Case Report

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Primary Subglottic Laryngeal Leiomyosarcoma: A Case Report

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1. Abstract

1.1. Aims: Laryngeal leiomyosarcoma (LLMS) is an extremely rare malignant mesenchymal tumor of the larynx. Clinical data are especially limited for ultra-elderly patients. This study aims to summarize the clinical features, diagnostic pitfalls, and standardized treatment strategies of LLMS for clinical reference.

1.2. Methods: We retrospectively analyzed the complete clinical course of a 91-year-old male patient with primary subglottic LLMS, including diagnosis, surgical treatment, pathological features and follow-up outcomes.

1.3. Results: The patient was diagnosed with LLMS by postoperative immunohistochemistry after an initial false-negative biopsy. He underwent minimally invasive tumor resection first. Early recurrence occurred 2 months later. Radical total laryngectomy with bilateral cervical lymph node dissection was then performed. Surgical margins were negative, and no lymph node metastasis was found. Follow-up to date has shown no local recurrence or distant metastasis.

1.4. Conclusion: LLMS has non-specific clinical features and a high rate of preoperative misdiagnosis. Immunohistochemistry is the gold standard for diagnosis. Radical resection with negative margins is essential for prognosis. Long-term follow-up is required to monitor for recurrence.

2. Keywords: Laryngeal leiomyosarcoma; Leiomyosarcoma; Laryngeal neoplasm; Immunohistochemistry; Surgical resection

3. Introduction

Laryngeal malignancies make up 1%-5% of all new malignant tumors worldwide. Squamous cell carcinoma (SCC) accounts for over 95% [1]. Mesenchymal malignancies of the larynx rarely occur, making up less than 1% of all laryngeal neoplasms. Laryngeal leiomyosarcoma (LLMS) is even rarer among these sarcomas [2,3]. Jackson first described LLMS in 1939. Fewer than 60 cases of LLMS have been reported in the global literature to date [1,15].

LLMS arises from smooth muscle cells of the laryngeal vascular wall, arrector pili muscles, or pluripotent mesenchymal cells [3,7]. Its incidence is low due to the scarcity of smooth muscle tissue in the head and neck region [1,3]. Epidemiologically, LLMS mostly affects males aged 50-70 years. The male-to-female ratio is 4:1 [3,7]. LLMS has no proven association with smoking or alcohol, unlike laryngeal SCC [1,2]. Predisposing factors include prior radiation, hereditary syndromes, abnormal mesenchymal changes, Epstein-Barr virus infection in immunosuppressed patients, and abnormal postoperative healing [1,5,17].

Because of its nonspecific manifestations and rarity, LLMS is often misdiagnosed before surgery. There is no international consensus on diagnostic and treatment protocols [9,14]. Here we report a rare case of primary subglottic LLMS in a 91-year-old male. We also review relevant literature to summarize key clinical diagnosis and treatment points for this rare disease.

4. Case Presentation

A 91-year-old Chinese male was admitted in August 2024 for worsening hoarseness and 1 month of post-exertional dyspnea. He had no history of smoking, alcohol consumption, chronic laryngeal disease, malignant tumors, or chronic systemic diseases, and was fully independent in activities of daily living before symptom onset.

Laryngoscopy showed the neoplasm had grown to approximately

Annals of Clinical and Medical Case Reports

0.9 cm in diameter. The tumor had a wide base and caused mild narrowing of the glottic space. Contrast-enhanced neck CT revealed a 9 mm × 6 mm nodular lesion in the anterior glottis. There was no laryngeal cartilage destruction or cervical lymphadenopathy. After ruling out surgical contraindications, low-temperature plasma-assisted resection was performed via suspension laryngoscopy with an operative microscope. Intraoperative frozen section showed squamous epithelial hyperplasia in the left vocal cord and anterior commissure, and hyperplastic myofibroblasts in the subglottic region. Only local tumor resection was performed to preserve laryngeal function.

On the 5th postoperative day, paraffin pathology and immunohistochemistry (IHC) confirmed laryngeal leiomyosarcoma. The subglottic tumor showed hyperplastic spindle cells with significant atypia, visible mitoses, and surface necrosis. IHC results: smooth muscle actin (SMA) (+), h-caldesmon (+), Desmin (-), S-100 (scattered +), Pan-Cytokeratin (Pan-CK) (-), and Ki-67 (40% positive in dense areas). After detailed communication, the patient and his legal guardian chose discharge and regular follow-up.

In October 2024, follow-up laryngoscopy identified a 0.1 cm recurrent neoplasm beneath the anterior commissure of the vocal cords. Preoperative assessment confirmed that the patient's cardiopulmonary function could tolerate radical surgery. Intraoperative frozen section via median thyrotomy confirmed leiomyosarcoma involving both vocal cords, anterior commissure, and subglottic region. Radical total laryngectomy with bilateral cervical lymph node dissection and permanent tracheostomy was performed. Surgical margins were negative, and there was no lymph node metastasis in all 32 dissected nodes. The patient and legal guardian declined postoperative adjuvant chemoradiotherapy due to his advanced age and treatment tolerance.

Up to the last follow-up, no local tumor recurrence or distant metastasis was found in the patient; the tracheostomy stoma was unobstructed, with no stenosis or infection; the surgical incision healed completely, and no abnormal symptoms such as neck pain or swelling occurred.

A literature review shows that LLMS most commonly involves the glottis (48%), followed by the supraglottis (32%). Primary subglottic LLMS accounts for only 5%-6% of all cases [1,8]. Our case is not only a rare primary subglottic LLMS, but also the oldest reported LLMS patient to date. Globally, only 6 cases of synchronous laryngeal SCC and LLMS and 3 cases of radiation-induced LLMS with a latency of up to 17 years have been reported [2,5,17]. This highlights the high clinical heterogeneity of this rare disease.

Figure 1 Clinical and pathological findings of the case

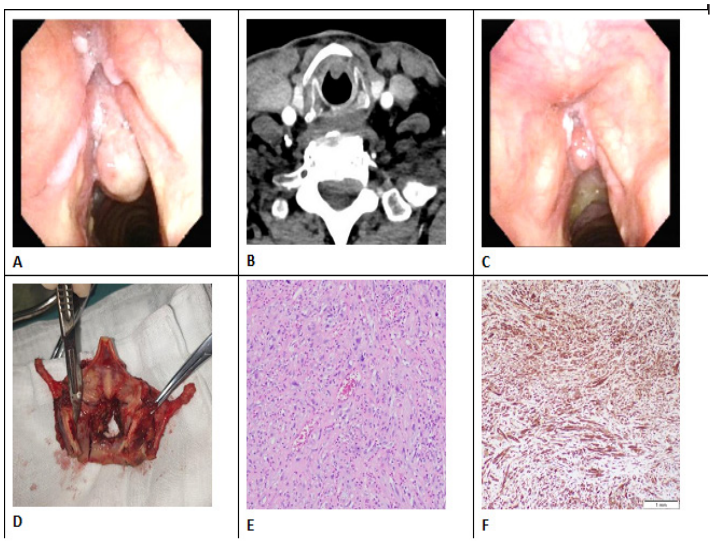

Figure 1.
A. Preoperative laryngoscopy in August.
B. Preoperative contrast-enhanced neck CT in August.
C. Follow-up laryngoscopy in October.
D. Intraoperative specimen image in October.
E. Microscopic hematoxylin and eosin (HE) staining of the tumor tissue.
F. Immunohistochemistry (IHC) staining showing diffuse positive expression of Smooth Muscle Actin (SMA) in the tumor tissue.

5. Discussion

5.1. Diagnostic Challenges and Pathological Confirmation of LLMS

Diagnosing LLMS is extremely challenging. Its non-specific manifestations are indistinguishable from those of laryngeal SCC and other benign laryngeal lesions [1,3]. Common symptoms are progressive hoarseness, dyspnea, dysphagia, and a sensation of a foreign body in the throat. Severe cases may present with acute airway obstruction [1,13]. The duration of symptoms varies from 2 weeks to 2 years. This is not reliable for differential diagnosis [3,7].

In our case, both the initial intraoperative frozen section and the superficial biopsy were false-negative. This is consistent with previous reports of diagnostic pitfalls in LLMS [9]. The main reasons are the tumor's submucosal growth pattern and the similarity between spindle cell morphology and reactive myofibroblast hyperplasia in frozen sections [9,16]. Multiple deep biopsies are required for long-standing laryngeal lesions to reduce missed diagnoses. Clinicians should be aware of the limitations of intraoperative frozen-section analysis for this rare tumor [9,16].

Definitive diagnosis of LLMS relies on histopathology combined with IHC. This is the key for differentiating LLMS from other laryngeal spindle cell tumors [1,6]. Histologically, LLMS shows interlacing fascicular spindle cells with blunt-ended, cigar-shaped

nuclei, eosinophilic cytoplasm, nuclear atypia, increased mitoses (usually >5 per 10 high-power fields), and tumor necrosis [1,15]. The typical IHC profile: positive for smooth muscle markers (SMA, h-caldesmon, Desmin, Vimentin) and negative for epithelial, neural, and myogenic markers [1,6,15]. Loss of Desmin expression does not rule out LLMS. Comprehensive judgment using multiple smooth muscle markers is needed [2,14].

The main differential diagnoses include rhabdomyosarcoma, malignant schwannoma, and sarcomatoid carcinoma. These can be excluded by specific IHC markers [1,13]. Electron microscopy helps in cases with unclear IHC results [1,8]. Neck CT and MRI are important for mapping tumor extent and guiding surgical planning [1,17]. LLMS rarely spreads to lymph nodes (incidence <10%). Elective cervical lymph node dissection is not recommended unless there are confirmed metastases [3,7,14,15].

5.2. Treatment Strategy for LLMS

There is no standardized treatment guideline for LLMS because it is extremely rare. Current evidence shows that radical surgery with wide negative margins is the main and most effective treatment [1,12,14]. The surgical procedure should be tailored to the tumor's features and the patient's general condition.

For early, localized, low-grade LLMS, conservative surgery can be used to preserve laryngeal function [14,16]. Our patient developed an early recurrence 2 months after local resection. This supports studies showing that endoscopic surgery often fails to achieve negative deep margins for subglottic lesions [9]. Conservative surgery should be used with caution for subglottic LLMS, especially with an unclear diagnosis [9]. Total laryngectomy is preferred for widely invasive, recurrent, or high-grade tumors. This reduces the risk of local recurrence [1,3].

The role of adjuvant radiotherapy and chemotherapy remains controversial. Radiotherapy is used only as an adjuvant modality for positive margins, residual disease, or recurrence, with limited efficacy as a primary treatment [1,17]. Routine adjuvant radiotherapy is not required for patients with negative margins [9,14]. Chemotherapy has a very limited role, and is only considered for distant metastasis or advanced unresectable disease, with doxorubicin-based regimens as the first choice [5,8].

5.3. Prognosis and Follow-up

The overall prognosis of LLMS is poor, with a reported 5-year overall survival rate of 35%-50% [1,3,7]. The local recurrence rate after surgery is 35%-50%, and distant metastasis (most commonly to the lungs and liver) occurs in 35%-38% of cases [1,7,17]. Adverse prognostic factors include high pathological grade, tumor diameter >5 cm, positive surgical margins, and distant metastasis at diagnosis [8,15]. LLMS can recur even years after initial treatment, so all patients require long-term, regular follow-up [1,3].

6. Conclusion

Laryngeal leiomyosarcoma is an extremely rare malignant mesenchymal tumor of the larynx, with non-specific clinical manifestations and a high preoperative misdiagnosis rate. Multiple deep biopsies and standardized immunohistochemistry are essential to avoid missed diagnosis, and immunohistochemistry is the gold standard for definitive diagnosis. Radical surgical resection with negative margins is the core treatment to improve patient prognosis, while the role of adjuvant radiotherapy and chemotherapy is limited. Long-term follow-up is required after treatment to monitor late recurrence and distant metastasis.

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Annals of Clinical and Medical Case Reports

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