International Journal of Otorhinolaryngology and Head and Neck Surgery
Ramakrishnan R et al. Int J Otorhinolaryngol Head Neck Surg. 2023 Nov;9(11):891-895
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20233221

Case Report

Spindle cell carcinoma of the larynx: a rare entity

Rajika Ramakrishnan[1], Kiran Natarajan[1]*, Sreenivas Kamath[1], Susruthan[2], Mohan Kameswaran[1]

[1]Madras ENT Research Foundation, Raja Annamalaipuram, Chennai, Tamil Nadu, India
[2]Susrutha Diagnostics, Kundrathur road, Madhananthapuram, Porur, Chennai, Tamil Nadu, India

Received: 07 July 2023
Accepted: 18 October 2023

***Correspondence:**
Dr. Kiran Natarajan,
E-mail: kirannatarajan2001@yahoo.co.in

ABSTRACT

Squamous cell carcinoma (SCC) is the commonest malignancy encountered in the larynx in the Indian population. Spindle cell carcinoma is an extremely rare malignant tumor and is a variant of SCC with a mesenchymal like malignant cell component. This is a case report of a 58 years old patient who presented with hoarseness of voice of 7 months duration. He was diagnosed to have a right vocal cord polypoidal growth with mobile vocal cords. He underwent direct laryngoscopy and biopsy of the lesion which was reported as spindle cell neoplasm/inflammatory myofibroblastic tumor (IMT). Immunohistochemistry (IHC) was carried out and confirmed the diagnosis of inflammatory myofibroblastic tumor. He was doing well and the follow up videolaryngoscopic examinations and PET CT were normal. At subsequent follow-up 19 months later, he was found to have a recurrent right vocal cord lesion. Direct laryngoscopy and biopsy was repeated along with laserization of the right vocal cord. Histopathology was reported as spindle cell malignant neoplasm. Immunohistochemistry was reported as spindle cell carcinoma. He was then sent for radiation therapy. The patient responded well to radiation and is tumor free at last follow-up. He has been advised regular follow-ups. Spindle cell carcinoma is an extremely rare laryngeal malignancy. It typically originates in the glottis. The treatment for spindle cell carcinoma includes surgery, radiation or a combination of these modalities. Its prognosis is worse than squamous cell carcinoma and patients require close follow-ups.

Keywords: Laryngeal spindle cell carcinoma, Radiation therapy, Surgery

INTRODUCTION

Spindle cell carcinoma (SpCC) represents 2 to 3% of all laryngeal tumors and 1% of head and neck cancers.[1] It is a variation of squamous cell carcinoma, which also includes a mesenchymal-like malignant spindle cell component and is a monoclonal epithelial neoplasm.[2] It predominantly occurs in males older than 65 years.

Smoking and excess alcohol consumption are the known risk factors. Patients typically have hoarseness of voice as the most frequently affected site is the glottis in 70% of patients.[2] The tumor usually has a polypoid appearance. On histopathological examination, laryngeal SpCC represents a biphasic tumor, composed of a squamous cell carcinoma and a malignant spindle cell component with mesenchymal appearance, but of monoclonal epithelial origin.[3]

Surgical excision is the mainstay of treatment and radiotherapy is indicated in recurrent cases or in more extensive tumors. Histopathology and immunochemistry help clinch the diagnosis.

On immunohistochemistry, tumor cells express epithelial and mesenchymal markers.[2]

The prognosis of laryngeal SpCC is worse than that of laryngeal SCC; hence patients have to be advised regular follow-ups.

CASE REPORT

This was a case report of a 58 years old male who presented with hoarseness of voice of 7 months duration. He was diagnosed to have a large right vocal cord polypoidal growth involving the anterior one thirds of the cord with mobile vocal cords (Figure 1). There was no palpable lymphadenopathy. He underwent direct laryngoscopy and biopsy of the lesion which was reported as polypoidal fragment lined by squamous epithelium with underlying lesion composed of spindle shaped cells showing mild atypia in a myxoid background. Necrosis/atypical mitosis were not seen. The diagnosis was spindle cell neoplasm/inflammatory myofibroblastic tumor (Figure 2).

Immunohistochemistry was carried out and confirmed the diagnosis of inflammatory myofibroblastic tumor. CD 34 was focally positive, ALK Negative, Ki 67 positive in 40% of lesional cells, Vimentin was positive, SMA was negative and S100 was negative. At follow-up a PET CT was done which was reported to be normal with no evidence of any enhancing lesion in the surgical bed (Figure 3). Subtle nodularity was noted in the right vocal cord with no abnormal metabolic activity- likely post-operative changes. On MRI screening, there was no evidence of a residual lesion. No significant metabolically active cervical lymphadenopathy was noted. There was no evidence of abnormal increased FDG accumulation in any other visceral organs or elsewhere in the head and neck (Figure 4). At subsequent follow-up 19 months later, he was found to have a recurrent right vocal cord growth involving the anterior one-thirds of the vocal cord with extension to the anterior commissure (Figure 5). Direct laryngoscopy and biopsy was repeated along with laserization of the right vocal cord with KTP/532 laser. Histopathology was reported as ulcerated stratified squamous epithelium with subepithelium showing a neoplasm composed of sheets of malignant spindle cells with pleomorphic hyperchromatic nuclei in a myxoid stromal background; atypical mitosis were seen – suggestive of malignant spindle cell neoplasm (Figure 6). Immunohistochemistry was done for further subtyping. IHC was reported as cytokeratin and vimentin positive, ALK-1 negative and reported as spindle cell carcinoma. He was then sent for radiation therapy.

The patient presented with a right vocal cord growth which was diagnosed as inflammatory myofibroblastic tumor. He was advised periodic follow-ups and during each visit, the videolaryngoscopic appearance of the vocal cord was found to be normal. A follow-up was done with PET CT which was reported to be normal. Nineteen months later, when he had a recurrent right vocal cord growth and a re-biopsy was done, the diagnosis of SpCC was confirmed. Due to the early detection of the tumor, the patient underwent surgical excision with KTP/532 laser and radiotherapy (IMRT) and has responded well to the treatment. He is tumor free at last follow-up six months post RT and has regained a good voice quality. He has been advised regular follow-ups.

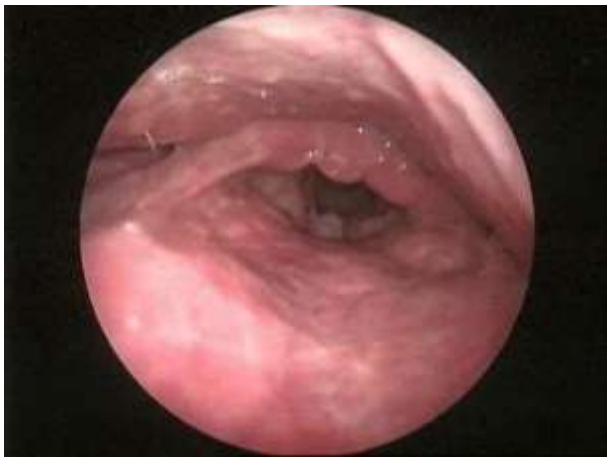

Figure 1: Videolaryngoscopy showing right vocal cord lesion with mobile vocal cords.

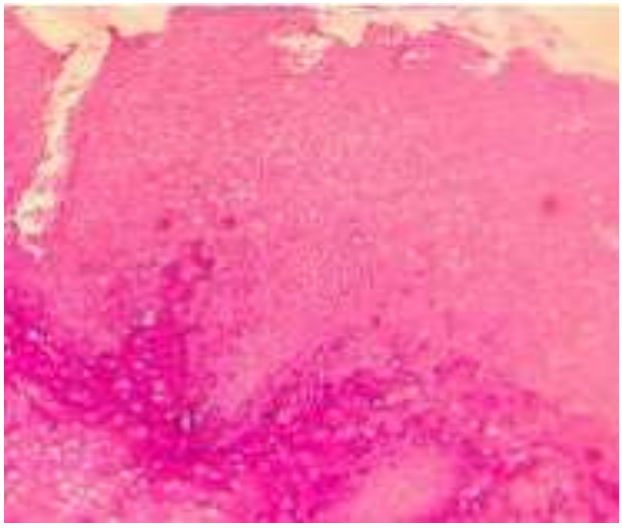

Figure 2: Histopathology reported as spindle cell neoplasm/inflammatory myofibroblastic tumor.

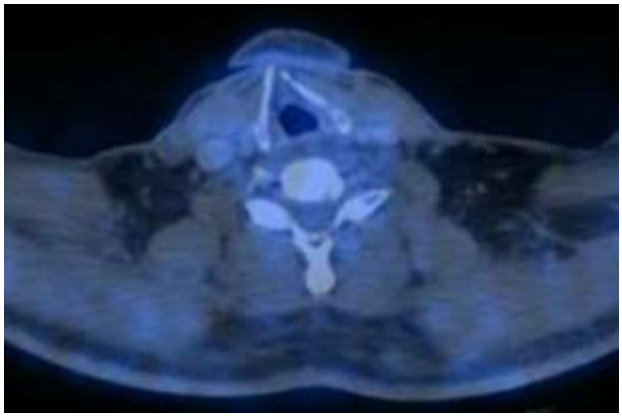

Figure 3: Post-operative PET CT showing normal larynx and neck.

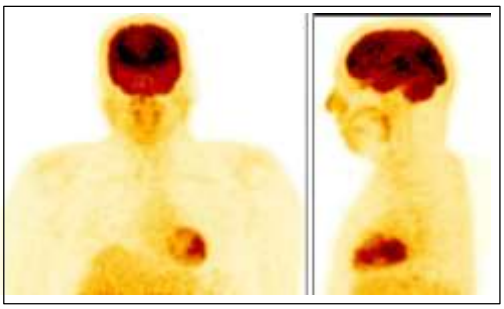

Figure 4: Post-operative normal PET CT scan.

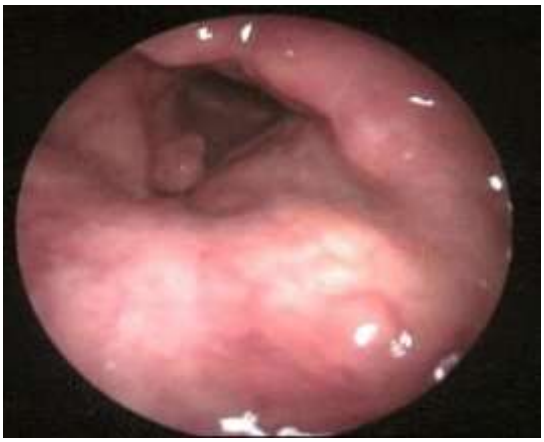

Figure 5: Recurrent lesion right vocal cord and anterior commissure.

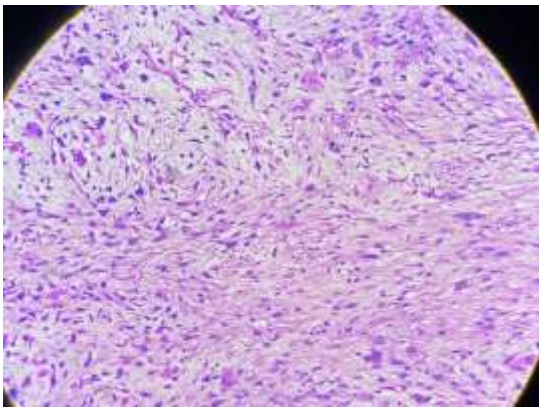

Figure 6: Histopathology suggestive of malignant spindle cell neoplasm.

DISCUSSION

SpCC is a rare malignancy of the larynx and comprises 1-3% of all laryngeal neoplasms.[4] It was first reported in the literature in 1933 by Figi, as 'larynx sarcoma'.[5] The oral cavity is the next most frequent site after the larynx, with the tumor affecting the lower lips, tongue and buccal mucosa.[6] The majority (>95%) of laryngeal carcinomas are squamous cell carcinomas (SCCs). Laryngeal SpCC is reported to occur predominantly in males older than 65 years. The male: female ratio has been reported to be 12:1.[7] The etiology remains unknown, but it is associated with smoking and excess alcohol consumption.[8] Although radiotherapy is not thought to be a causative factor, tumors arising in irradiated patients may have a more aggressive course.[2] The most frequently affected site in the larynx (70%) is reported to be the glottis, and patients present with hoarseness of voice.[9] Dyspnea, cough, and dysphagia may occur in large lesions.[7] SpCC of the larynx following pulmonary SpCC has been reported.[10]

Laryngeal SpCC typically presents with a polypoid appearance.[11] When these tumors involve the true vocal cords, they may be misdiagnosed as a laryngeal polyp.[12] The imaging finding of laryngeal SpCC has no specificity. A thorough histopathological and immunohistochemical evaluation is vital to ensure the correct diagnosis. SpCC is a variant of SCC, which also includes a mesenchymal-like malignant spindle cell component.[2] With the advances in pathological techniques, it has been proven that SpCC of the larynx is a monoclonal epithelial neoplasm.[13] The spindle cells evolve from the SCC component by undergoing epithelial-mesenchymal transition.[14] Two distinct epithelial-derived components include squamous cells and sarcomatoid spindle cells.[2] The spindle cells are arranged in storiform pattern, solid, or fascicular pattern, and may vary from bland to pleomorphic cytology. Hypocellular lesions with mild atypical cells can lead to misdiagnosis of the tumor.[1] The squamous-cell component typically expresses AE1/AE3, CK1, CK1, 8, 9, epithelial membrane antigen KI and K18, and p63. The spindle-cell component typically expresses vimentin and other mesenchymal markers.[2] For spindle cell carcinomas with poorly differentiated epithelial tumor components, it has been shown by Lewis et al. that p53, a transcription factor that is important for epithelial proliferation and differentiation, is particularly useful for diagnosing SpCC of the head and neck region.[7]

The differential diagnosis of laryngeal SpCC includes a number of benign and malignant conditions, such as inflammatory myofibroblastic tumor, fibrosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, osteosarcoma, mesenchymal chondrosarcoma, Kaposi's sarcoma, angiosarcoma, synovial sarcoma, malignant melanoma, fibromatosis, leiomyoma, nodular fasciitis, and reactive epithelial proliferations.[15] The differential diagnosis of SpCC and IMT can be difficult for the pathologist.[3] The lack of any inflammatory cells rules out the possibility of inflammatory myofibroblastic tumor.[16] Immunohistochemistry is crucial in differentiating the two entities - for SpCC , cytokeratin and vimentin positive, ALK-1 negative and for IMT, ALK-1 and vimentin positive, cytokeratin negative. [3]

The goals of treatment include cure of the cancer, laryngeal preservation, good post-operative voice quality and a low risk of complications.[15] Surgical excision of SpCC with a wide margin is the primary treatment as the tumor has low radiochemosensitivity.[2] Polypectomy and wide local excision can completely eliminate the tumor because of noninvasion of the underlying stroma at an

early stage.[7] Endoscopic microsurgery using cold knife and/or KTP laser has been reported.[16] Stage T2 tumors can be managed conservatively with irradiation which helps preserve the patient's voice.[7] In our patient, the KTP/532 laser was useful to completely excise the tumor and radiotherapy was subsequently given as it was a recurrent lesion. Tumors that are staged 3-4 can be treated with local resection, partial laryngectomy, total laryngectomy with or without lymph node dissection followed by a combination of radiation and chemotherapy.[7]

The prognosis of laryngeal SpCC is worse than that of laryngeal SCC as it is a highly malignant tumor and is determined by tumor subsite, stage, and tumor size.[2] Spector et al. have reported that laryngeal SpCC has a high local recurrence rate. [2] Dubal et al. reported that the involvement of regional lymph nodes and distant metastases is relatively rare.[2] The five-year survival rate is reported to be 65-95%.[3] The majority of laryngeal spindle cell tumors are detected early in stages T1 and T2 and are therefore associated with a better prognosis. Low tumor staging, glottic location, vocal cord mobility, absence of previous irradiation indicate a better prognosis.[3] Poor prognostic factors include high tumor staging, large tumors (>3 cm) with a predominance of epithelial component, nonglottic tumors, vocal cord fixity, previous radiotherapy, metastasis to regional lymph nodes and distant metastasis.[7] Improved survival rates have been found to be associated with a low level of cytokeratin expression.[3] A long-term term follow-up is essential after treatment.

CONCLUSION

Laryngeal SpCC is a rare malignancy seen in otolaryngology practice. It poses a significant diagnostic challenge. The clinical appearance, age, gender, history of smoking/alcohol consumption help points towards the diagnosis. For confirmatory diagnosis, histopathology with immunochemistry using epithelial and mesenchymal markers is mandatory. Owing to the aggressive nature of the disease, a high index of suspicion is essential as the presentation may be like a laryngeal polyp. Treatment involves surgical excision; radiotherapy is necessary in recurrent or more extensive disease. Rarely, more aggressive surgery such as total laryngectomy may be required. Understanding the biology of this tumor is essential for appropriate management.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Zghal M, Makni S, Mellouli M, Bouhamed M, Chaari C, et al. Spindle Cell Squamous Cell Carcinoma of The Larynx: A Report of Three Cases. Clin Oncol Res. 2020;3(11):3-4.
2. Chen L, Chen Q, Li C, Zhou L, Wang S, Zhang M. Clinical Analysis of Laryngeal Spindle Cell Carcinoma. ORL J Otorhinolaryngol Relat Spec. 2020;82(6):310-7.
3. Völker HU, Scheich M, Höller S, Ströbel P, Hagen R, Müller-Hermelink HK, et al. Differential diagnosis of laryngeal spindle cell carcinoma and inflammatory myofibroblastic tumor--report of two cases with similar morphology. Diagn Pathol. 2007;2:1.
4. Stefani A, Boffano P, Bongioannini G. Review of histologic and immunohistochemical features of spindle cell carcinomas (carcinosarcomas) of the larynx. J Craniofac Surg. 2014;25(5):e430-3.
5. Bostanci A, Ozbilim G, Turhan M. Spindle Cell Carcinoma of the Larynx: A Confusing Diagnosis for the Pathologist and Clinician. Case Rep Otolaryngol. 2015;2015:831835.
6. Roy S, Purgina B, Seethala RR. Spindle cell carcinoma of the larynx with rhabdomyoblastic heterologous element: a rare form of divergent differentiation. Head Neck Pathol. 2013;7(3):263-7.
7. Boamah H, Ballard B. A case report of spindle cell (sarcomatoid) carcinoma of the larynx. Case Rep Med. 2012;2012:370204.
8. Rutt AL, Mintz I, Jackson-Menaldi C, Johns M, McHugh JB, Rubin AD. Spindle cell carcinoma of the larynx presenting as a vocal fold cyst. J Voice. 2014;28(4):524-9.
9. Miyahara H, Tsuruta Y, Yane K, Ogawa Y. Spindle cell carcinoma of the larynx. Auris Nasus Larynx. 2004;31(2):177-82.
10. Mamanov M, Yener M, Yilmaz M, Akil F, Ibrahimov M, Karaman E. Spindle cell carcinoma of the larynx following spindle cell pulmonary carcinoma: second primary or metastasis? J Craniofac Surg. 2012;23(6):1935-6.
11. Gerry D, Fritsch VA, Lentsch EJ. Spindle cell carcinoma of the upper aerodigestive tract: an analysis of 341 cases with comparison to conventional squamous cell carcinoma. Ann Otol Rhinol Laryngol. 2014;123(8):576-83.
12. Randall G, Alonso WA, Ogura JH. Spindle cell carcinoma (pseudosarcoma) of the larynx. Arch Otolaryngol. 1975;101(1):63-6.
13. Thompson LD, Wieneke JA, Miettinen M, Heffner DK. Spindle cell (sarcomatoid) carcinomas of the larynx: a clinicopathologic study of 187 cases. Am J Surg Pathol. 2002;26(2):153-70.
14. Viswanathan S, Rahman K, Pallavi S, Sachin J, Patil A, Chaturvedi P, et al. Sarcomatoid (spindle cell) carcinoma of the head and neck mucosal region: a clinicopathologic review of 103 cases from a tertiary referral cancer centre. Head Neck Pathol. 2010;4(4):265-75.
15. Thompson LD, Wieneke JA, Miettinen M, Heffner DK. Spindle cell (sarcomatoid) carcinomas of the larynx: a clinicopathologic study of 187 cases. Am J Surg Pathol. 2002;26(2):153-70.

16. Barber SR, Kopach P, Genega EM, Carroll TL. Low grade spindle cell sarcoma of the true vocal folds, Otolaryng Case Rep. 2017.

Cite this article as: Ramakrishnan R, Natarajan K, Kamath S, Susruthan, Kameswaran M. Spindle cell carcinoma of the larynx: a rare entity. Int J Otorhinolaryngol Head Neck Surg 2023;9:891-5.