Case Report

A case of well-differentiated liposarcoma of the larynx histologically indistinguishable from spindle cell lipoma

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Abstract

Correctly identifying atypical lipomatous tumors/well-differentiated liposarcomas (WDLs) can be exceedingly difficult, as they account for <0.5% of all laryngeal neoplasms. Diagnosis is further complicated by their morphologic similarity with other more benign lipogenic tumors, such as spindle cell lipoma. We describe a 63-year-old Caucasian man who presented with a left aryepiglottic mass clinically suspicious for a simple cyst. On excision, a frozen section diagnosis of benign fibrolipomatous lesion was reported. Permanent sections revealed an adipocytic neoplasm comprising cellular fibrosis and monomorphic spindle cells, histologically suggestive of a spindle cell/pleomorphic lipoma. Immunostains were positive for CD34 and negative for smooth muscle actin, desmin, and S-100 protein, also consistent with spindle cell/pleomorphic lipoma. However, amplification of MDM2 by fluorescence in situ hybridization confirmed the diagnosis of WDL. The case was reviewed by two soft-tissue pathologists, and they both favored the diagnosis of spindle cell lipoma until reviewing the relevant MDM2 result. The morphology and immunophenotype of WDL have previously been reported as closely related to that of spindle cell lipoma, and this case provides a striking example of how unmistakable these two entities can be on histologic examination alone.

Keywords: Atypical lipomatous tumor/well-differentiated liposarcoma, larynx, MDM2 gene amplification, spindle cell lipoma

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INTRODUCTION

Atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL) has been described as the most common subtype of liposarcoma, generally occurring within the limbs and retroperitoneum. Whereas only 5.6% arise in the head and neck, the larynx has been described as the primary site of origin in only 20% of all head-and-neck liposarcomas, with most occurring in the regional soft tissues.[1] When they present in the larynx or hypopharynx, these tumors constitute <0.5% of all laryngeal neoplasms. A male-to-female predominance has been described, and the average patient is within the sixth decade of life. Definitive therapy is complete surgical excision; local recurrences are common, but the prognosis is exceptional – a 5-year survival of essentially 100% has been reported.[2] The differential diagnosis includes spindle cell lipoma, which features bland spindle cells within an abundant myxoid stroma that can be difficult to distinguish from ALT/WDL in the absence of identifiable cellular atypia. As a result, overexpression of the MDM2 gene has become the gold standard for separating liposarcomas from other more

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benign entities.[3] Without MDM2 testing, the diagnosis of ALT/WDL would likely have been impossible in the case presented here, which was histologically indistinguishable from a spindle cell lipoma.

CASE REPORT

A 63-year-old Caucasian man presented in August 2014 with a 1-year history of throat clearing and voice changes. His past medical history was notable for multiple nonmelanoma skin cancers and no previous head-and-neck issues. Per the patient, his voice had become "gravelly" over the past 6–8 months, and he would occasionally experience some nonexertional shortness of breath that would resolve instantaneously. His symptoms worsened upon reclining, and he denied dysphagia.

Laryngoscopy revealed a submucosal lesion along the left aryepiglottic fold that was mobile and could be displaced between the laryngeal introitus and the piriform sinus; it did not penetrate to the level of the vocal fold. The mass was consistent with an aryepiglottic cyst, although malignancy could not be excluded clinically. Therefore, the patient opted to proceed with microdirect laryngoscopy and complete excision of the lesion using a carbon dioxide laser.

A 1.6 cm × 0.9 cm × 0.7 cm soft-tissue fragment was submitted to pathology, and representative frozen sections were consistent with a benign fibrolipomatous lesion. Permanent sections of the remaining specimen demonstrated an adipocytic neoplasm that was traversed by ropy collagen and cellular fibrous bands populated by monomorphic spindle cells and rare atypical stromal cells with hyperchromatic nuclei [Figure 1]. No necrosis or mitoses were identified. Immunostains were positive for CD34 but negative for smooth muscle actin, desmin, and S-100 protein. Fluorescence *in situ* hybridization (FISH) amplification for MDM2 was abnormal, with an average MDM2 signal number per cell >10.0 in 20 counted cells.

The case was reviewed in consultation by two soft-tissue pathologists who agreed that although the morphologic features of the tumor and the associated immunostains were strongly suggestive of a benign spindle cell lipoma, MDM2 testing confirmed the diagnosis of ALT/WDL.

DISCUSSION

Our patient is among the less than 40 individuals with reported liposarcoma of the larynx/hypopharynx. Most cases occur in the supraglottic area, with only four having been documented within the true vocal cords.[4] The average age of patients is 55 years (range: 28–83 years). This tumor

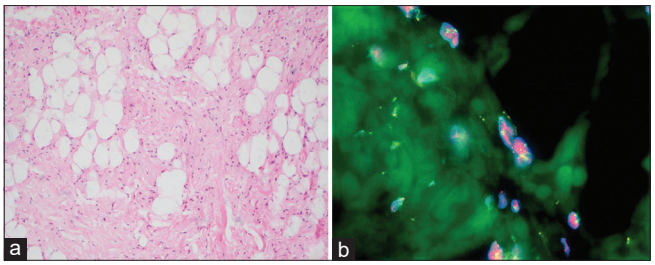

Figure 1: (a) Hematoxylin and eosin staining of the patient's laryngeal tumor at × 200 demonstrates collections of adipocytes disrupted by ropy, cellular fibrous bands punctuated by monomorphic spindle cells. (b) Immunostains (not pictured) are positive for CD34 and negative for smooth muscle actin, desmin, and S-100 protein. Fluorescence *in situ* hybridization demonstrates greater than 10 MDM2 signals per cell, consistent with gene amplification

is more common in men (male-to-female ratio of 8:1) and is often clinically mistaken for cysts causing hoarseness and breathing difficulties.

While other liposarcoma subtypes (including myxoid/round cell, pleomorphic, and dedifferentiated) have been rarely described in the larynx, the majority of cases are described as ALT/WDL.[5-7] This subtype is locally aggressive but does not generally involve regional lymph nodes, and distant metastasis is not expected.[8] Essentially 100% survival is reported at 5 years. Although surgical resection is the definitive treatment, recurrence is common. Therefore, long-term follow-up is required, and a total laryngectomy may eventually become necessary.[9] Some clinicians advocate postoperative low-dose radiation, but only a few patients have been treated by this modality due to the rarity of the tumor, and no systematic comparison studies have been completed.[10]

Ultimately, ALT/WDL demonstrates a more locally aggressive nature than its benign lipomatous counterparts, such as spindle cell lipoma. Therefore, proper clinical management is contingent upon proper pathologic diagnosis, which would not have been possible in our case without MDM2 testing. Two consulting soft-tissue pathologists were misled by the morphologic characteristics of our patient's tumor, which they considered pathognomonic for spindle cell lipoma. Clay *et al*. documented a similar diagnostic difficulty for 303 other ALTs and was able to successfully classify 108 as liposarcoma only by MDM2 FISH.[10] This study demonstrated that MDM2 gene amplification remains the most sensitive and specific method for confirming the diagnosis of ALT/WDL.

CONCLUSION

Pathologists must remain vigilant when examining ALTs and always consider molecular testing so as to prevent

misdiagnosis. Fortunately, for our patient, his tumor type was detected by MDM2 gene amplification, and he since has undergone multiple surveillance laryngoscopies, which suggest that his lesion was entirely excised without evidence of recurrence.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Mateva S, Nikolova M, Valkov A, Todorova-Doneva J. Well-differentiated liposarcoma of the larynx: A case report and review of literature. J Biomed Clin Res 2016;9:85-9.
2. Zhu H, Sun J, Wei S, Wang D, Brandwein M. Well-differentiated laryngeal/Hypopharyngeal liposarcoma in the MDM2 era report of three cases and literature review. Head Neck Pathol 2017;11:146-51.
3. Jakobiec FA, Nguyen J, Bhat P, Fay A. MDM2-positive atypical lipomatous neoplasm/well-differentiated liposarcoma versus spindle cell lipoma of the orbit. Ophthalmic Plast Reconstr Surg 2010;26:413-5.
4. Han Y, Yang LH, Liu TT, Wang J, Li H, Yu G, *et al*. Liposarcoma of the larynx: Report of a case and review of literature. Int J Clin Exp Pathol 2015;8:1068-72.
5. Krausen AS, Gall AM, Garza R, Spector GJ, Ansel DG. Liposarcoma of the larynx: A multicentric or a metastatic malignancy. Laryngoscope 1977;87:1116-24.
6. Ferlito A. Primary pleomorphic liposarcoma of the larynx. J Otolaryngol 1978;7:161-6.
7. McCormick D, Mentzel T, Beham A, Fletcher CD. Dedifferentiated liposarcoma. Clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. Am J Surg Pathol 1994;18:1213-23.
8. Powitzky R, Powitzky ES, Garcia R. Liposarcoma of the larynx. Ann Otol Rhinol Laryngol 2007;116:418-24.
9. Maheshwari GK, Baboo HA, Gopal U, Mehta S, Shah NM. Liposarcoma of the larynx treated with radiotherapy. Indian J Otolaryngol Head Neck Surg 1998;50:269-71.
10. Clay MR, Martinez AP, Weiss SW, Edgar MA. MDM2 amplification in problematic lipomatous tumors: Analysis of FISH testing criteria. Am J Surg Pathol 2015;39:1433-9.