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Case Report

Spindle Cell Squamous Cell Carcinoma of The Larynx: A Report of Three Cases

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ARTICLE INFO

Article history:
Received: 3 October, 2020
Accepted: 17 October, 2020
Published: 2 November, 2020

Keywords:
Spindle cell squamous cell carcinoma
larynx
sarcomatous transformation
osteosarcoma
immunohistochemistry

ABSTRACT

Spindle cell squamous cell carcinoma (SCSCC) is a rare malignant tumor, which involves both squamous cell carcinoma and sarcomatoid proliferation. It remains uncommon in the larynx and represents only 1 % of SCSCC of the head and neck. This tumor still poses diagnostic and therapeutic challenges. In the present report, three cases of laryngeal SCSCC were investigated; their clinical, pathological findings, treatment and outcomes are described. The patients were smoker men aged 50, 66 and 66 years old respectively. Dysphonia was the mean symptom. The tumor involves the vocal cord in all cases. The patient underwent laryngectomy with bilateral neck dissection. Histological examination confirmed the diagnostic of SCSCC. One case showed basaloid squamous cell carcinoma with sarcomatous transformation and osteosarcoma. Immunohistochemical analysis performed in one patient was positive for vimentin, SMA, PS100, focally for EMA and negative for keratin and P63.One case presented lymph nodes metastases and an adjuvant radiotherapy was preconised for this patient. All patients were well controlled after treatment and there was no recurrence during the following up.

Introduction

Spindle cell squamous cell carcinoma (SCSCC) of the larynx is a rare variant of squamous cell carcinoma (SCC) [1]. It represents 2 to 3% of all laryngeal tumors and 1% of head and neck SCSCC [2]. Considerable controversy has long surrounded this tumor due to its heterogeneous terminology, rarity and disputed histogenesis [3]. SCSCC was considered as a biphasic tumor with both carcinomatous and sarcomatous components. This tumor has now been proved to be monoclonal, evolving from conventional squamous carcinoma with sarcomatoid dedifferentiation [4]. This uncommon tumor still poses a challenge in diagnosis, prognosis and therapeutic approach.

Methods

Three cases of laryngeal SCSCC were identified at our institution during a period of 12 years from 2009 to 2020. Their clinical characteristics, treatment, pathological features and outcomes were retrospectively reviewed.

Case Reports

Case 1

A 50-year-old-man, with a 20 pack-year smoking history, presented dysphonia that dates back 3 months. Laryngoscopy showed an exophytic tumor involving the right vocal cord. Pathology revealed *in situ* squamous cell carcinoma with sarcomatous invasive component (Figure 1). Immunohistochemical analysis was positive for vimentin, SMA, PS100, focally for EMA and negative for keratin and P63 (Figure 2). A total laryngectomy with bilateral neck dissection was performed. Macroscopically, it was an exophytic tumor of the right vocal cord with 2, 2× 2, 5 ×1, 8 cm in size reaching the anterior commissure and the subglottis. Histological analysis of surgical specimen showed sarcomatous proliferation; the spindle cells are arranged in fascicular architecture with moderate to highly nuclear atypia and many mitoses. A final diagnosis of spindle cell squamous carcinoma was made considering the presence of *in situ* SCC. All margins were negative and

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http://dx.doi.org/10.31487/j.COR.2020.11.01

lymph nodes metastases were absent. The patient remains free of disease at 3-years follow-up.

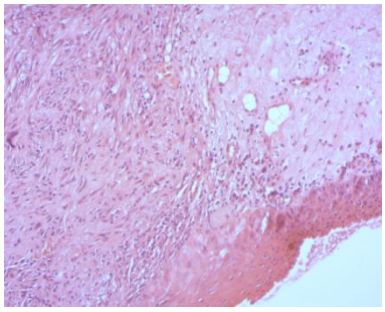

Figure 1: *In situ* squamous cell carcinoma of the overlying epithelium with sarcomatous invasive component (HE × 25).

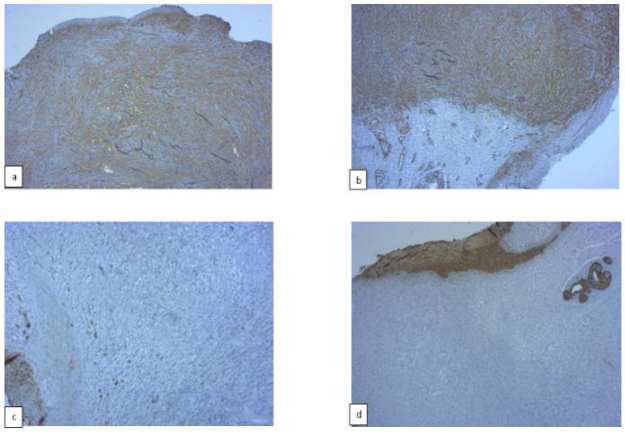

Figure 2: Spindle cells immunoreactivity: positive for **a)** vimentin and **b)** SMA; **c)** focally positive for EMA and **d)** negative for Keratin.

Case 2

A 66-year-old man, with a 40 pack-year smoking history, presented dysphonia and dysphagia. Laryngoscopy revealed a glottis exophytic tumor. Diagnosis given on biopsy was moderately differentiated squamous cell carcinoma with sarcomatous component. The patient underwent partial laryngectomy with bilateral neck dissection.

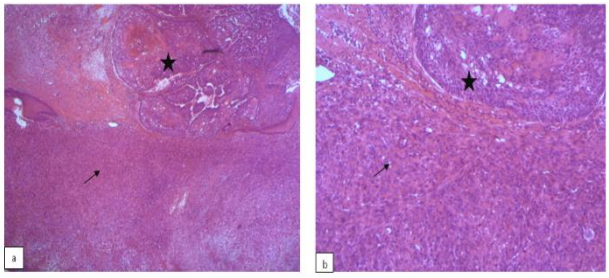

Figure 3: Basaloid squamous cell carcinoma (★) with atypical basaloid cells showed peripheral palisading among sarcomatous transformation (↗) (**a.** HE × 25), (**b.** HE × 50).

Macroscopically, it was an ulceroproliferative tumor involving the right vocal cord. Histologically, it presented several components (Figure 3): basaloid region, of which tumor cells have hyperchromatic nuclei, scanty basophilic cytoplasm and showed peripheral palisading, comedo necrosis and hyalinized stroma ; conventional keratinizing squamous component and highly undifferentiated sarcoma (Figure 4); there was focal osteosarcomatous differentiation (Figure 5). All margins were negative. Multiple ipsilateral lymph nodes were metastatic. An adjuvant radiotherapy was preconised. There was no recurrence in the following 7 months.

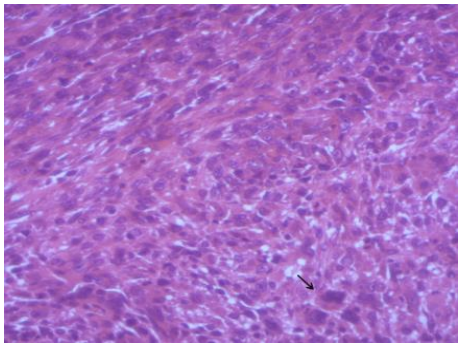

Figure 4: Sarcomatous component: higher power reveals spindle cells exhibiting pleomorphism, hyperchromatism and abnormal mitoses with pleomorphic cells (↘) (HE × 100).

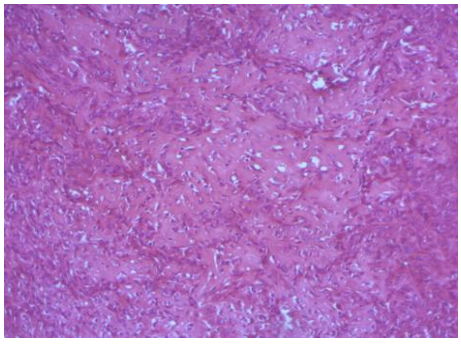

Figure 5: Foci of obvious osteosarcoma are hypercellular with atypical osteoblasts and osteoid matrix (HE ×50).

Case 3

A 66-year-old man was suffering from dysphonia and inspiring dyspnea. A large polypoid obstructive tumor of the left vocal cord was detected under laryngoscopy. The pathological diagnosis based on biopsy was spindle cell squamous carcinoma; the tumor was made of moderately differentiated squamous cell carcinoma with sarcomatous component (Figure 6). The patient underwent partial laryngectomy with bilateral neck dissection. A residue of SCC has been identified on final histological examination. The margins were negative with no lymph nodes metastases. The patient has been free of the tumor for 2 months after surgery.

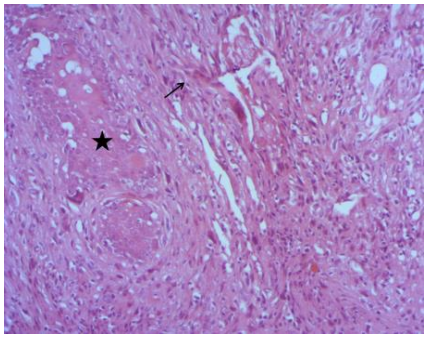

Figure 6: Invasive moderately squamous cell carcinoma (★) with sarcomatous component (↗) (HE × 25).

Discussion

SCSCC is a rare and highly malignant variant of SCC [4]. It is a bimorphic tumor made up of a squamous cell carcinoma component and a spindle cell proliferation. Given the controversy surrounding its histogenesis, this tumor was termed as sarcomatoid carcinoma, pleomorphic carcinoma, pseudocarcinoma, carcinosarcoma [3]. Laryngeal SCSCC is strongly associated with tobacco and alcohol abuse, prior radiation to the larynx has been noted in a few studies [1]. Men are much more affected, especially in the seventh decade of life [5]. In our series, all patients were male and heavy smokers; the median age was 60,6 year. This tumor typically presents as a polypoid mass, usually involving the glottis (70% of cases) which is similar to our report [6]. Hoarseness is the most frequent symptom; dysphonia, dysphagia, or airway obstruction and cough were usually observed [3, 7]. Dysphonia was the main symptom in our cases.

Histopathologically, SCSCC show the presence of two distinct components: a squamous cell carcinoma and sarcomatoid spindle cell component. The squamous cell component forms a minor portion of the tumor mass which may be represented by dysplasia, carcinoma *in situ* or invasive carcinoma [8]. The patient in case one exhibited SCC *in situ* without invasive conventional squamous component. The spindle cells are arranged in storiform, solid, or fascicular pattern, and may vary from bland to pleomorphic cytology. Hypocellular lesions with mild atypical cells can lead to misdiagnosis [6]. Foci of osteosarcoma and chondrosarcoma can be seen. Mesenchymal component is positive for vimentin and other markers, depending on the differentiation expressed by the tumor [9]. This component is usually positive for keratin, EMA ,CK5/6, and p63 which confirm the epithelial nature of the spindle cell; but these markers are absent in 30% of cases proposing that SCSCC can undergo a molecular alteration and lose of epithelial expression [8]. Thus, explaining that EMA expression was focally positive in case 1.

The differential diagnosis of SCSCC includes benign spindle cell proliferation, such as nodular fasciitis and inflammatory myofibroblastic tumor or malignant tumor like osteosarcoma, chondrosarcoma, or low-grade myofibroblastic sarcoma [10]. The squamous component can be a basaloid variant. We presented one case of Basaloid squamous cell carcinoma (BSCC) with sarcomatous transformation and osteosarcoma in our series (case 2). Laryngeal tumors composed of BSCC and spindle cells are exceedingly rare; few cases were reported in literature and only one case presented osteosarcomatous differentiation [11, 12]. It is characterized by basal palisading, high nuclear to cytoplasmic ration and central necrosis, consistent with a basaloid morphology [13]. The standard therapeutic protocol of laryngeal SCSCC is still not standardized [14]. Partial or total laryngectomy with neck nodes dissection is the preferred method [5]. Polypectomy is curative in many cases (T1, T2 stages) [2]. Radiotherapy is recommended in cases of nodal metastasis or positive surgical margin [8].

The prognosis of SCSCC is controversial and seems to be worse than that of squamous cell laryngeal carcinoma [9]. Five-year survival is reported to be 65 to 95% [6]. lymph nodes metastases are more frequent (25%) and distant metastases occur in 5 to 15% [3]. Our patients continued to do well during the following up. High-stage disease, non-glottic tumors, high size (>3 cm), previous radiotherapy, necrosis, and epithelium positive immunoreactivity were found to be poor prognostic factors [6]. For BSCC with sarcomatous transformation, the longest postoperative follow-up reported was12 months. It has been associated with a high rate of local recurrence, lymph node metastasis, and early distant metastasis [15].

Conclusion

Laryngeal SCSCC is extremely rare with no randomized clinical trials. Histological and immunohistochemical evaluation are essential for correct diagnosis. Laryngeal SCSCC pose a significant diagnostic challenge to the pathologist given morphologic overlap with other benign and malignant spindle cell tumors. Understanding the biological behaviour of this tumor is essential for appropriate prognostic factors and treatment modalities.

Conflicts of Interest

None.

Funding

None.

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