Age Limit and Radiotherapy Option for Sarcomatoid Carcinoma of the Larynx: A Case Report with Literature Review

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Abstract
Sarcomatoid carcinomas, also known as spindle cell carcinomas (SPCCs), are rare carcinomas, predominantly developing in the lung. They have lots of features of sarcoma in their histological features. The standard laryngeal carcinoma classification is based on tumor size, lymph node affection, and metastasis (TNM), it is the classification scheme of the American Joint Committee on Cancer Staging (AJCC), and it is used in the same way for stage spindle cell carcinoma (SPCC). We present a case report of a young female along with a literature review of sarcomatoid carcinoma of the larynx.

Keywords: carcinosarcoma, Oncology, spindle cell carcinomas, laryngeal sarcomatoid carcinoma

Introduction
Sarcomatoid carcinomas, also known as spindle cell carcinomas (SPCC), are rare carcinomas that predominantly develop in the lung. They have lots of features of sarcomas in their histological features [1-3]. In the larynx, sarcomatoid carcinomas are considered high-grade variants of squamous cell carcinomas, with no randomized clinical trials, conducted to specify a treatment modality [2]. The standard laryngeal carcinoma classification scheme of the American Joint Committee on Cancer Staging (AJCC) is used in the same way as to stage SPCC [3]. The classification is based on tumor size, lymph node affection, and metastasis (TNM) [3]. Most laryngeal SPCCs give symptoms early, predominantly hoarseness of voice. The reason for hoarseness of voice is that they most commonly appear as glottic pedunculated polypoidal masses (T1 or T2 lesions) with minimal invasion of the underlying stroma. The presenting gross appearance allows early wide complete transoral local excisions [3]. Scholars suggested good disease-controlled outcomes for early-stage glottic sarcomatoid carcinomas when treated with irradiation, comparing favorably with early glottic squamous cell carcinomas [4].

Case Presentation
A 24-year-old female patient presented to the otolaryngology clinic with a six-month history of progressive hoarseness of voice. In addition, she has a recent history of mild dyspnea on exertion and dry cough. The patient did not have any weight loss nor dysphagia. The patient was a cigarette smoker of around one pack per day for five years. There was no past family history of cancer, and she did not have any medical illness of significance. The patient also did not have any prior history of radiotherapy. In the clinic, fiberoptic nasoendoscopy showed a right vocal fold mass reaching the anterior commissure. The vocal fold mobility was normal. The neck examination was unremarkable. Our clinical impression, at this stage, was that the patient had early glottic laryngeal cancer. Consequently, the patient had a computed tomography (CT) scan showing the mass with no cervical lymphadenopathy (Figure 1).
FIGURE 1: CT scan findings: A lesion at the glottic level, without any lymphadenopathy.

CT: computed tomography

The vocal fold mobility was normal. The neck examination was unremarkable. The patient underwent a laryngotracheoscopy under general anesthetic, with a biopsy taken from the lesion, which appeared to be arising from the right vocal fold without a subglottic extension. The initial histopathology report confirmed sarcomatoid carcinoma and subsequent immunohistochemistry was positive for epithelial membrane antigens (EMA), cytokeratin CK 5/6, and cytokeratin AE1/AE3AE1/3 (Figures 2-4).
FIGURE 2: Histopathology stained with H&E: Spindle cells with short fascicles and pleomorphic nuclei.
The patient’s spindle cell (sarcomatoid) carcinoma stage was T2N0M0 according to the AJCC cancer staging system for laryngeal carcinomas. The options for management were evaluated by the head and neck multidisciplinary team, who preferred a transoral surgical excision as a modality of treatment. We discussed the treatment options with the patient, who refused surgical intervention. Consequently, she received intensity-modulated radiotherapy (IMRT). The patient had followed up at a six-month interval, and she remains free of the disease (Figure 5).
FIGURE 5: Follow-up by laryngoscope after six months showed no recurrence. Respiration (1) shows the posterior commissure and respiration (2) shows the anterior commissure.

### Discussion

#### Methods

We also conducted a review of the literature based on a search performed on June 9, 2018, in PubMed. We discovered 167 articles, and on further screening, we excluded 103 articles, as they were not related to our topic or we could not download it. Then, 49 studies were excluded in the full-text analysis due to irrelevant disease. Fifteen articles were included in our review of the literature. We reviewed 59 patients with laryngeal carcinosarcoma having different ages, sexes, and modalities of carcinosarcoma treatment. The following table illustrates the review of the included patients (Table 1).

| ID | Article | Age (Years) | Gender | Specific Habits/ Symptoms/Duration | Site/Classification | Treatment | Pathology Report of Surgical Specimen | Subsequent course/Follow-Up |
|----|---------|-------------|--------|-----------------------------------|---------------------|-----------|---------------------------------------|-----------------------------|
| 1  | Randall et al. [5] | 58/M | Smoker/hoarseness for two Mo | Rt anterior commissure/T1bN0M0 | Local excision | Pseudo-Sarco carcinoma in situ | Neck metastasis four Mo, and FOD eight Y later |
| 5  | Fransawy Alkomos et al. [10] | 56/M | Smoker/hoarseness for two Wks | Lt anterior commissure/ T2N1M0 | SSL | Carcinoma in situ and invasive epidermoid carcinoma pseudo sarcoma | Neck metastasis nine Mo, Lt RND, one node has cancer/FOD four Mo before death from MI |
| 4  | Fransawy Alkomos et al. [10] | 43/F | Smoker/hoarseness for four Mo | Lt TVC/T1aN0M0 | Lt HL | Invasive epidermoid carcinoma with underlying pseudosarcoma | FOD nine and a half Y |
| 7  | Fransawy Alkomos et al. [10] | 74/M | Smoker/hoarseness for one Y | Anterior commissure/T2N0M0 | Frontal HL | Pseudosarcoma | FOD four Y |
| 6  | Fransawy Alkomos et al. [10] | 60/M | Smoker/hoarseness for three Mo | Rt PVC/T3N0M0 | SSL with foldover Rt RND | Osteosarcoma | FOD three and a half Y |
| Age/Gender | Symptoms | Site | Treatment | Diagnosis | Outcome |
|------------|----------|------|-----------|-----------|---------|
| 67/M       | Dysphagia for three Mo | FVC/TV (bilater/T2N1M0) | TL | Pseudosarcoma | Died with cancer three Y |
| 55/M       | Dysphagia for three Mo | Epiglottis r T2N1M0 | SSL, Bilateral RND | Pseudosarcoma | Died with cancer three Y |
| 80/F       | Dysphagia for eight Mo | Lt A2/ T3N0M0 | SSL, LT RND | Pseudosarcoma, carcinoma in situ | Died Free of Dis two Y |
| 80/M       | Dysphagia for three Y | Lt TVC/ T3N0M0 | TL | Pseudosarcoma | Died with cancer 13 M0 |
| 55/M       | Dysphagia for three Mo | Ri ventricle, Ri VC | Radiotherapy | Fusion of SCC and SPOC | Local recurrence, 10 Mo/died one and a half Y |
| 51/M       | Dysphagia for three Mo | Anterior half of Ri VC | HL | SCC with sarcoma-like areas | Died Free of Dis two Y |
| 72/M       | Hoarseness for three mo | Base of the epiglottis | Rd | Fusion of SCC and spindle cells | Local recurrence, 5 Mo, radium implant/died 1-months later |
| 49/M       | None | Right arytenoid | Snare excision +radiotherapy | SCC intermixed with spindle cells; osteoid and chondroid areas | Died five Mo |
| 56/M       | Hoarseness for three mo | Left true cord | None | Predominant bizarre spindle cell neoplasm | Died eight Mo |
| 59/M       | Difficulty swallowing for six mo | Hypopharynx, false cord | None | SCC intermixed with spindle cells; osteoid and chondroid areas | Died five mo |
| 49/M       | Dysphagia for seven Mo | Right, true cord | Rd then local recurrence, Four yr.; total laryngectomy | SCC intermixed with spindle cells; osteoid metaplasia | Died, five and i half Y, cervical node metastasis |
| 42/M       | Hoarseness (nine mo) neck pain (one Mo) | Right, true cord | HL | Fusion of SCC and spindle cells | Alive and all after 13.5 Y |
| 59/M       | Hoarseness for two yr, dysphagia for three Mo. | Both true cords and commissure | TL/Metastasis in cervical lymph nodes, three Mo then RD | Fusion of SCC and spindle cells | Died, 10 Mo |
| 73/F       | Hoarseness, dysphagia, weight loss, six Wks | Right ventricular fold | TL/regional recurrence, cervical lymph node metastasis, 13 Mo followed by radiotherapy | Fusion of SCC and spindle cells | Died two and a half Y later |
| 77/M       | Hoarseness for 10 mo | Right, true cord | TL | SCC with demarcated sarcoma-like areas | Died one and a half year later |
| 50/M       | Smoker/hoarseness | LT VC/T1A1N0M0 | Radiotherapy | Interlacing bundles of large spindle-shaped cells with pleomorphic nuclei and nucleoli. | FOD 22 Mo |
| 59/M       | Smoker/hoarseness for one year | Ri VC | TL | Sarcomatoid carcinoma | FOD two Y |

References:
2. Appelman et al. [2]
6. Katholm et al. [6]
7. Alguacil-Garcia et al. [7]
| Age/Gender | Duration of Hoarseness | Site | Treatment | Follow-Up |
|------------|------------------------|------|-----------|-----------|
| 64/M       | 7 Mo                   | VC   | TL+Radio  | FOD 8 and a half Y |
| 65/F       | 8 Mo                   | Epiglottis | Rad   | FOD three and a half Y |
| 54/M       | 3 Mo                   | VC   | TL   | FOD three Y |
| 69/M       | 4 Mo                   | VC   | Excision, rad | FOD one and a half Y |
| 71/M       | 2 Mo                   | VC   | Rad/than recurrence after five Y, then laryngofissure | FOD eight and a half Y |
| 62/F       | 3 Mo                   | VC   | Excision | FOD one and a half Y |
| 57/M       | 4 Mo                   | VC   | TL+Radio | FOD one and a half Y |
| 63/M       | 5 Mo                   | VC   | Radio | FOD two Y |
| 75/F       | 6 Mo                   | VC   | Radio | FOD 11.5 Y |
| 58/M       | 3 Mo and a half Mo     | VC   | Radio | FOD six Y |
| 67/M       | 2 Mo                   | VC   | Excision+radio | FOD 10.5 Y |
| 57/M       | 2 Mo                   | VC   | Excision | FOD six Y |
| 69/M       | 2 Mo                   | VC   | Excision | FOD six Y |
| 64/F       | 7 Mo                   | VC   | TL   | FOD 11.5 Y |
| 56/F       | 8 Mo                   | VC   | TL   | FOD six Mo |
| 65/F       | 8 Mo                   | VC   | TL+Radio | FOD six Mo |
| 54/M       | 3 Mo                   | VC   | TL   | FOD three Y |
| 69/M       | 2 Mo                   | VC   | Rad   | FOD six Y |
| 76/M       | 2 Mo                   | VC   | Extirpation | FOD six Y |

**Lassaletta et al.**

| Age/Gender | Duration of Hoarseness | Site | Treatment | Follow-Up |
|------------|------------------------|------|-----------|-----------|
| 88/M       | 6 Mo                   | Smoker | RT VC/T1aN0 | Died seven Y |
| 68/M       | 7 Mo                   | Smoker | RT VC/T1aN0 | Died seven Y |
| 69/M       | 2 Mo                   | Smoker | RT VC/T1aN0 | Died seven Y |
| 76/M       | 2 Mo                   | Smoker | VC/T1aN0 | Died eight M0 |

**Miyahara et al.**

| Age/Gender | Duration of Hoarseness | Site | Treatment | Follow-Up |
|------------|------------------------|------|-----------|-----------|
| 73/M       | 2 Mo                   | Smoker | LVI VC/T1a(N1aM0) | Died eight M0 |

**Onishi et al.**

| Age/Gender | Duration of Hoarseness | Site | Treatment | Follow-Up |
|------------|------------------------|------|-----------|-----------|
| 64/M       | 7 Mo                   | VC   | TL   | Carcinosarcoma |
| 65/F       | 8 Mo                   | Epiglottis | Rad   | FOD six Y |
| 54/M       | 3 Mo                   | VC   | TL   | Spindle cell carcinoma |
| 69/M       | 2 Mo                   | Anterior commissure/T1a(N0) | Rad. | Spindle cell carcinoma |
| 76/M       | 2 Mo                   | VC/T1aN0 | Extirpation | Spindle cell carcinoma |

**Hellquist et al.**

| Age/Gender | Duration of Hoarseness | Site | Treatment | Follow-Up |
|------------|------------------------|------|-----------|-----------|
| 54/M       | 4 Mo                   | VC   | Radio | LNs metastasis |
| 57/M       | 2 Mo                   | VC   | Excision | Died seven Y |
| 62/M       | 3 Mo                   | VC   | Radio | Died seven Y |
| 57/M       | 2 Mo                   | VC   | Excision | Died seven Y |
| 69/M       | 2 Mo                   | VC   | Excision | Died seven Y |
| 64/M       | 7 Mo                   | VC   | TL   | Carcinosarcoma |
| No. | Name et al. | Age | Sex | Diagnosis | Clinical Symptoms | Treatment | Pathology | Outcome |
|-----|-------------|-----|-----|-----------|-------------------|-----------|-----------|---------|
| 9   | Fransen et al. [12] | 61/M | Hoarseness four Mo, dysphonia two Wks | Right VC and anterior commissure/T2 N0 M0 G3 | Partial laryngectomy and modified radical neck dissection | | | |
| 10  | Boamah et al. [13] | 67/M | Smoker/swallowing difficulty 2 Mo, weight loss > 12 kg | Right laryngeal wall of the sinus piriformis and the aryepiglottic fold/T3 N2B Mo | Right-sided laryngeal hypopharyngeal resection and neck dissection | Light microscopic and immunohistochemically becomes a biphasic tumor (carcinosarcoma) | | |
| 11  | Rutt et al. [14] | 69/M | Smoker (15 Y) quitter, dysphonia | Right VC/T1N0M0 | Micro flap excision then wider excision | SCC, spindle cell variant | FOD one Y |
| 12  | Zheng et al. [15] | 61/M | Smoke, hoarseness | Bilateral vocal folds/T3N0M0 | TL | SCC, malignant fibrous histiocytoma | 88 Mo/AWD |
|     |             | 64/M | Smoke, hoarseness | Left vocal VC, laryngeal ventricle/T2N0M0 | Vertical partial laryngectomy | SCC, malignant fibrous histiocytoma | 62/AWD |
|     |             | 59/M | Smoke, hoarseness | Left vocal VC, laryngeal ventricle/T2N1M0 | Total laryngectomy + RND | Poorly differentiated Ca, leiomyosarcoma | 60/DDD |
|     |             | 60/M | Smoke, hoarseness, dysphoria | Left vocal fold, bilateral vocal folds/T3N0M0 | Total laryngectomy + RND | Mucinous adenocarcinoma, fibrosarcoma | 24/AWD |
|     |             | 57/M | Smoke, hoarseness, dysphoria | Bilateral vocal folds/T3N0M0 | Total laryngectomy + SND | Poorly differentiated Ca, osteosarcoma | 20 Mo/AWD |
|     |             | 50/M | Abnormal throat sensation | Epiglottis, Right aryepiglottic fold/T3N0M0 | Total laryngectomy + RND | Poorly differentiated Ca, embryonal rhabdomyosarcoma | 17 Mo/AWD |
|     |             | 42/M | Smoke, hoarseness | Right VC/T2N0M0 | Vertical partial laryngectomy | Ca in situ, leiomyosarcoma | 13 Mo/AWD |
| 13  | Zheng et al. [16] | 55/M | Smoker, neck mass | Left pyriform sinus | Excision, reconstruction, and neck dissection | SPCC | Free eight Mo |
|     |             | 62/M | Smoke, hoarseness | Left VC | TL+ dissection | SPCC | Pulmonary metastasis six M0 |
|     |             | 57/M | Smoke, foreign body | Posterior wall of hypopharynx | Total hypopharyngectomy | SPCC | Free five and half M0 |
| 14  | Bozianci et al. [17] | 69/M | Smoke, hoarseness, dysphoria | Right VC/T1N0M0 | Excision + Radiotherapy | Atypical spindle cells/spindle cell component positive cytokeratin and p53 | FOD 12 M0 |
| 15  | Ras et al. [18] | 65/M | Smoker, hoarseness, difficulty in swallowing and breathing six Mo | Right VC/T1N0M0 | Mass excision | Pleomorphic spindle-shaped cells | FOD three Mo |

**TABLE 1**: Clinical characteristics of patients with laryngeal sarcomatoid carcinoma described in the literature (n=59)
Results
The included articles described a total of 59 patients, 52 of which were males and seven were females. The age range was between 36 and 88 years. The reported cases were from 1960 till 2016. Most of the patients were smokers, and most of them underwent total laryngectomy followed by radiotherapy. On the other hand, eight patients received radiotherapy only, while the rest had different types of surgery. The general survival outcome was better with a combination of both surgery and radiation, compared to radiotherapy alone.

Discussion
Carcinosarcoma is a rare lesion; it can be present in many body parts, including the larynx. The larynx appears to be an unusual site, as only a few cases can be found in the literature. Carcinosarcoma is considered a malignant tumor composed of both epithelial and mesenchymal components. It accounts for less than 1% of all malignant tumors of the larynx and hypopharynx [19]. In our review of the literature, we noticed that there is a broad age range for laryngeal carcinosarcoma (36-88 years), while our case was 24 years old. Despite being a rare condition, spindle cell carcinoma should be considered a valid diagnosis in any age group, especially if the patient presents with hoarseness of voice or dyspnea and a history of smoking. Surgical intervention was the first line of management in the treatment of most of the laryngeal carcinosarcomas mentioned in our literature with a favored outcome. However, scholars suggested good disease-controlled results for early-stage glottic sarcomatoid carcinomas when treated with irradiation, comparing favorably with early glottic squamous cell carcinomas [4]. We had eight patients in our review that received radiotherapy only, without any surgical intervention [2,6,8,10]. These patients had different ages, cancer stages, and laryngeal cancer locations. Five out of the eight patients who were treated only with radiation have no evidence of the disease at a range of two to 11.5 years while the other three developed a recurrence and died of the disease later on. So radiotherapy might be a valid alternative option instead of surgical therapy in selected patients. Our patient has stage T2N0M0 glottic carcinoma. Due to the early detection of the tumor and its site, the surgical excision was a valid and reasonable option for management. However, the patient preferred the radiotherapy option. The follow-up plan will be the same as for other glottic carcinomas.

Conclusions
Spindle cell carcinoma (SPCC) or sarcomatoid carcinoma of the larynx is a rare, highly malignant variant of squamous cell carcinoma. It can present at an early age with symptoms and diagnosis is possible in the early stages. Although in some patients, surgery is the best modality of therapy, radiation only can be a reasonable alternative.

Additional Information

Disclosures
Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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