Liposarcoma is the most common type of soft tissue sarcoma accounting for 20% of all mesenchymal malignancies (1). Liposarcomas of the head and neck represent only 3% of all liposarcomas and are often subcutaneous, low grade, early stage, and with fewer nodal metastases than liposarcomas in non-head and neck sites (2). Well-differentiated spindle cell liposarcoma (WIDC) was first described by Des Tos AP et al. in 1994 (3). It represents a rare variant of well-differentiated liposarcoma composed predominantly of spindle cells admixed with atypical lipogenic cells. Histologically, the tumor contains CD34-positive spindle cells with slightly enlarged, fusiform nuclei in short fascicles in a collagenous or fibromyxoid stroma. WIDC is frequently subcutaneous and occurs in the trunk, lower extremities, and head and neck region. It is a rare and locally aggressive growing mesenchymal tumor and may recur, whereas metastasis and dedifferentiation have been rarely reported. Therefore, wide local excision with long-term follow-up looking for recurrence and metastasis is necessary in this rare variant of liposarcoma (4, 5). Herein we report the first case, to our knowledge, of WIDC of the larynx.

Case Report

A 59-year-old male with no significant past medical history presented with change of voice and phlegmy cough for several months. Laryngoscopy revealed a mucosal covered pedunculated mass on the supraglottis. A computerized tomography (CT) scan of the neck showed a well-defined low-attenuation mass causing moderate narrowing of the airway (Figure 1A). A laryngoscopy-driven excisional biopsy was performed. Intraoperatively, a smooth solid mass extending from the right supraglottic region underneath the right arytenoid and interarytenoid mucosa was noted (Figure 1B). Grossly, the mass was ovoid, solid and soft with homogeneously white-gray and rubbery cut surface and measured 4.2 cm in greatest dimension (Figure 1C). Microscopically, sections of this mass revealed a well-demarcated neoplasm composed of predominantly atypical and focally pleomorphic spindle cells distributed in a
prominent collagenous stroma, with admixed adipocytes showing variation in cell size and rare lipoblasts (Figure 2). There was no tumor necrosis. A rare mitotic figure was noted. Immunohistochemically, the spindle cells were strongly positive for MDM2 and CDK4. There was also multifocal positivity for CD34 and rare cells positive for desmin, while S100 protein was negative (Figure 3). Staining for retinoblastoma (Rb) was positive (normal/retained). The combined histology and immunoprofile are consistent with WDSCCL. Due to positive resection margin, the patient subsequently received endoscopic local wide re-excision with carbon dioxide laser. At 4 months after primary excision, the patient was doing well with no evidence of recurrence or metastasis.

Discussion

WDSCCL occurs most commonly in the subcutaneous tissue of extremities, trunk, and neck and cheek region but rarely seen in the larynx. Morphologically, WDSCCL consists of spindled tumor cells in short fascicles set in a fibrous, collagenous or fibromyxoid stroma. Areas of traditional lipoma-like morphology can be found. The differential diagnoses of this case include reactive or benign spindle cell lesions such as nodular fasciitis, fibromatosis, spindle cell lipoma, inflammatory myofibroblastic tumor, and leiomyoma, or malignant mesenchymal tumors such as liposarcoma, myxofibrosarcoma, malignant peripheral nerve sheath tumor, and low-grade fibromyxoid sarcoma. Laryngeal fibromatosis in adults is a rare, locally infiltrative and rapidly progressive disease (6). It is composed of relatively bland and collagenous spindled cells without significant cytological atypia or mitosis. Fibromatosis is characterized by mutations in the beta-catenin gene or the adenomatous polyposis coli (APC) gene, most are sporadic but some are associated with several syndromes such as Gardner’s syndrome. Diffuse nuclear beta-catenin stain is helpful to make the diagnosis. Laryngeal inflammatory myofibroblastic tumors consist of fibroblastic and myofibroblastic spindle cells in a myxoid background with significant mixed inflammatory infiltrate. The diagnosis can be confirmed by the presence of anaplastic lymphoma kinase (ALK) overexpression and by fluorescence in situ hybridization (FISH) rearrangement (7). Spindle cell lipoma is a benign lipomatous tumor composed of admixture of mature adipocytes and fibroblast-like spindle cells in myxoid stroma. Compared to liposarcoma, spindle cell lipoma does not contain lipoblasts and lacks MDM2 and CDK4 amplification (8).

WDSCCL and other sarcomas such as myxofibrosarcoma or low-grade fibromyxoid sarcoma share many clinical and histological features making the differential diagnosis difficult in some cases. Morphologic features that can help differentiate between those tumors include the presence of lipoblasts and prominent “chicken wire” pattern vasculature in WDSCCL (9, 10).

Ancillary tests including immunohistochemistry and molecular studies can be very helpful to make the correct diagnosis of WDSCCL. Immunohistochemically, the spindle cells in all WDSCCL cases are at least focally positive for CD34. Only a portion of the WDSCCL cases were positive for MDM2 (5). Although MDM2 amplification has been estimated to occur in the majority of well-differentiated liposarcoma/atypical lipomatous tumors and dedifferentiated liposarcomas (~98%) (11), previous studies showed that soft tissue WDSCCLs of the extremities do not contain MDM2 gene amplifications. Instead, it has been reported to harbor RB1 gene deletions and loss of RB expression (5, 12). More recently, in-frame TRIO-TERT fusion gene has been described in a case of spindle cell liposarcoma of the thigh through next-generation sequencing (13). This type of in-frame TRIO-TERT fusion has been identified in some non-
translocation-related sarcomas such as dedifferentiated liposarcoma, undifferentiated pleomorphic sarcoma, or leiomyosarcoma. The gene arrangement can lead to significantly increased TERT mRNA expression levels, causing increased telomerase activation in these sarcomas. The TRIO-TERT fusions have not been identified in any RB1-deleted spindle cell lipomatous tumors, suggesting that this may represent a biologically distinct pathway (14). Our case is unique in that the spindled tumor cells are strongly and diffusely positive for MDM2 and CDK4, consistent with amplification of these genes on the long arm of chromosome 12. No RB loss of expression is identified. The findings suggest that laryngeal WDSCL exhibits similar molecular alterations compared to conventional well-differentiated liposarcoma. Identifying molecular genetic alterations of this rare entity with additional cases in the future are required to better classify this type of spindle cell lipomatous neoplasm.

WDSCL is a locally aggressive mesenchymal tumor with recurrent potential and low risk of metastasis (5). Wide local excision with negative margins is the preferred treatment (15). In general, anatomic site is the most important prognostic factor for conventional well-differentiated liposarcoma, with higher risk of recurrence in tumors of body cavities compared to those in extremities (16). Our patient recovered uneventfully after the surgery. No evidence of recurrence or metastasis was noted at 4 months after primary excision. Due to the limited number of case reports, the prognosis of WDSCL, particularly those in the larynx, is still unknown.

Figure 2. Histological features (Hematoxylin and Eosin staining) of laryngeal WDSCL. (A, B): Low- and high-power view of the tumor showing predominantly atypical and focally pleomorphic spindle cells admixed with adipocytes (C) in a fibromyxoid background. (D): High-power magnification showing nuclear pleomorphism and atypical vacuolated lipoblasts. Magnifications: A, ×20; B and C, ×100; D, ×200.
In conclusion, we report the first case of WDSCL of the larynx which was completely excised. The results suggest that WDSCL should be considered in the differential diagnosis of patients presenting with a spindle cell neoplasm in the larynx. Ancillary tests are helpful to make the diagnosis. Long-term follow-up is required to monitor the progression of this rare tumor.

Conflicts of Interest

The Authors declare no conflicts of interest with regard to the study.

Authors’ Contributions

X.L. and D.Z. contributed to the design and implementation of the study, to the analysis of the results and to the writing of the article. S.F. contributed to the data collection.

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Figure 3. Immunohistochemical stains of laryngeal WDSCL. (A, B): Spindled tumor cells are diffusely positive for CD34. (C, D): Atypical and pleomorphic spindled tumor cells showing a strong nuclear expression of CDK4 (C) and MDM2 (D). Magnification: ×100.
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Received March 4, 2021
Revised June 1, 2021
Accepted June 3, 2021