

Laryngeal leiomyosarcoma with coexistent tuberculous mediastinal lymphadenopathy

Eşlik eden tüberküloz mediastinal lenfadenopati ile birlikte larengeal leiomyosarkom

Nesibe Gül Yüksel Aslier, MD,¹ Ersoy Doğan, MD,¹ Sülen Sarıoğlu, MD,² Ahmet Ömer İkiz, MD¹

¹Department of Otolaryngology, Medical Faculty of Dokuz Eylül University, İzmir, Turkey

²Department of Pathology, Medical Faculty of Dokuz Eylül University, İzmir, Turkey

ABSTRACT

Laryngeal leiomyosarcoma is an extremely rare malignancy originating from the smooth muscles of blood vessels. Herein, we present the first case of leiomyosarcoma arising from the glottic area of the larynx with coexistent tuberculous mediastinal lymphadenopathy. The patient was treated with vertical laryngectomy and anti-tuberculous medication. He has been disease-free for 24 months since initial treatment.

Keywords: Larynx; leiomyosarcoma; mediastinal lymphadenopathy; vertical laryngectomy.

ÖZ

Larengeal leiomyosarkom, kan damarlarının düz kaslarından köken alan, son derece nadir bir malignitedir. Bu yazıda, eşlik eden tüberküloz mediastinal lenfadenopati ile birlikte larenksin glottik bölgesinden köken alan ilk leiomyosarkom olgusu sunuldu. Hasta vertikal larenjektomi ve antitüberküloz ilaçlar ile tedavi edildi. İlk tedaviden bu yana 24 aydır hasta hastalıksızdır.

Anahtar Sözcükler: Larenks; leiomyosarkom; mediastinal lenfadenopati; vertikal larenjektomi.

Soft tissue sarcomas comprise less than 1% of head and neck malignant tumors. Eeles et al.^[1] reviewed histological slides from 103 of 130 patients with head and neck sarcomas in their study and found nine patients diagnosed as leiomyosarcoma. When a Pubmed search using the MeSH keywords 'laryngeal leiomyosarcoma' and 'larynx, leiomyosarcoma', 62 cases reported in 55 case reports from 1959 till September 2013 can be found. In past years with the absence of immunohistochemistry, diagnosis of laryngeal leiomyosarcoma (LLMS) was more problematic.

Nowadays differential diagnosis of the laryngeal sarcomatous tumors is still disputable and late diagnosis might result in inappropriate and/or incomplete management of the disease.

In the present report a new case of LLMS with simultaneous tuberculous mediastinal lymphadenopathy (TML) is presented with physical examination findings, diagnosis, management and follow-up results in order to contribute and discuss the literature about this rare malignant tumor of the larynx.





Figure 1. Axial computed tomography scan of the neck: tumor in the right glottic area.

CASE REPORT

A 68-year-old man with a past history of diabetes mellitus, hypertension and thyroidectomy for multinodular goiter presented with hoarseness in the last three months. He had quit smoking 10 years ago with a past smoking history of 30 pack years. At his first visit to another otolaryngology clinic, microlaryngoscopy and biopsy was performed on the right vocal cord and pathology was reported as 'mucosal ulceration'. The biopsy was repeated two months later and this time it was reported as 'suspicious for leiomyosarcoma'. The patient was referred to our department.



Figure 2. Axial computed tomography scan of the thorax, mediastinal window: mediastinal lymph nodes.

Consultation of the biopsy material with our Pathology Department was reported as "spindle cell tumor with mild pleomorphism (vimentin, actin, desmin positive, caldesmon focal positive; myogenin and pan-cytokeratin negative), consistent with leiomyosarcoma, but due to small biopsy size correlation with clinical findings is recommended". Computed tomography (CT) of the neck disclosed a tumor in the right glottic area and its diameter was approximately 15 mm (Figure 1). Computed tomography of the thorax showed paratracheal, pericarinal, subcarinal and mediastinal lymphadenopathies and pleural thickening but parenchymal neoplastic disease was not detected (Figure 2). Tuberculin skin test gave a wheal of 22 mm in the patient. Sputum smears and cultures failed to grow acid-fast bacilli.

We performed microlaryngoscopy under general anesthesia and broad-based deep biopsies were taken from the smooth surface of a polypoid tumor located at the anterior two thirds of the right vocal cord with extension to the right ventricle (Figure 3). Histopathological examination revealed a submucosal spindle cell tumor with moderate nuclear polymorphism, Ki-67 positivity in 30% of the tumor cells and mitotic activity (4 in 10 high power field), compatible with leiomyosarcoma (Figure 4). The mediastinal lymphadenopathies biopsied



Figure 3. Microlaryngoscopic view: tumor in the anterior two thirds of the right vocal cord extending to right ventricle.

concurrently by thoracic surgeons revealed necrotizing granulomatous inflammation diagnosed as tuberculosis.

Following the elimination of the possibility of distant disease by positron emission tomography (PET) a right vertical hemilaryngectomy was performed. Intraoperative frozen-sections performed for surgical margin control were all tumor negative. The final pathology report was also reported as leiomyosarcoma with negative surgical margins. The patient was decannulated on the eighth postoperative day. The patient was discussed at our Multidisciplinary Head and Neck Tumor Board and close follow-up without additional therapy was decided. The patient was also referred to Pulmonary Medicine Department for TML. The patient was given antituberculosis treatment -- a six-month course of rifampicin and isoniazid supplemented initially by pyrazinamide for two months. The patient is still disease-free on his postoperative 24th month of follow-up.

DISCUSSION

Leiomyosarcomas are rarely seen in the head and neck as there are not many smooth muscle

derived structures in this region. Eppsteiner et al.^[2] reported a laryngeal location as 2.2% (13 of 578 cases) for leiomyosarcoma of the head and neck. Unlike ulcero-vegetating squamous cell carcinomas of the larynx, they are generally polypoid or submucosal lesions. As it has been shown in Figure 3, the lesion was also polypoid in our case.

Even though Chizh has described a case of LLMS in an eight-year-old girl, the tumor frequently occurs in middle aged men.^[3] Radiation induced sarcomas or sarcomatoid dedifferentiation of squamous cell carcinomas after irradiation has been proposed; however radiotherapy has not been found to be present in the history of most patients with LLMS.^[4] An interesting case of LLMS that occurred after primary laryngeal squamous cell carcinoma reported by Völker et al.^[4] had also not received radiotherapy after surgical treatment of his primary disease. Kara et al.^[5] reported two cases of LLMS with rare association of squamous cell carcinoma of the larynx. Unlike squamous cell carcinoma of the larynx, there is no proven link between smoking and/or alcohol intake for occurrence of this tumor.^[6]

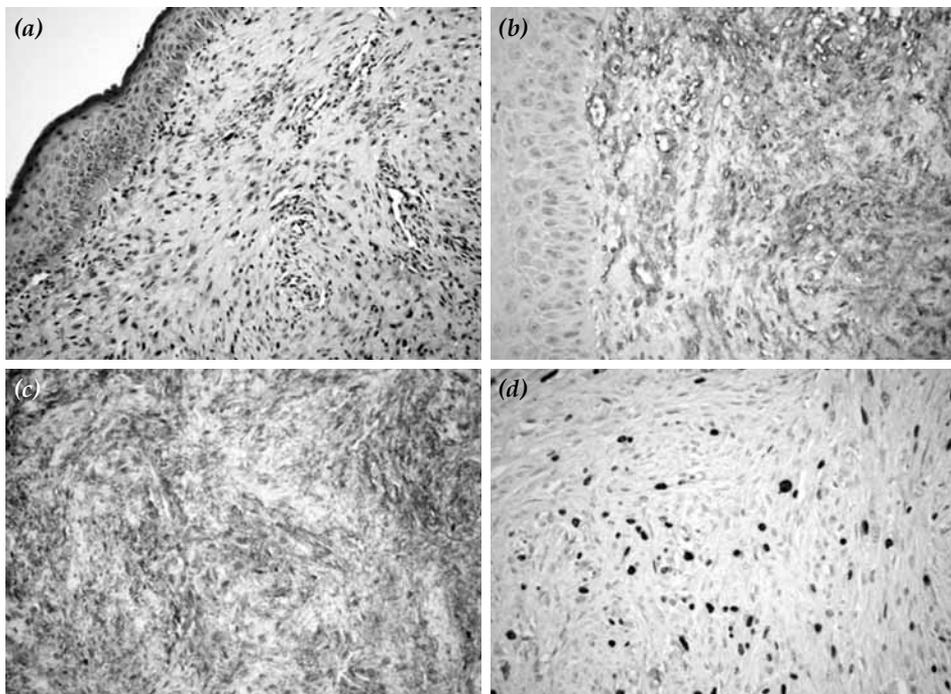


Figure 4. (a) Spindle cell neoplasm with atypia and pleomorphism underlying squamous epithelium (H-E x 200). (b) Actin expression (IHC x 400). (c) H-Caldesmon expression (IHC x 400). (d) Ki-67 expression (IHC x 400).

Laryngeal leiomyosarcoma is most frequently located at the supraglottic or the glottic area as seen in our case. There are only two cases reported in the subglottic region.^[6,7] Hoarseness is the most common complaint on admission. Dyspnea or stridor due to progressive sessile growth of the tumor may necessitate emergency tracheotomy.^[8] Occasionally a foreign body sensation in the throat, dysphagia, referred otalgia and neck mass can be the initial complaints especially in supraglottic tumors.

On light microscopy, intersecting and interlacing fascicular arrangements of spindle cells with cytoplasmic extensions and elongated nuclei are seen. The presence of nuclear pleomorphism and increased mitotic activity detected under high power magnification are the most important criteria for malignancy. Immunohistochemistry is the most valuable study for diagnosis. The tumor cells are often positive for muscle-specific actin, vimentin and desmin on immunohistochemical staining, whereas they are negative for cytokeratin, epithelial membrane antigen, CD34 and S100 protein. H-caldesmon is also believed to be specific for leiomyosarcoma.^[9] Tumor size, cellularity, cytologic atypia, necrosis, and hemorrhage may correlate with the malignant behavior of the smooth muscle tumors but the most dependable predictor is the level of mitotic activity and Ki67 proliferation index also has supportive importance.^[10] Electron microscopy may be required to figure out ultrastructural characteristics including pinocytic vesicles, desmosomes and myofibrils in cases with nonspecific light microscopic findings and obscure immunohistochemical staining. Our case was a spindle cell tumor expressing markers of muscle differentiation including h-caldesmon, atypia, increased mitotic activity and increased ki-67 expression, which were diagnostic for leiomyosarcoma.

Similar to other sarcomatous tumors, metastatic spread via the bloodstream to lungs, liver and skeleton may be seen. That is why PET scan was performed in our patient with paratracheal, pericarinal, subcarinal and mediastinal lymphadenopathies and pleural thickening reported on CT of the thorax. The involvement of the lymph nodes in the neck does not exceed 10-15% of patients.^[6] Skoulakis et al.^[11] presented a case report with literature review of 30 previous cases of LLMS. None of the patients

presented with nodal or distant metastases at the time of diagnosis. Two of them (6.45%) developed nodal metastases and six of them (19.35%) developed distant metastases mainly to lungs. Co-occurrence of mediastinal lymphadenopathy has not been reported in the literature. Even primary pulmonary leiomyosarcoma does not generally expected to involve mediastinal lymph nodes, mediastinal nodal disease of LLMS is also not known.

In previous case reports, there is a broad range of treatment options from local excision alone by transoral laser resection to total laryngectomy with elective neck dissection and adjuvant chemoradiotherapy.^[4-8,11-15] In general, partial laryngectomy is recommended for patients with early stage tumors and postoperative radiotherapy might have a role in allowing a more limited surgical resection or it might be a complementary therapy to improve loco-regional control.^[4-8,11-15] Neck dissection is indicated for clinically positive cervical nodal disease.^[14] Elective neck dissection is not indicated unless there are clinically positive nodes.^[11,13] Radiotherapy by itself is generally not a treatment of choice for LLMS and the tumor is mostly believed to be resistant to radiotherapy.^[6] Cocks et al.^[12] also concluded that radiation therapy on its own has not been shown to be useful. However, in a cohort study of Eppsteiner et al.,^[2] patients with leiomyosarcoma of the head and neck who received surgery alone had improved survival compared to those who received primary or adjuvant radiotherapy. They deduced that adjuvant radiotherapy could be reserved for patients who had poor prognostic factors such as large, invasive tumors with poorly differentiated histological features.^[2] The place of chemotherapy in LLMS is generally at the metastatic stage of disease but information is limited for this treatment modality.^[11] In our case, right vertical hemilaryngectomy was performed and there was no indication for additional treatment postoperatively. For TML, patient was treated by antituberculous medication. The patient has been free of disease for 24 months.

The first case report of LLMS from our country was published in 1989.^[16] The number of LLMS cases presented in our national and international journals do not exceed five. Whereas it is expected for tuberculosis to be associated with any medical condition in our country, LLMS with a coexistent

TML was first presented herein with the intent to make a contribution to the literature on clinical findings, diagnosis, treatment modalities and follow-up results of this unusual malignant tumor of the larynx and to show TML is likely to be the reason for mediastinal disease without any involvement of primary tumor. Even though the initial treatment modality establishes disease control, because local recurrence, nodal and distant disease may be seen unpredictably in the early years, close follow-up is crucial for patients with LLMS. As there is scarce accumulation of knowledge regarding optimal treatment modalities and postoperative follow-up results of the laryngeal leiomyosarcoma, the tumor behavior needs to be emerged from obscurity by additional case reports.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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