Case Report

Spindle Cell (Sarcomatoid) Carcinoma of the Larynx
-- Case Report --

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Abstract

A 56 year old male patient presented with a history of recurrent attacks of progressive hoarseness and stridor for the last 9 months, he underwent six laryngeal surgery and the biopsy results were negative for malignancy except the last pathology report which revealed the diagnosis of spindle cell carcinoma of the larynx confirmed by immunohistochemistry. The patient refuses radiotherapy and went to India where they failed to diagnose the disease. The presented case demonstrates that spindle cell carcinoma or sarcomatoid carcinoma is very rare malignant tumor of the larynx but should be suspected in spindle cell tumours of the larynx and awareness of the pathologist to the unusual immunohistochemical presentation of this tumor with the use of expanded immunohistochemical markers panel.

Key words: Larynx, Sarcomatoid Carcinoma, Spindle cell carcinoma, Spindle squamous cell carcinoma, Head and neck tumors.

Introduction

Spindle cell (sarcomatoid) carcinoma of the larynx is a rare tumor and comprises 2% to 3% of all laryngeal cancers. (1) Squamous cell carcinoma is the most common malignant carcinoma of the larynx, and spindle cell (sarcomatoid) tumor is considered a highly malignant variant of squamous cell carcinoma. Spindle cell carcinoma is considered to be a biphasic tumor that is composed of a squamous cell carcinoma (in situ or invasive) and spindle cell carcinoma with sarcomatous appearance. (2) Although it is generally accepted that spindle cell carcinoma is a monoclonal epithelial neoplasm (3-7), and the sarcomatous components are derived from squamous epithelium with divergent mesenchymal differentiation (8), the diagnosis, classification and management of this tumor infrequently may become subject matter deluded of its histological variety in sarcomatous components. These sarcomatous components commonly resemble to fibrosarcoma or malignant histiocytoma (9,10), and while rare, foci resembling to chondrosarcoma and/or osteosarcoma differentiation may be observed. (11) Laryngeal spindle cell (sarcomatoid) carcinomas (LSCSCs) have been the focus of a great deal of discussion over the years, harkening back to the original descriptions of these tumors. (12,13) Over the years many terms have been applied to the confounding neoplasm under consideration (Table 1). These tumors were considered to be collision tumors, combination tumors, or composition tumors. It was believed that the absence of mingling of the stromal and epithelial elements militated against their being transformed carcinomas; therefore, the spindled process was reactive or reparative. (12,13,14,15) With the passage of time leading to a better understanding of these malignant tumors, the medical community (as reflected in the

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literature) has come to recognize this peculiar, morphologically biphasic tumor process as a carcinoma that has surface epithelial changes (in situ to invasive carcinoma) and an underlying spindle-shaped neoplastic proliferation. When the malignant surface epithelium is histologically evident, the diagnosis of a spindle cell (sarcomatoid) carcinoma is made with confidence. However, when the surface epithelium is ulcerated or denuded, the correct diagnosis is more difficult to render.\textsuperscript{13,15-31}

<table>
<thead>
<tr>
<th>Table 1. Terms used for spindle cell (sarcomatoid) carcinoma</th>
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<tr>
<td>Carcinosarcoma</td>
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<td>Pseudosarcoma</td>
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<td>Pseudocarcinoma</td>
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<td>Pseudocarcinosarcoma</td>
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<td>Pseudosarcomatous carcinoma</td>
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<tr>
<td>Carcino(pseudo)sarcoma</td>
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<td>Spindle cell carcinoma</td>
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<td>Spindle cell variant of squamous carcinoma</td>
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<td>Squamous cell carcinoma with pseudosarcoma( Lane tumor )</td>
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<td>Squamous cell carcinoma with sarcoma-like stroma</td>
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<td>Bizarre squamous cell carcinoma</td>
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<td>Carcinoma with pseudosarcoma</td>
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<td>Pleomorphic carcinoma</td>
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<td>Metaplastic carcinoma</td>
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<td>Polypoid squamous cell carcinoma</td>
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**Case Report**

A 56 year old male patient presented with nine month history of progressive hoarseness that has been affecting his ability to speak with no dysphagia. He had neither a history of smoking nor alcohol abuse. Patient looked apparently well nourished, physical examination and laboratory investigations did not reveal any other abnormality. The patient gave a history of previous three operations for the larynx in the last seven months, direct laryngoscopy, and biopsies were taken and the pathology reports were negative for malignancy (Fig. 1 A,B,C). The patient underwent a flexible laryngoscopy that showed the presence of a bluish pink polypoidal mass obscuring the view of both vocal cords. A CT scan of his neck revealed a 12X11 mm enhancing polypoid mass involving the left vocal cord; however the nasopharynx, pharynx, parapharyngeal space and epiglottis appeared unremarkable with no adenopathy (Fig. 2). A new direct laryngoscopy was performed under general anesthetia. A soft polpoidal pedunculated mass arising from the left vocal cord excised and sends for histopathology, the pathology report was also negative for malignancy (Fig. 3). The slides and paraffin block revised with other pathologist who gave same results. Within the next two months the patient experienced two same attacks of recurrence of hoarseness and strider and two operations were done for him in one month interval, only the last biopsy revealed the diagnosis of spindle cell carcinoma of the larynx confirmed by immunohistochemistry (Fig. 4 A, B, C, D, E). The patient refuse treatment option, radiotherapy, and he went to India where a new microlaryngeal surgery and excisional biopsy were done in Asian Institute of Medical Sciences, Faridabad. The biopsy report reveals no malignancy and he came back to Iraq with same compliant.

**Discussion**

Sarcomatoid carcinomas of the head and neck pose a significant diagnostic challenge to the pathologist with remarkable morphological and immunohistochemical overlap with other benign and malignant spindle cell tumors.\textsuperscript{10,32} The differential diagnosis includes benign and malignant soft tissue neoplasms and malignant melanoma, and a definitive diagnosis sometimes can be difficult based on histologic features alone,
especially with small biopsy specimens.\(^{(33)}\)

Fig. 1: (A) Laryngeal biopsy showing intact, benign looking stratified squamous epithelium, with normal looking underlying submucosal stroma, X 100 H&E stain. (B) Show only bland looking spindle cell proliferation of low density with cellular atypia, X 100 H&E stain. (C) Show intact stratified squamous epithelium with underlying cellular submucosal stroma, with no significant atypia or mitotic activity X100 H&E stain.

The diagnosis of spindle cell carcinoma requires histological demonstration of both the squamous cell component and the spindle shape cells with sarcomatous appearances.\(^{(2)}\) In addition to histological studies, immunohistochemical studies of epithelial and mesenchymal markers are used to diagnose the tumor. Epithelial markers include keratin (AE1/AE3, CK1, 8, 9), epithelial membrane antigens, K1, and K18. Mesenchymal markers include vimentin, desmin, S-100, Osteopontin, and BMP (2, 4).\(^{(9)}\) The individual tumor cells of LSCSC reacted variably to the immunohistochemical markers. Even in cases when immunoreactivity was noted, none of the markers decorated all of the lesional tumor cells. The most sensitive and reliable epithelial markers in LSCSCs appear to be keratin (AE1/AE3), K1, K18, and epithelial membrane antigen. All of the
other epithelial markers analyzed seemed to react with only a limited number of cases and often with only a limited number of tumor cells. However, if only keratin, epithelial membrane antigen, K1, and K18 are included, then 64% of cases tested were immunoreactive for at least one of these four antibodies.

Fig.4: (A) Cellular spindle cell proliferation with marked atypia and frequent mitotic figures (some are atypical mitosis, arrow), X400 H&E stain. (B) CD34 negativity in tumor cells, X400. (C) Cytokeratine negativity in tumor cells, X400. (D) Ki-67 proliferative index 40-50% of the tumor cells, X400. (E) Vimentine positivity in tumor cells, X400.

Where the surface epithelium was present, it was strongly and diffusely immunoreactive for the epithelial markers analyzed. The intermediate filament vimentin was present in all cases, other mesenchymal markers
were focally expressed. Epithelial expression decreases from 100% in the surface epithelium to nonexistent in the spindle cell component in a fair percentage of cases, vimentin has the exactly inverse relationship (100% of the spindle cells to nonreactive in the surface epithelium).

Consequently, the presence of mesenchymal marker immunoreactivity, even in the absence of epithelial immunoreactivity, does not preclude the diagnosis of an LSCSC but may indeed lend support to the true nature of the neoplasm that has become so transformed. Thus, a single case may be negative for immunoepithelial antibodies and still be an LSCSC. Furthermore, a number of technical or histologic factors may confound the pathologist's ability to demonstrate epithelial differentiation. These conditions include subjectivity of the reviewer, sampling error or nonhomogeneous tumors, poor preservation or fixation, inappropriate antibody or technique, or epithelial features less than the threshold of detection immunohistochemically or ultrastructurally. As noted in our case, in the first biopsy, the pathological report of benign laryngeal nodule is due to the benign looking of surface epithelium, while in the second biopsy there is a noticeable underlying fibrous stroma with no significant atypia making the diagnosis still in the benign side. In the third biopsy the cellular atypia started to be more obvious but less than that required to diagnose the lesion in malignant side and the tumor cells appear to be spindle in shape, and with the use of a limited available immunohistochemical markers which revealed negative EMA, CK and positive vimentin, the diagnosis of spindle cell type of squamous cell carcinoma had been excluded because of the negativity of epithelial markers which are usually positive in the epithelial tumors and this lead to diagnostic pitfall of a benign myofibroblastic tumor which can arise in such location and characterized by frequent recurrence after excision but the recurrence rate of such tumor is very slow and it is not compatible with our case. The fourth and fifth operations, the biopsy readed by other pathologist in another center and the results were inconclusive. In the sixth operation, after expanding the panel of immunohistochemical markers and adding a proliferative marker (Ki-67), which showed a high proliferative index > 60% which explain the rapid recurrence rate and by review of literatures, which showed that about 35% of spindle cell squamous cell carcinoma are negative for epithelial markers and positive for vimentin, finally the diagnosis of spindle cell type of laryngeal squamous cell carcinoma was done. The presented case demonstrates that spindle cell carcinoma or sarcomatoid carcinoma is very rare malignant tumor of the larynx but should be suspected in spindle cell tumours of the larynx and awareness of the pathologist to the unusual immunohistochemical presentation of this tumor with the use of expanded immunohistochemical markers panel.

References

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