course.

In addition to histological studies, immunohistochemistry also demonstrates two distinct pathologies. The epithelial component is positive for a panel of keratin markers (AE1/AE3 "CK1"), epithelial membrane antigen, K1 and K18 and the mesenchymal component is positive for variable smooth muscle actin, S-100 protein, muscle specific actin, desmin-D33 and desmin-DR11. But both components are positive for vimentin, however, it's more expressed in sarcomatoid component of the tumour or in those epithelial cells that shows metaplastic mesenchymal transformation while losing their ability to react with epithelial markers. p53 is an epithelial cell proliferation and differentiation marker and is important in confirming the diagnosis of SpCC of head and neck region.

SpCC is staged according to AJCC TNM staging system based on tumour size and presence or absence of loco-regional lymph node and distant metastasis. There is no consensus available yet on treatment modality of SpCC. The goals of the treatment include cancer cure, organ preservation, good voice quality and low risks of complications. Surgery and radiation are the two treatment options available but surgery remains the mainstay of the treatment. The choice depends on stage and location of tumour. For small stage tumours T1 and T2 polypectomy, microlaryngoscopic excision or vocal cord stripping followed by adjuvant radiotherapy is considered the treatment of choice. However, L.D.R. Thompson et al, in his study showed that patients who were managed by surgery alone had a better outcome than the patients who were treated with surgery and adjuvant radiotherapy. The group of patients that was treated with radiation alone and those that were treated with radiation and surgery both had a better survival (3.6 years) compared to those that were treated with surgery alone (1.9 years). Theoretically, some studies also show that the use of radiation therapy in SpCC is not suggested because mesenchymal component of the disease is highly resistant to radiation. For advance, high stage (T3 and T4) and recurrent tumours a more aggressive approach is adapted including hemi-laryngectomy or total laryngectomy with or without lymph node dissection followed by post-op radiotherapy [12-15]. In one of our case reports advance SpCC with extensive liver and lung metastasis is discussed in which salvage surgery and palliative radiotherapy was adopted that showed survival of 2 years. Radiation alone might not be the control of the disease but when combined with salvage surgery it has a survival of 79-98% in recurrent diseases.

Conclusion:
Spindle cell carcinoma is a rare but aggressive variant of squamous cell carcinoma. As there are chances of local as well as distant metastatic disease so cross sectional imaging of lungs and liver should be incorporated in routine staging work-up. Origin of the tumour remains controversial so is its definitive mode of treatment. With our case series we conclude that surgery must be the mainstay of treatment but adjuvant radiation should be combined to have good loco-regional controls.

Abbreviation:
SpCC: Spindle cell carcinoma, FOL: Fibre-optic laryngoscopy, MRI: Magnetic resonance imaging, CT: Computerized tomography, Gy: Grey
References:


