Cervical Dedifferentiated Liposarcoma with Meningothelial-Like Whorling

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Abstract Liposarcomas are the most common soft-tissue sarcoma of adults, but rare in the head and neck. Recently, a subtype of dedifferentiated liposarcoma with meningiothelial-like whorls was reported and we present the first description of such a tumor in the head and neck. A 65 year old male underwent a resection of a calcified retroesophageal mass that was in close relation to the left hemithyroid and recurrent laryngeal nerve. It was resected en bloc with the left thyroid lobe. Initial pathologic evaluation suggested the mass was a schwannoma of the recurrent laryngeal nerve, but positive staining for MDM2 and CDK4 indicated the tumor was a dedifferentiated liposarcoma. Further evaluation elucidated the unique meningiothelial-like whorls within the tumor. This case demonstrates dedifferentiated liposarcomas do appear in the head and neck. Furthermore, this is the first report in the head and neck of the meningiothelial-like whorling pattern type of dedifferentiated liposarcoma.

Keywords Liposarcoma · Dedifferentiated · Meningiothelial-like whorls · Cervical

Introduction

Sarcomas represent less than 1 % of malignancies in the US; of those, liposarcomas are the most common and account for 17–25 % of all adult sarcomas [1–3]. They are most commonly found in the retroperitoneum, trunk and extremities. The head neck region remains a rare location demonstrated by a 60-year retrospective analysis of liposarcomas at MD Anderson showing a 2 % incidence in the head and neck region [3]. Liposarcomas are classified into four major types: well-differentiated liposarcoma (WDLS), myxoid liposarcoma, pleomorphic liposarcoma, and mixed liposarcoma, with WDLS being the most common. Dedifferentiated liposarcomas (DDLs) are classified with WDLS and generally described as a progression of the sarcoma to a higher-grade lesion, though low-grade dedifferentiation has been described [1, 2]. DDLs are most commonly found in the retroperitoneum with only a few cases occurring in the head and neck [4]. Even rarer is a particular histologic pattern of dedifferentiation characterized by formation of meningiothelial-like whorls, which until now have only been described in the retroperitoneum, extremities, scrotum and one in the anterior mediastinum [5–11]. Here we present, to our knowledge, the first case of a dedifferentiated liposarcoma of the neck with meningiothelial-like whorling patterns.

Case Report

A 65-year-old male presented to the ENT clinic after a non-contrast CT chest performed to evaluate the size of an ascending aortic aneurysm demonstrated bilateral thyroid nodules with a notable left dominant calcified mass extending posterior to the trachea. At his initial ENT evaluation he presented with symptoms of globus sensation, dysphagia and

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a change in the character of his voice all thought to be consistent with a compressive goiter. He denied shortness of breath, symptoms consistent with hyper- or hypothyroidism or history of radiation exposure.

Physical exam demonstrated a well-appearing obese male with a strong voice. Neck exam revealed palpable masses in the right thyroid and in the left lower neck. His cranial nerves, including the recurrent laryngeal nerve, were intact.

Further radiographic evaluation with contrast-enhanced CT imaging characterized the mass as a paratracheal calcified lesion compressing both the esophagus and trachea, appearing to arise from the left lobe of the thyroid (Fig. 1a, b). Ultrasonographic evaluation of the thyroid showed an enlarged gland with heterogeneous echotexture and multiple bilateral lesions, including a right centrally necrotic/cystic lesion measuring 5.4 cm in its greatest dimension. The left dominant nodule of interest was described as a solid, peripherally-calcified nodule measuring $4.7 \times 2.5 \times 3.1$ cm with regions of central calcification (Fig. 1c). A fine needle aspiration was attempted but failed to produce adequate sample for cytologic evaluation.

The left paratracheal mass and thyroid were approached using a low transverse cervical incision. After dissection to expose the left thyroid lobe, a 3×3 cm mass was encountered immediately lateral to the tubercle of Zuckerkandl. Intraoperative nerve monitoring (NIM nerve monitoring system, Medtronic) was used to aid in identification of the left recurrent laryngeal nerve which was stretched thinly over the mass and within the fascia surrounding the lesion (Fig. 2). After mobilizing the left thyroid lobe, the recurrent laryngeal nerve was dissected off of the paratracheal mass, which was removed en-bloc with the left thyroid lobe. The recurrent laryngeal nerve stimulated with a strong signal proximally, but a very weak signal distally.

The left thyroid lobe weighed 10.4 g and contained a 0.5 cm irregular nodule diagnosed as sclerosing papillary

Fig. 2 Intraoperative photograph demonstrating the retroesophageal tumor with its intimate relationship with the recurrent laryngeal nerve *asterisk*

microcarcinoma without extracapsular extension or neurovascular invasion. The associated retroesophageal lesion was a 4 cm tan-pink, firm ovoid mass. On histologic examination, this tumor was entirely comprised of low-grade dedifferentiated liposarcoma, consisting of a proliferation of bland to mildly atypical spindle cells with vesicular nuclei and delicate fibrillary cytoplasm arranged in short fascicles and loose whorls set in paucicellular, diffusely fibrotic and focally sclerotic stroma (Fig. 3a, c–f). Areas of well-differentiated liposarcoma were not present in the limited number of sections submitted for histologic evaluation. Dedifferentiated liposarcoma was associated with mature woven bone with no evidence of atypia (Fig. 3b). Throughout the tumor there were areas of small, well-delineated, tight concentric meningothelial-like eddies of bland spindle and epithelioid cells, accounting for approximately 10 % of the total tumor volume (Fig. 4a, b).

Fig. 1 Coronal (a) and axial (b) CT chest demonstrating left retroesophageal calcified mass. Ultrasound (c)

Meningothelial-like whorls were scattered individually within the dedifferentiated liposarcoma and composed of plump spindle and epithelioid cells with dark oval to elongated nuclei and scant eosinophilic fibrillary cytoplasm. Mitotic activity was low (<2/10 high-power fields). No necrosis was seen. The meningothelial-like whorls showed focal, moderate nuclear expression of MDM2 and CDK4 (Fig. 5a, b). Vimentin, SMA, and CD99 expression was also present. No immunostaining was observed for AE1/AE3, Cam 5.2, EMA, S-100, Bcl-2, CD117, DOG1, desmin, GFAP, β -catenin, ALK, CD34, CD57, h-caldesmon, or CD68.

The patient's postoperative course was uneventful and was discharged home on post-operative day two. Fiberoptic laryngoscopy at post-operative follow-up revealed left vocal fold weakness, but did not significantly impact the patient's ability to phonate, breath or swallow.

Discussion

Dedifferentiated liposarcomas were originally thought to represent a distinct entity of high-grade disease within a WDLS [1, 2]. First classified by Evans in 1979, DDLS were described as a “tumor composed of areas of a non-lipogenic sarcoma associated with an atypical lipomatous

tumor or WDLS” [12]. Current research concludes DDLS likely represent a progression of disease from WDLS to either a high or low-grade lesion. This is supported by WDLS and DDLS sharing a genetic profile. These tumors contain a large scale amplification of sequences in the 12q13-15 region, which contain the MDM2 gene and 90 % contain an amplification of CDK4, as seen in our tumor. These mutations work in concert to extend cell survival and underlie the neoplastic process, with MDM2 as a known strong inhibitor of p53 thereby decreasing apoptosis, and with CDK4 phosphorylating Rb gene products thereby helping the cell to proceed unchecked through the G1–S checkpoint [1, 2].

The dedifferentiation of LPS demonstrates a wide morphological spectrum, with most of the high-grade poorly DDLS resembling malignant fibrous histiocytoma and fibrosarcoma. Five to ten percent can show divergent differentiation into myogenic or osteochondromatous elements and rare components of angiosarcoma. In 1998, Nasciamento et al. and Fanburg-Smith et al. independently reported in short succession an extremely unusual histologic pattern of DDLS described as containing neural-like whorling patterns associated with metaplastic bone [9]. To date, 39 cases of this distinct histologic variant have been reported, though never in the head and neck [5–11]. This pattern tends to be described as meningothelial-like whorls

Fig. 3 **a** Low-power microphotograph demonstrates low-grade dedifferentiated liposarcoma. Cellular areas form discrete nodules and nests alternate with hyalinized sclerotic areas (H&E, $\times 40$). **b** Areas of metaplastic bone are readily identifiable adjacent to the cellular component (H&E, $\times 40$). **c** and **d** Tumor cells show fascicular and storiform arrangement (H&E, $\times 100$). **e** The tumor predominantly

consists of a proliferation of spindle cells with elongated vesicular nuclei and delicate fibrillary cytoplasm arranged in short fascicles and loose whorls (H&E, $\times 200$). **f** A high-power view of neoplastic cells demonstrates mild atypia including slight pleomorphism and nuclear contour irregularities (H&E, $\times 400$)

Fig. 4 Medium- and high-power microphotograph shows meningotheelial-like whorls scattered throughout the tumor, comprising discrete, concentrically organized eddies of spindle and epithelioid cells (H&E, $\times 100$ and $\times 200$, respectively)

Fig. 5 **a** Nuclear expression of CDK4 is present in the meningotheelial-like whorls. **b** MDM2 immunostain highlights nuclei in the whorled areas

or spherical bodies found in clusters and scattered throughout the tumor. In addition, one report of 17 cases of this variant demonstrated metaplastic bone in ten of the cases and this pattern has repeated itself as a characteristic of this histologic subtype, as seen in our case. This type of dedifferentiation is one that has augmented the notion of dedifferentiation as only transforming into a high-grade lesion. This neural-type dedifferentiation is considered low-grade and may portend a survival benefit [2].

DDLs tend to occur later in life with a mean age of 50 without a clear sex predilection [1, 4]. They are most commonly seen in the retroperitoneum (80 %), extremities, spermatic cord and other sites of the internal trunk [1, 14, 15]. Demonstrating the rarity of these lesions in the head and neck, an analysis of 60 years of head and neck liposarcomas at MD Anderson produced a cohort of 30 patients. Twelve of the thirty occurred in the neck or parotid, with none of the dedifferentiated sub-type [3]. Similarly, a study from Tunisia reported 15 cases in 32 years of LPS in the head and neck, of which four were in the neck

and one was dedifferentiated [13]. A few other case reports/series have reported dedifferentiated liposarcomas in the head and neck, specifically in the parapharyngeal space, buccal mucosa, tongue and parotid gland [16–18].

Treatment for liposarcomas throughout the body largely consists of primary resection. Survival, however, is greatly varied. A multi-variate analysis at Memorial Sloan Kettering (MSKCC) of patients with LPS primarily resected from the extremities, trunk or retroperitoneum showed histologic type, age, margin status, presentation status, primary site and tumor burden as independent predictors of disease-specific survival. Specifically, they found 5-year and 12-year disease specific survival for DDLs as 44 and 38 %, respectively. In addition, they demonstrated microscopically negative, positive or grossly positive margins to predict a 74, 68 and 25 % disease-specific survival [4, 14]. Though this data did not include cases of LPS of the head and neck, one could apply these principles. The studies of head and neck LPS at MD Anderson and in Tunis showed 5-year disease free survival of 72.8 and 87 %, respectively,

but included only one case of DDLS. Additionally, the MD Anderson study clearly demonstrated a survival benefit for lower grade histologic types concurring with the MSKCC study. Interestingly, both head and neck reviews found lower disease free survival for patients receiving multimodality therapy, likely reflecting the prescription of those regimens for patients with more locally aggressive histologic types and increased tumor burden. Recurrence is a significant risk for patients with LPS. Disease free survival ranges from 50 to 91 % and is highly dependent on location [14]. More succinctly, the MSKCC study found presentation status, histological type, and tumor burden to be independent predictors of recurrence [14, 15]. With significantly less power, the MD Anderson review corroborated a high rate of recurrence with 20 of their 30 cases recurring, though one-third of their cohort were initially misdiagnosed, but, interestingly, they found smaller lesions were more likely to recur [3].

In conclusion, liposarcomas and, specifically, DDLS of the head and neck is an exceedingly rare entity, but one that should be considered when approaching sarcomatous tumors in this region. Furthermore, our case demonstrates the first reported incidence of dedifferentiated liposarcoma of the neck with metaplastic bone, meningothelial-like whorling and neural-like histology.

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