



# Radiation-Induced Low Grade Fibromyxoid Sarcoma of the Larynx: a Case Report and Literature Review

Dariya L. Chivchibashi<sup>1</sup>, Pavel Pavlov<sup>2</sup>, Maria Tzaneva<sup>2</sup>, Nikolay Sapundzhiev<sup>3</sup>, Georgi Davidov<sup>3</sup>

<sup>1</sup> Department of Physiology and Pathophysiology, Medical University of Varna, Varna, Bulgaria

<sup>2</sup> Department of General and Clinical Pathology, St Marina University Hospital, Varna, Bulgaria

<sup>3</sup> Department of Neurosurgery and Otorhinolaryngology, Medical University of Varna, Varna, Bulgaria

**Corresponding author:** Dariya Chivchibashi, Department of Physiology and Pathophysiology, Medical University of Varna, 55 Marin Drinov St., 9002 Varna, Bulgaria; E-mail: dariya.chivchibashi@mu-varna.bg; Tel.: +359 896 825 848

**Received:** 8 July 2020 ♦ **Accepted:** 24 Sep 2020 ♦ **Published:** 30 June 2021

**Citation:** Chivchibashi DL, Pavlov P, Tzaneva M, Sapundzhiev N, Davidov G. Radiation-induced low grade fibromyxoid sarcoma of the larynx: a case report and literature review. *Folia Med (Plovdiv)* 2021;63(3):433-7. doi: 10.3897/folmed.63.e56150.

## Abstract

Low grade fibromyxoid sarcoma (LGFMS) is an uncommon variant of fibrosarcoma with high risk of local recurrence, immense metastatic potential and frequently protracted period between tumour presentation and metastasis. This unusual malignancy rarely affects the region of the head and neck which makes cases of laryngeal LGFMS extremely infrequent. To date, LGFMS of the larynx has been scatteredly mentioned in the literature. Neither incidence nor causes and risk factors for laryngeal LGFMS have been clarified so far. To the authors' knowledge, this is the first case report that discusses the clinical course, imaging diagnosis, histopathological evaluation and surgical approach to radiation-induced laryngeal LGFMS.

We present a case of a 70-year-old man who developed a LGFMS after previous radiotherapy (RT) for squamous cell carcinoma (SCC) of the larynx. The latency period between the time of radiation exposure and the diagnosis of LGFMS was twenty-seven months. After re-confirming the diagnosis with second biopsy and extensive imaging evaluation the patient was subjected to an open partial resection of the larynx. Owing to the rarity of the tumour, there is no established protocol with follow-up recommendations.

This case highlights the importance of considering the RT history of the patient in order to monitor radiotherapy-related complications, including the occurrence of LGFMS.

## Keywords

rare, soft tissue, tumour

## INTRODUCTION

Low grade fibromyxoid sarcoma (LGFMS) is a rare variant of fibrosarcoma. It is characterized by a high risk of local recurrence, an immense metastatic potential and protracted period between tumour presentation and metastasis.<sup>1,2</sup> LGFMS is a well-described but sporadically observed

neoplasm which makes it easily misdiagnosed; hence it is with undetermined incidence rate.<sup>3,4</sup> Usually, middle aged adults are affected.<sup>5,6</sup> Laryngeal LGFMS cases have been scatteredly mentioned in the literature with only a few contributable to previous radiation therapy.<sup>3,6-8</sup> We present a case of radiation-induced LGFMS of the larynx. Imaging findings, surgical approach, histopathology and immunohistochemistry are discussed.

## CASE REPORT

A 68-years-old man presented to the hospital with dysphonia. Histopathology following endoscopic cold-steel excision revealed moderately differentiated squamous cell carcinoma (SCC) with no signs of regional or distant spread (T1N0M0). After completion of cobalt RT with a total dose of 60 Gy, the patient was discharged. Twenty-seven months after the RT, the patient presented with dyspnea. Endoscopy and enhanced computed tomography (CT) detected an exophytic lesion measuring 2.1×2.3×3.4 cm in close proximity to the former SCC (Fig. 1). Following the endoscopic debulking of the tumour, the patient was soon discharged.

Histopathology revealed lesions lined by keratinized stratified squamous epithelium surrounded by myxoid areas with curvilinear blood vessels (Fig. 2A, 2B), foci of necrosis and mitotic figures. Tumour cells were spindle shaped with irregular eosinophilic cytoplasm and elliptical pleomorphic nuclei (Fig. 2C). Immunohistochemistry showed CD99 (Fig. 3A), Vimentin (Fig. 3C), and Bcl-2 positive expression (Fig. 3B), while EMA was only focally expressed (Fig. 3D). Immunoreactivity with MUC4 revealed a characteristic moderate-to-strong and diffuse granular cytoplasmic expression (Figs 3E, 3F). AE1/AE3, CK 5/6, p63 expression remained negative.

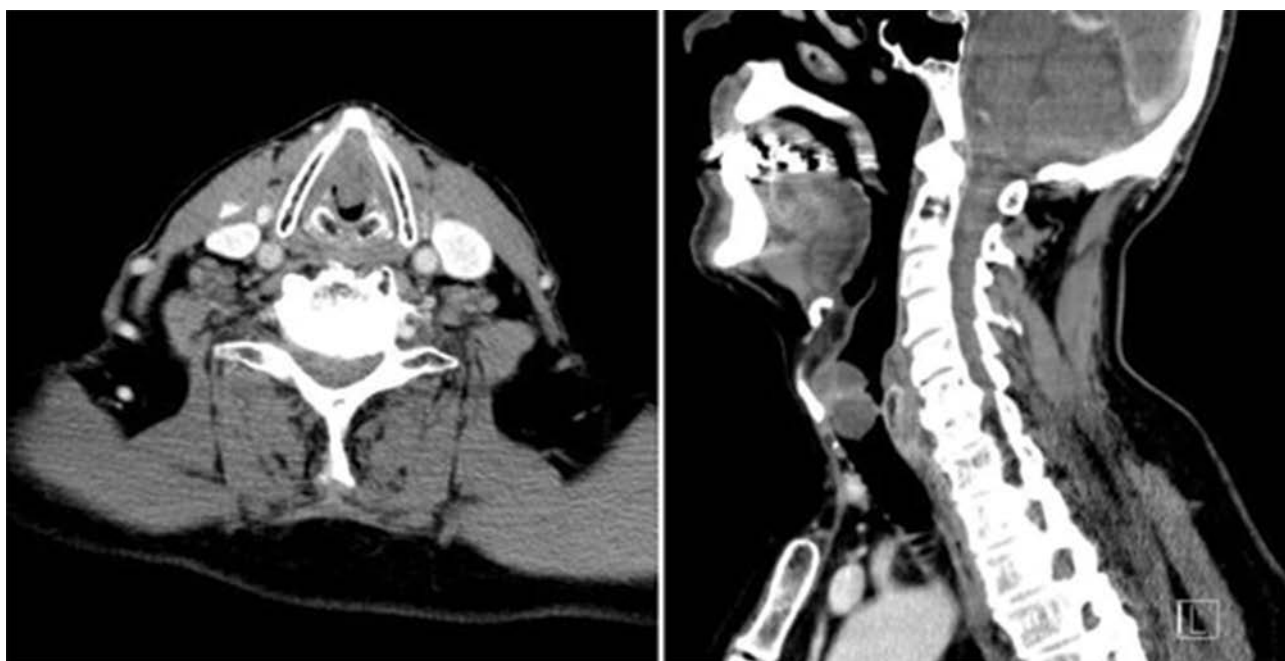
## DISCUSSION

LGFMS is a rare tumour. Laryngeal involvement is even more rare.<sup>1,6,10,11</sup> Usually, middle-aged adults are affected<sup>2</sup>, although pediatric and geriatric cases have been also reported<sup>12,13</sup>. According to Harish et al., this malignancy has a

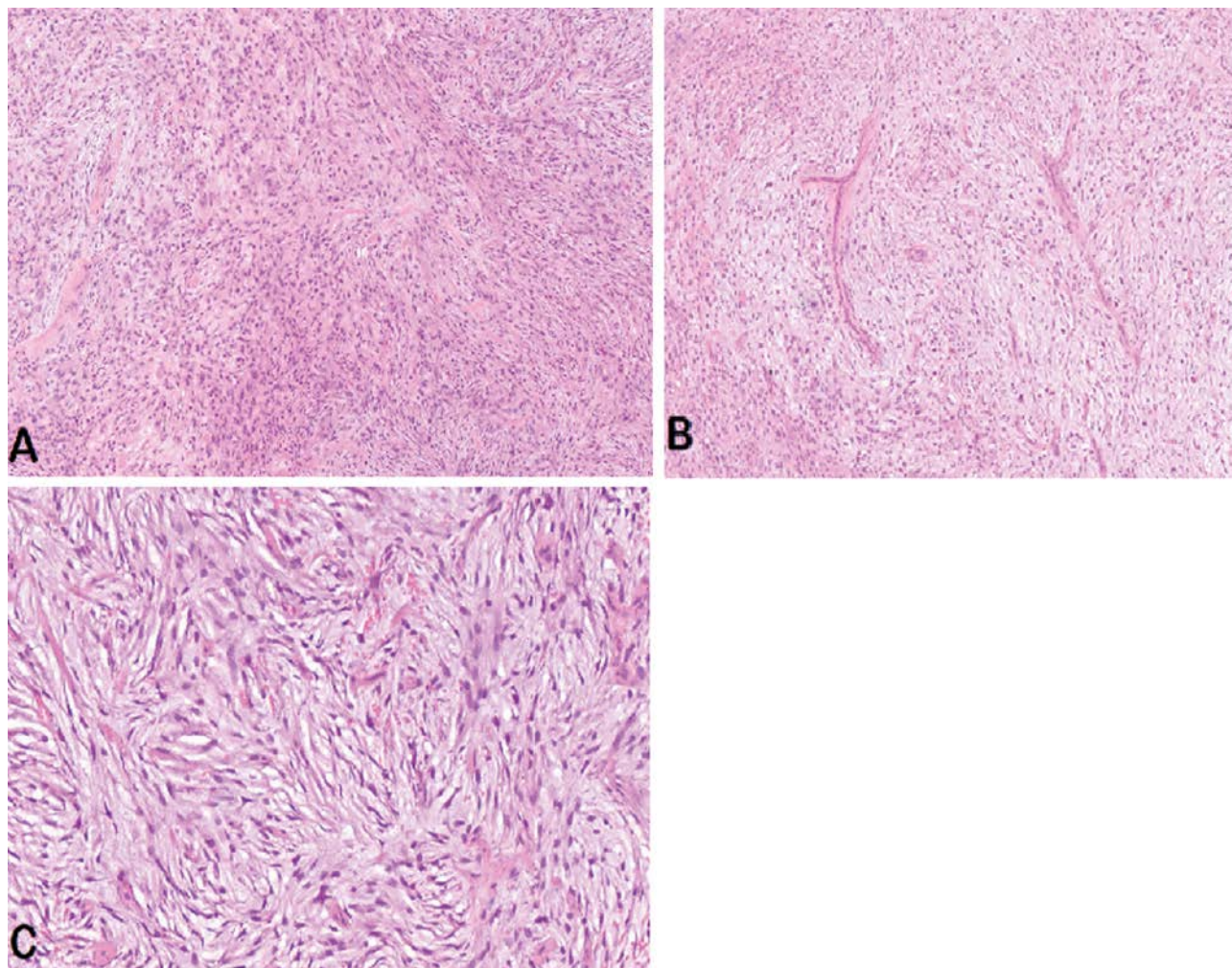
higher incidence rate among males.<sup>5</sup> It has been reported to be aggressive with local recurrence in 68%, metastasis in 41%, and death from disease in 18%.<sup>1,3,6</sup> Typically, LGFMS presents as a painless lesion with a pre-biopsy duration of over 5 years in 15% of patients.<sup>10</sup> However, head and neck LGFMS may have fast clinical presentation.<sup>9,11</sup> LGFMS is sporadically observed neoplasm; hence it is easily misdiagnosed.<sup>3,4</sup> Morphologically, it is characterized by a combination of myxoid and fibrous areas with whorled growth pattern. Tumour cells are small with poor eosinophilic cytoplasm, elliptical nuclei and absent nucleoli. Mitoses or necrosis are infrequent.<sup>1,4,6,14</sup> MUC4 has been shown to be a specific immunohistochemical marker for LGFMS. Still, MUC4-negative neoplasms have been also reported. Usually Vimentin, CD99, EMA and Bcl-2 show positive expression, while S100, desmin, caldesmon, cytokeratin, and CD117 remain negative.<sup>4,6,12</sup> In our case, MUC4, Vimentin, Bcl-2, and CD99 were strongly positive while EMA was only focally expressed. Epithelial markers, in particular AE1/AE3, CK 5/6, and p63 showed negative expression.

To date, the etiology of LGFMS has been little discussed. Some authors have linked this tumour with previous RT. Shibata et al., for instance, described a case of radiation-induced LGFMS of the chest wall in a patient with a history of RT for breast carcinoma 9 years earlier.<sup>8</sup> Marglani and colleagues reported a case of LGFMS of the sternocleidomastoid muscle, 30 years subsequent to RT to the cervical region for Hodgkin lymphoma.<sup>7</sup>

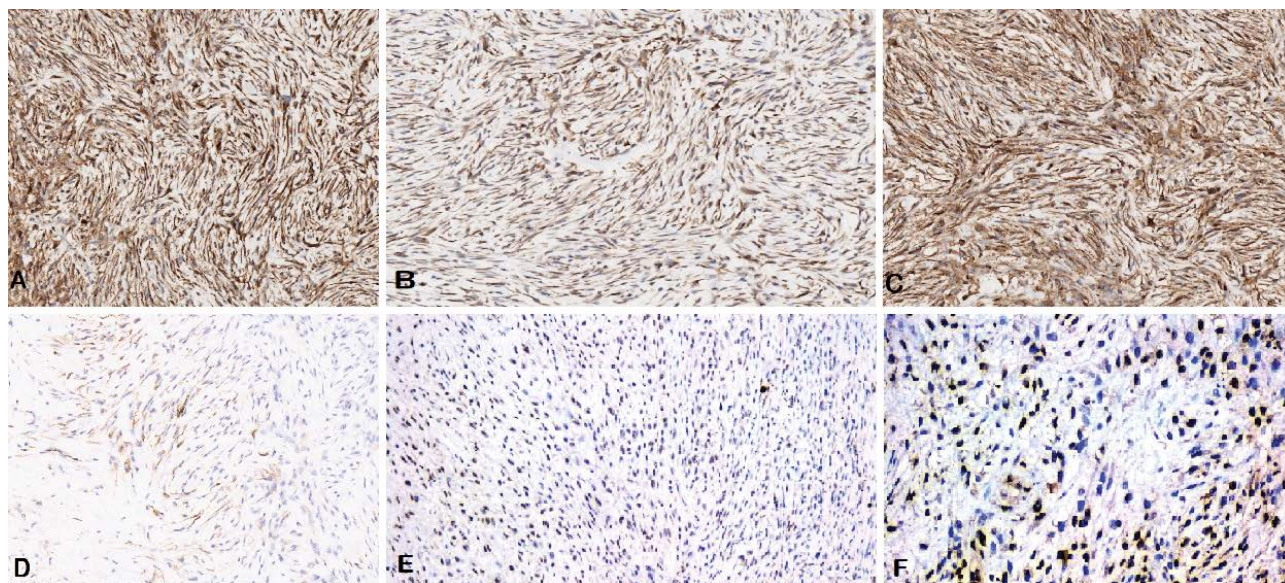
When presented as a RT-related complication in unusual location, LGFMS becomes a challenging issue. And what is challenging is neither the diagnostic procedure, nor the surgical approach. As the diagnosis of LGFMS is usually not difficult, a wide surgical resection is considered



**Figure 1.** Axial and sagittal CT: well delineated tumour mass in the larynx and critical airway.

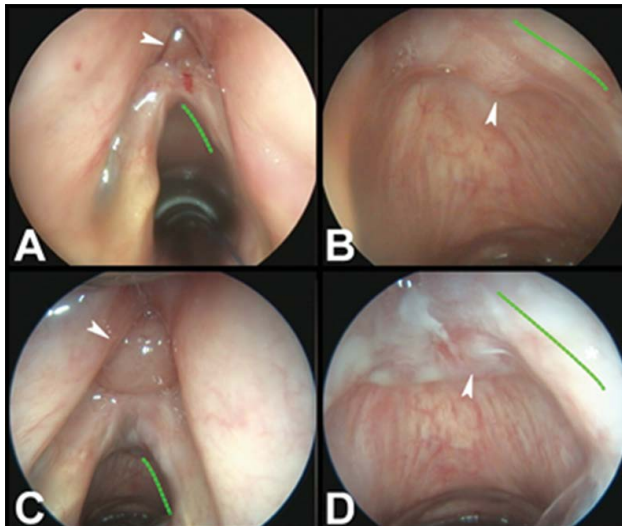


**Figure 2.** LGFMS with: **A.** Alternating fibrous and myxoid areas. HE stain ( $\times 100$ ); **B.** Myxoid area with curvilinear vessels. HE stain ( $\times 100$ ); **C.** Swirling and whorled pattern cell arrangement. HE stain ( $\times 200$ ).



**Figure 3.** Immunohistochemistry with positive expression for: **A.** CD-99  $\times 200$ ; **B.** Bcl-2  $\times 200$ ; **C.** Vimentin  $\times 200$ ; **D.** EMA  $\times 200$ ; **E.** MUC4  $\times 100$ ; **F.** MUC4  $\times 400$ .

the most adequate treatment approach to LGFMS.<sup>7,9</sup> It is the long-established follow-up that becomes an issue due to protracted period between tumour presentation and metastasis.<sup>1,15</sup> In our case, 27 months after RT for SCC of the larynx, the patient presented with laryngeal LGFMS. (Fig. 4) The tumour originated from a region in close proximity to the former SCC. This unusual LGFMS behaviour raises a doubt whether surgery alone is sufficient therapy for this malignancy. And the insensitivity of the LGFMS to



**Figure 4.** Control endoscopy 2 months after debulking (A&B) and endoscopy 45 days later immediately before frontolateral vertical laryngectomy (C&D). Two residual tumor lesions could be identified (arrows) above the anterior commissure (A&C) and in the subglottic space right from the midline (B&D). The lesions in A&B were excised to confirm their nature so C&D represent regrowth over 45 days. The scar after the initial endoscopic excision and radiotherapy of the initial SCC is marked with the green dotted line.

RT and CTX stresses the importance of a clinical follow-up performed for an extended period of time.<sup>9,14</sup>

## CONCLUSIONS

We report in detail one of the few cases of laryngeal LGFMS. It appears that it is attributable to a previous RT. To the authors' knowledge, this is the first case report that discusses the clinical course, imaging diagnosis, histopathological evaluation and surgical approach to radiation-induced laryngeal LGFMS. This case stresses the importance of considering the RT history of the patient in order to monitor RT-related complications, including the occurrence of LGFMS.

## Potential competing interests

No potential conflict of interest relevant to this article was reported.

## Funding

No funding was available for this publication.

## REFERENCES

1. Evans HL. Low-grade fibromyxoid sarcoma. A report of two metastasizing neoplasms having a deceptively benign appearance. *Am J Clin Pathol* 1987; 88(5):615–9.
2. Hornick JL. Practical soft tissue pathology. 1st ed. Saunders; 2013.
3. Kanato T, Kalyani S, Lailiang T, et al. Low grade fibromyxoid sarcoma in oral cavity: a rare case report. *Indian J Otolaryngol Head Neck Surg* 2019; 71(1):25–6.
4. Arnaoutoglou C, Lykissas MG, Gelalis ID, et al. Low grade fibromyxoid sarcoma: A case report and review of the literature. *J Orthop Surg Res* 2010; 5(1):49.
5. Harish K, Ashok AC, Alva NK. Low grade fibromyxoid sarcoma of the falciform ligament: a case report. *BMC Surg* 2003; 3:7.
6. Cowan ML, Thompson LD, Leon ME, et al. Low-grade fibromyxoid sarcoma of the head and neck: a clinicopathologic series and review of the literature. *Head Neck Pathol* 2016; 10(2):161–6.
7. Marglani O, Lamothe A, Commons S. Radiation-induced low-grade fibromyxoid sarcoma of the sternocleidomastoid muscle. *The Journal of otolaryngology* 2007; 36(5):E73–5.
8. Shibata S, Shiraiishi K, Yamashita H, et al. Radiation-induced low-grade fibromyxoid sarcoma of the chest wall nine years subsequent to radiotherapy for breast carcinoma: A case report. *Oncol Lett* 2016; 11(4):2520–4.
9. Tatari MM, Elhariti L, Abou-elfadl M, et al. Low grade fibromyxoid sarcoma of the neck: a case report. *Ann Clin Case Rep* 2016; 1:1056.
10. Folpe AL, van den Berg E, Molenaar WM. Low grade fibromyxoid sarcoma. In: Fletcher CDM, Unni KK, Mertens F. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon: IARC Press; 2002. p 104–5.
11. Saito R, Kumabe T, Watanabe M, et al. Low-grade fibromyxoid sarcoma of intracranial origin. *J Neurosurg* 2008;108(4):798–802.
12. Almaskati J, Patil D, Sarsam S, et al. Low-grade fibromyxoid sarcoma: a rare distinctive soft tissue tumor. *Bahrain Medical Bulletin* 2013; 158(1187):1–3.
13. Canpolat C, Evans HL, Corpron C, et al. Fibromyxoid sarcoma in a four-year-old child: case report and review of the literature. *Med Pediatr Oncol* 1996; 27(6):561–4.
14. Maretty-Nielsen K, Baerentzen S, Keller J, et al. Low-grade fibromyxoid sarcoma: incidence, treatment strategy of metastases, and clinical significance of the FUS gene. *Sarcoma* 2013; 2013.
15. Wu X, Petrovic V, Torode IP, et al. Low grade fibromyxoid sarcoma: problems in the diagnosis and management of a malignant tumour with bland histological appearance. *Pathology* 2009; 41(2):155–60.

# Радиационно-индуцированная фибромиксоидная саркома гортани низкой степени злокачественности: клинический случай и обзор литературы

Дария Чивчибаши<sup>1</sup>, Павел Павлов<sup>2</sup>, Мария Цанева<sup>2</sup>, Николай Сапунджиев<sup>3</sup>, Георги Давидов<sup>3</sup>

<sup>1</sup> Кафедра физиологии и патофизиологии, Медицинский университет – Варна, Варна, Болгария

<sup>2</sup> Кафедра общей и клинической патологии, УМБАЛ „Св. Марина“, Варна, Болгария

<sup>3</sup> Кафедра нейрохирургии и оториноларингологии, Медицинский университет – Варна, Варна, Болгария

**Адрес для корреспонденции:** Дария Чивчибаши, Кафедра физиологии и патофизиологии, Медицинский университет – Варна, ул. „Марин Дринов“ №55, 9002 Варна, Болгария; E-mail: dariya.chivchibashi@mu-varna.bg; Тел.: +359 896 825 848

---

**Дата получения:** 8 июля 2020 ♦ **Дата приемки:** 24 сентября 2020 ♦ **Дата публикации:** 30 июня 2021

**Образец цитирования:** Chivchibashi DL, Pavlov P, Tzaneva M, Sapundzhiev N, Davidov G. Radiation-induced low grade fibromyxoid sarcoma of the larynx: a case report and literature review. Folia Med (Plovdiv) 2021;63(3):433-7. doi: 10.3897/folmed.63.e56150.

## Резюме

Фибромиксоидная саркома низкой степени злокачественности (ФМСНСЗ) – это редкий вариант фибросаркомы с высоким риском местного рецидива, огромным метастатическим потенциалом и часто длительным периодом между наличием опухоли и метастазированием. Это необычное злокачественное новообразование редко поражает область головы и шеи, что делает ФМСНСЗ гортани чрезвычайно редкими. На сегодняшний день ФМСНСЗ гортани упоминается в литературе редко. На сегодняшний день не выяснены ни частота, ни причины, ни факторы риска ФМСНСЗ гортани. Насколько известно авторам, это первый клинический случай, в котором обсуждаются клиническое течение, визуализация, гистопатологическая оценка и хирургический подход к ФМСНСЗ гортани, вызванной лучевой терапией.

Мы представляем случай 70-летнего мужчины, у которого развился ФМСНСЗ после предыдущей лучевой терапии (ЛТ) по поводу плоскоклеточного рака (ПКР) гортани. Латентный период между воздействием радиации и постановкой диагноза ФМСНСЗ составлял двадцать семь месяцев. После повторного подтверждения диагноза с помощью второй биопсии и оценки с помощью обширной визуализации пациенту была выполнена открытая частичная резекция гортани. Из-за редкости опухоли протокол для рекомендаций по контролю не разработан.

Этот случай подтверждает важность лучевой терапии в анамнезе пациента для отслеживания связанных с лучевой терапией осложнений, включая наличие ФМСНСЗ.

---

## Ключевые слова

редкий, мягкие ткани, опухоль