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Case Report

Pathology Section

LMP1-Positive Composite Tumour of Larynx: A Diagnostic Quandary

KAUSALYA KUMARI SAHU[1], SARASWATHY SREERAM[2], PANDURANGA KAMATH[3], VIJENDRA SHENOY[4], NIMI MOHAMMED ALI[5]

ABSTRACT

Malignant spindle cell tumours of the larynx are rare, of which the most common are Spindle Cell Squamous Carcinomas (SCSCs). Sarcomas are extremely infrequent in the larynx. Composite tumours, further, are quite unheard of, except for rare case reports. This case report describes a spindle cell malignancy of the larynx in an elderly male, which posed a diagnostic difficulty due to its unique morphological and immunohistochemical features. The tumour was superficial, polypoidal with the proliferation of malignant spindle cells and abundant mitoses under an ulcerated epithelium. Occasional squamous cell rests with keratin pearls were present. Spindle cells were strongly immunoreactive for vimentin, smooth muscle actin and squamoid cells were p63 positive. Desmin was negative. The dilemma in diagnosis was of a SCSC with smooth muscle differentiation against a composite tumour. The tumour also turned out to be positive for Epstein Barr Virus Latent Membrane Protein-1 (EBV-LMP1), establishing a noteworthy association.

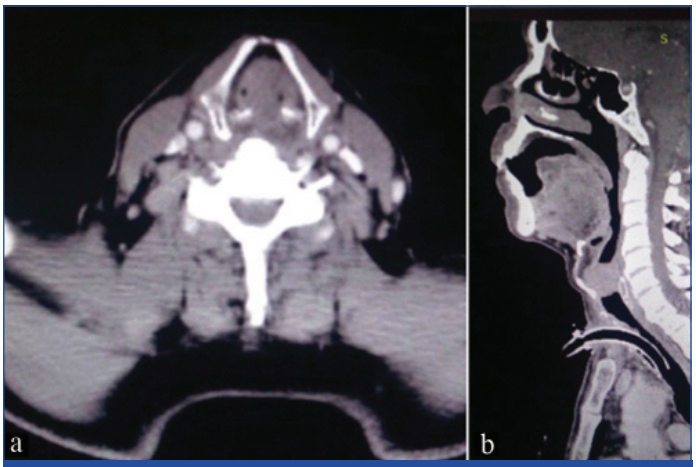
Keywords: Laryngeal malignancy, Leiomyosarcoma, Spindle cells, Squamous cell carcinoma

CASE REPORT

A 60-year-old man presented to Department of Otorhinolaryngology with hoarseness of voice since one year, dysphagia and dyspnea since two months and noisy breathing since two weeks. He had undergone emergency tracheostomy for stridor in another hospital a week before. He gave a history of smoking 15 cigarettes per day for 40 years, which, he stopped four years back. He denied the history of fever, loss of weight, alcohol abuse and previous irradiation. Cervical lymph nodes were not palpable. Indirect laryngoscopy revealed a globular mass (1×1 cm) arising from the right false cord.

Computed tomography showed a heterogeneously enhancing mass in the right false cord measuring 27×25×23 mm causing complete obliteration of the laryngeal air column. Right true cord was not seen separately from the lesion. Posteriorly, the lesion was abutting cricoid and posterior laryngeal wall with loss of fat planes. Laterally, lesion was abutting both arytenoids, both aryepiglottic folds and bilateral cornua of hyoid. Anteriorly, lesion was abutting body of hyoid. There was no evidence of bony erosions or invasion of laryngeal cartilages. The lesion was causing complete airway obstruction at the level of glottis. [Table/Fig-1]. Biopsy showed a tumour composed of spindle cells intermingled with squamoid cells and areas of necrosis. It was reported as SCSC [Table/Fig-2a-c]. Confirmation with Immunohistochemistry (IHC) was not done on biopsy since tumour tissue was scant and inadequate for a panel of markers. Also, malignancy was unequivocally proven. Investigations for distant metastasis were performed and proved negative. Total laryngectomy was done.

The resected specimen measured 9×7×5 cm with a sessile, polypoid growth in the right vocal cord measuring 2.5×1.3 cm. Tumour was 4 cm and 2.5 cm away from epiglottic and tracheal resected margins, respectively [Table/Fig-2d,e]. Microscopy showed malignancy composed of pleomorphic spindled cells in fascicles with moderate eosinophilic cytoplasm, hyperchromatic to vesicular nuclei, some with prominent nucleoli [Table/Fig-2f,g]. Mitotic rate was 20 per ten HPF [Table/Fig-2g]. Tumour was lined by ulcerated, thinned out squamous epithelium [Table/Fig-2h]. Among the spindle cells were scattered, cells with epithelioid features. An occasional keratin pearl was seen. [Table/Fig-2i]. Lymphovascular and perineural invasion were not identified. Surgical pathology was reported as malignant spindle cell tumour and IHC panel was ordered for confirmation.

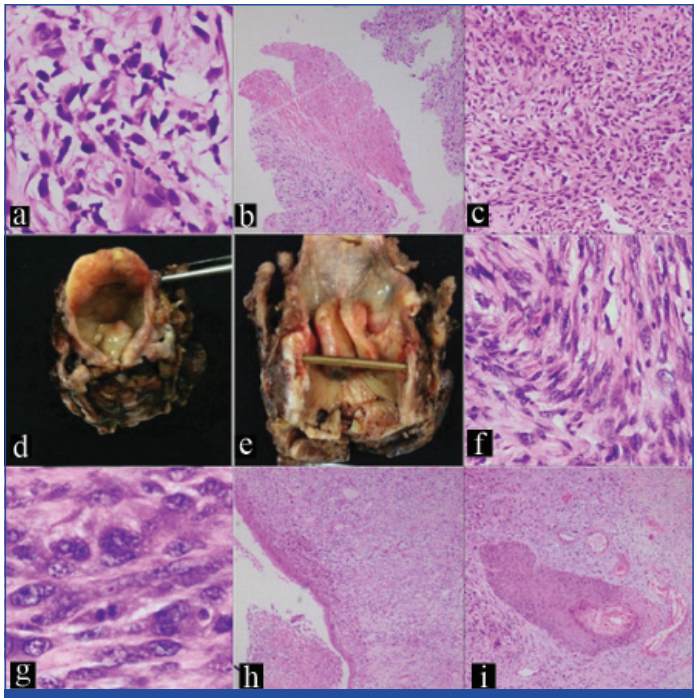


[Table/Fig-1]: Computed tomography of head and neck. Glottic tumour (a-Coronal view; b-sagittal view).

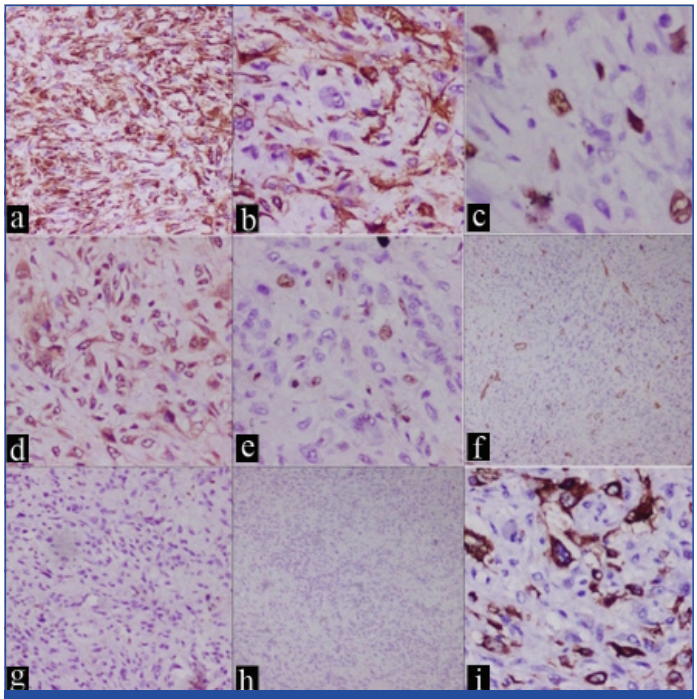
Immunohistochemically, 95% tumour cells were strongly positive for vimentin [Table/Fig-3a] and 80% for Smooth Muscle Actin (SMA) [Table/Fig-3b]. However, 20% of cells with epithelioid appearance, which stained negative for SMA, were positive for p63 [Table/Fig-3c]. EBV-LMP1 was strongly positive in the cytoplasm of tumour cells [Table/Fig-3d]. Ki-67 proliferation index was 20% [Table/Fig-3e]. Beside these, the tumour cells were negative for S100 [Table/Fig-3f], CD34 [Table/Fig-3g] and desmin [Table/Fig-3h]. Based on the morphological and IHC features, SCSC with smooth muscle differentiation could not be ruled out. Pancytokeratin showed positivity similar to p63 only in the squamoid cells [Table/Fig-3i]. The final diagnosis given was combined leiomyosarcoma (LMS) with SCC based on the IHC pattern. The tumour was given a pathological stage of T2 Nx according to the American Joint Committee on Cancer (AJCC) 2017 staging [1]. Surgical margins were free of tumour. The postoperative period was uneventful. The patient was discharged on the tenth postoperative day. Radiotherapy was not administered.

DISCUSSION

Laryngeal malignancies, histologically, are mostly SCCs [2]. Spindle cell morphology of tumour cells is rare and most frequently seen in SCSC (0.5% of all laryngeal cancers) [3]. However, extremely rarely,



[Table/Fig-2]: Laryngeal biopsy: a) Hyperchromatic spindle cells (20X); b) Necrosis (4X); c) Intersecting fascicles of cells with squamous differentiation (20X); d&e) Laryngectomy showing polypoid growth; f-i) Histopathology; f) Spindle sells with moderatelly pleomorphic hyperchromatic nuclei (20X); g) Numerous mitotic figures (40X): h) Lining squamous epithelium with dysplasia and ulceration (10C); i) Reactive squamous islands within tumour (10X). All stained with Haematoxylin and Eosin



[Table/Fig-3]: Immunohistochemistry: a) Vimentin strongly positive in 85% of cells (10X); b) SMA: Strongly positive in 80% of cells (40X); c) p63 in 25% of tumour cells (40X), d) EBV-LMP1 positive (20X); e) Ki-67 20% (20X); f) CD34 negative (4X); g) S100 negative (10X); h) Desmin negative (4X); i) Pan CK positive in 30% tumour cells (20X).

sarcomas can occur in the larynx and show characteristic malignant spindle cell proliferation [4]. Composite tumours of the larynx are rare and most of them are a combination of SCC and small cell/neuroendocrine carcinoma. Globally, very few cases have been published so far to the best of present knowledge, out of which the most recent was in 2012 [5]. This case was a composite LMS with SCC, which is extremely unique, as only five cases have been published till date [6-9].

In this case, differential diagnoses were LMS with squamous differentiation, SCSC with smooth muscle differentiation or composite tumour of LMS with SCC. Rare differentials of myofibroblastic sarcoma and melanoma were also considered. SCSC is composed of conventional SCC (in-situ or invasive) along with malignant spindle-shaped or pleomorphic component. Squamous component is scant to nil in some SCSCs, especially when the surface is ulcerated. However, the occasional keratin pearl seen in one of the ten tumour sections in this case could be part of conventional SCSC. Surface epithelium shows variable dysplasia along with intimate association of tumour cells. Heterologous elements like bone and cartilage, benign or malignant, can be seen. Tumour cells in SCSC co-express CK, p63 and SMA on IHC [2].

LMS is exceptionally scarce and comprises of <0.1% of laryngeal cancers. Less than 100 cases have been published so far [3]. Only five cases of composite or metachronous tumours of larynx with SCC have been reported worldwide. Three of these were composite LMS whereas others were chondrosarcoma and adenocarcinoma. In all, the two composite tumours were present as separate foci [6-9].

Mesenchymal intermediate filaments like vimentin, desmin, SMA and muscle-specific actin can be seen in SCSCs. SMA positivity in SCSCs is usually focal and can be present in up to 40% of cases [2]. However, strong positivity in 80% of cells, like in this case, is not surmised in SCSCs. h-caldesmon is considered a more specific marker for LMS. This antibody marker was not available in the institution where this case was reported. LMS can show focal CK staining. The clinching diagnostic feature in this case, however, was the exclusive reverse staining pattern of CK and p63 with that of SMA. The same tumour cells in SCSC stain for both p63, CK and SMA [2]. Therefore, a diagnosis of LMS with SCC was given.

In the larynx, a possible role of EBV has been reported in SCCs [10]. Rare cases of EBV-associated smooth muscle tumours of larynx in immunocompromised have been published [10]. The LMP-1 positivity in this case could just indicate a latent co-existence of this virus in airway. Nonetheless, LMP-1 is neither specific nor sensitive for EBV, and the gold standard test Epstein Barr encoding region in-situ hybridization (EBER-ISH) was not done in this case due to financial constraints [11].

Wide surgical excision along with radical neck lymph node dissection and radiotherapy is the mode of treatment for SCSC [2]. LMS has been treated with endoscopic resection, partial and total laryngectomy, however, due to rarity of cases, there is no general consensus [6]. The line of management of composite tumours is not known due to same reason. Individual case evaluation is needed for optimal therapeutic decisions.

CONCLUSION

The vastness of differential diagnosis of spindle cell malignancies of larynx is exasperating for the pathologist. A biopsy diagnosis of this entity is difficult. IHC is usually the final resort to provide a solution to the diagnostic conundrum. In fact, the diagnosis is implausible even in resected specimens without resorting to IHC. Adding to the arduousness is the overlapping features in IHC as well. One such case is described here, where a final diagnosis was enigmatic despite doing the ancillary tests. A unique case of laryngeal composite tumour of LMS and SCC with LMP1 positivity, posing a diagnostic dilemma, resolved with IHC, is reported here. Presence of EBV-LMP1 brought out a unique, perhaps causal, association in this case.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Pathology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.
2. Assistant Professor, Department of Pathology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.
3. Professor, Department of Otorhinolaryngology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.
4. Professor and Head, Department of Otorhinolaryngology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.
5. Junior Resident, Department of Otorhinolaryngology, Kasturba Medical College, Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Saraswathy Sreeram,
Assistant Professor, Department of Pathology, Kasturba Medical College, Lighthouse Hill Road, Hampankatta,
Mangalore-575001, Karnataka, India.
E-mail: swameeram@gmail.com

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