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Radiation-Induced Leiomyosarcoma of the Larynx: A Case Report and Literature Review

Diango Keita, Serge Kumbi, Abir Oufrid, Sara Nejjari, Chaymae Chbihi, Hafssa El Hilali, Samia El Hakym, Mehdi Alem, Lamiae Amaadour, Karima Oualla, Zineb Benbrahim, Samia Arifi, Nawfel Mellas

Department of Medical Oncology, Hassan II University Hospital, Fez, Morocco
Email: keitadiango96@gmail.com

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Abstract

Leiomyosarcomas are rare malignant tumors arising from smooth muscle cells and may develop in various anatomical locations. Laryngeal involvement is exceptionally rare, accounting for less than 1% of malignant laryngeal tumors, particularly in a post-radiotherapy context. We report the case of a 75-year-old patient treated in 2005 for an undifferentiated carcinoma of the nasopharynx with induction chemotherapy followed by concomitant chemoradiotherapy. Seventeen years after the initial treatment, the patient presented with chronic cervical pain associated with dysphonia. Nasofibroscopy and cervicothoracic imaging revealed a supraglottic tumoral process. Histopathological examination combined with immunohistochemical analysis confirmed the diagnosis of laryngeal leiomyosarcoma. The patient underwent total laryngectomy followed by adjuvant radiotherapy at a dose of 60 Gy. A favorable clinical and radiological outcome was observed for two years, after which pulmonary recurrence occurred. Laryngeal leiomyosarcoma is an exceptionally rare entity, often associated with a poor prognosis. Its late occurrence after radiotherapy, as illustrated in our case, highlights the importance of prolonged clinical follow-up in irradiated patients.

Keywords

Leiomyosarcoma, Larynx, Radio-Induced, Head and Neck, Pulmonary, Case Report

1. Introduction

Laryngeal leiomyosarcomas are rare malignant tumors arising from smooth muscle cells and represent a very small proportion of laryngeal tumors. They account for less than 1% of laryngeal malignancies and approximately 3% of head and neck

tumors [1] [2].

First described by Franken in 1941, fewer than 50 cases have been reported in the literature to date [3]. They typically occur in elderly patients, with a mean age of over 50 years [4]. Radiation-induced occurrence remains rare and is characterized by a long latency period and a generally poor prognosis.

We report a case of laryngeal leiomyosarcoma occurring seventeen years after radiotherapy for an undifferentiated carcinoma of the nasopharynx in an elderly patient.

2. Case Presentation

A 75-year-old male patient, a former smoker who had quit smoking 20 years earlier and had no history of alcohol consumption, was included in this report.

He was initially followed for an undifferentiated carcinoma of the nasopharynx, treated in 2005 with induction chemotherapy followed by concomitant chemoradiotherapy at a total dose of 60 Gy (end of treatment: August 11, 2005). The clinical course was marked by prolonged locoregional control.

Seventeen years after the initial treatment, in 2022, the patient presented with chronic cervical pain associated with dysphonia and recurrent episodes of aspiration during swallowing.

Nasofibroscopy revealed a supraglottic tissue lesion centered on the epiglottis. Cervico-thoraco-abdomino-pelvic computed tomography showed an irregularly contoured supraglottic mass centered on the epiglottis, extending to the right preepiglottic space with obliteration of the ipsilateral vallecula, measuring 27 × 20 mm.

Cervical magnetic resonance imaging demonstrated a lesion involving the base of the epiglottis, right-sided, measuring 20 mm in diameter, staged as T2N0MX.

Histopathological examination of the biopsy specimen revealed a malignant spindle cell tumor. Immunohistochemical analysis was consistent with a high-grade leiomyosarcoma according to the FNCLCC grading system (differentiation score 3, necrosis score 2, mitotic score 2) (Table 1).

Table 1. Immunohistochemical profil of the tumor demonstrating smooth muscle differentiation consistent with a high-grade leiomyosarcoma.

Immunohistochemical marker	Resultat	Interpretation
CK AE1/AE3	Negative	Excludes epithelial origin
P40	Negative	Excludes squamous cell carcinoma
CD34	Negative	Not suggestive of vascular tumor
S-100 protein	Negative	Excludes neural or vascular tumor
Myogenin	Negative	Excludes rhabdomyoblastic differentiation
Desmin	Positive	Confirms smooth muscle origin
H-caldesmon	Positive	Specific marker of smooth muscle differentiation
Smooth muscle actin (SMA)	Positive	Confirms smooth muscle origin
Ki 67	20% - 30%	Indicates high proliferative activity

After multidisciplinary discussion in an ENT tumor board, a total laryngectomy without cervical lymph node dissection was performed, followed by postoperative radiotherapy at a total dose of 60 Gy in 30 fractions, delivered between November 23, 2022, and January 9, 2023.

Clinical and radiological follow-up was favorable for two years. Subsequently, pulmonary recurrence occurred, leading to the initiation of first-line systemic chemotherapy with doxorubicin at a dose of 75 mg/m^2.

3. Discussion

Leiomyosarcoma is a malignant mesenchymal spindle cell tumor, accounting for approximately 7% - 9% of all soft tissue sarcomas. The most frequently affected anatomical sites are the gastrointestinal tract, uterus, and retroperitoneum. Only 3% - 10% of cases occur in the head and neck region, likely due to the relative scarcity of smooth muscle tissue in this area [5].

Leiomyosarcoma primarily affects adults, most commonly during the fifth decade of life, with a marked male predominance (male-to-female ratio of 4:1), which is consistent with the profile of our patient [2].

Topographically, laryngeal leiomyosarcoma most commonly involves the glottis (48%), followed by the epiglottis (32%), and more rarely the subglottic region (5% - 6%) [6]. The clinical presentation is nonspecific and similar to that of other laryngeal tumors, including dysphonia, dyspnea, and dysphagia [2]. In patients with a history of radiotherapy, the onset or change in pain characteristics within the irradiated field should raise suspicion of a radiation-induced sarcoma [5], as observed in our case.

Several predisposing factors have been described, including radiotherapy, neurofibromatosis, Werner syndrome, Gardner syndrome, abnormalities of mesenchymal differentiation, and Epstein-Barr virus (EBV) infection. Unlike laryngeal squamous cell carcinoma, leiomyosarcoma is not associated with smoking, alcohol consumption, or human papillomavirus (HPV) infection [2]-[7].

In our patient, cervicofacial radiotherapy had been performed seventeen years earlier for an undifferentiated nasopharyngeal carcinoma. The diagnosis of radiation-induced sarcoma is based on the criteria defined by Cahan *et al.* in 1948, which include: prior exposure to radiotherapy; development of the radiation-induced tumor within the previously irradiated field; histological confirmation of sarcoma; a latency period of at least five years between irradiation and tumor onset to exclude recurrence; and evidence that the primary tumor and the secondary tumor belong to different histological entities. Our case fulfills the criteria for radiation-induced sarcoma as defined by Cahan *et al.* in 1948 [5].

Histopathological diagnosis may be challenging due to its resemblance to leiomyoma. Immunohistochemistry is therefore essential, typically showing positivity for smooth muscle actin, vimentin, and desmin, and negativity for cytokeratins, epithelial membrane antigen (EMA), and S-100 protein [4], as observed in our patient.

Therapeutic management depends on tumor extent, size, and location, as well as patient age. Total laryngectomy with negative surgical margins remains the treatment of choice, with adjuvant radiotherapy considered in selected cases [2]-[4]. In our patient, the indication for re-irradiation at a dose of 60 Gy was established due to the aggressive nature of the leiomyosarcoma and the high risk of local recurrence. However, the international medical literature does not report a clearly defined minimum cumulative radiation dose nor a correlation between radiation modality or type and the incidence of radiation-induced sarcomas.

Despite multimodal management, prognosis remains poor. Reported recurrence rates range from 25% to 40%, with approximately 25% occurring at the laryngeal level. In addition, distant metastases—particularly pulmonary and osseous—have been reported in 35% - 38% of cases [4]. The unfavorable outcome observed in our patient illustrates the aggressive biological behavior of this tumor and highlights the need for prolonged and rigorous follow-up. In cases of recurrence or advanced disease, systemic chemotherapy may be considered; doxorubicin remains the reference agent in the treatment of soft tissue sarcomas, including leiomyosarcomas, despite the absence of studies specifically dedicated to radiation-induced laryngeal forms [8].

4. Conclusion

Laryngeal leiomyosarcoma is an extremely rare malignancy. Diagnosis relies exclusively on histopathological and immunohistochemical evaluation. Its occurrence several years after radiotherapy highlights the importance of long-term follow-up in irradiated patients. Despite multimodal treatment, prognosis remains guarded due to the high risk of local recurrence and distant metastasis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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