

CASE STUDY**DEDIFFERENTIATED LIPOSARCOMA OF THE LARYNX****¹Clarke, J., ¹Medford, S., ^{*}²Islam, S., ³DeNoon, S. and ²Juman, S.**¹Department of Otolaryngology, San Fernando General Hospital, Trinidad and Tobago²Department of Clinical Surgical Science, St Augustine, Trinidad and Tobago³Department of Pathology, San Fernando General Hospital, Trinidad and Tobago**ARTICLE INFO****Article History:**Received 29th June, 2017

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ABSTRACT

Liposarcomas of the Head and Neck region are rare. Laryngeal liposarcomas are even rarer with only 40 reported cases in the world literature. However, dedifferentiated laryngeal liposarcomas are even scarcer. These tumours are often misdiagnosed and mistreated as other tumours, in some cases even benign lipomas. There is no reported case of high gradedifferentiated laryngeal liposarcomas from the Caribbean countries. We report the first case of a dedifferentiated laryngeal liposarcoma from the Caribbean with up to date literature search and its management options are outlined.

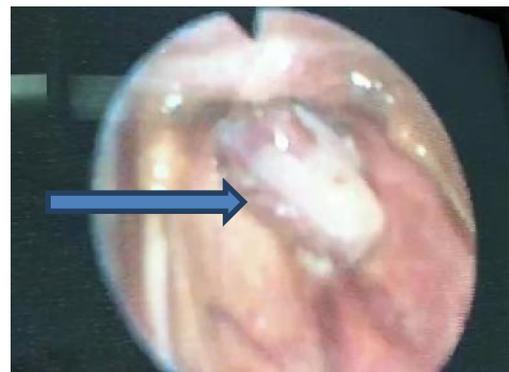
INTRODUCTION

Liposarcomas, while representing one of the most common types of malignant soft tissue sarcomas, account for only 0.5% of laryngeal tumours (Barnes *et al.*, 2007), with less than 50 cases reported in the literature (Han *et al.*, 2015; Kodiyar *et al.*, 2015 and Zhu *et al.*, 2016). Due to the rare nature of this entity, dilemmas are encountered in making the diagnosis and little data exists to ascertain best surgical and adjuvant management of these patients. In the present paper, we present the first documented case to our knowledge of a liposarcoma of the larynx, dedifferentiated variant, occurring within the Caribbean region. We also review current literature on the clinical and pathologic features, diagnostic challenges and management of this rare laryngeal tumour.

Case History

Our patient was a 64 year old male who presented to the Accident and Emergency to our institution with a history of a hoarse voice, a chronic cough and stridor which progressively worsened over a two month period. His history was also positive for weight loss of greater than 30 lbs. and dysphagia which also progressed over the two month period. Patient denied any history of night sweats, fever, haemoptysis or neck

lumps. A complete examination was done which included a flexible naso-endoscopy which showed a large smooth submucosal lesion approximately 2 – 3 cm in largest diameter. The lesion was noted to be "ball-valving" in the vestibule of the larynx with almost complete obstruction of the vestibule (Figures 1 and 2). The patient was immediately transferred to emergency theatre where he underwent a tracheostomy under local anaesthesia. A direct laryngoscopy was then performed under general anaesthesia and the tumour was de-bulked piecemeal from its point of attachment to the entire length of the left true vocal cord. A report was issued which indicated that sections revealed a malignant spindle cell tumour with overlying normal appearing mucosa (Figures 3 and 4).

**Fig.1.**

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Fig.2.

Figures 1 and 2 showing a flexible laryngoscopy with the mass "ball-valving"; Figure 1 denotes the position of the mass during expiration while Figure 2 shows the mass during inspiration. The blue arrows in both Figure 1 and 2 point to the laryngeal tumour

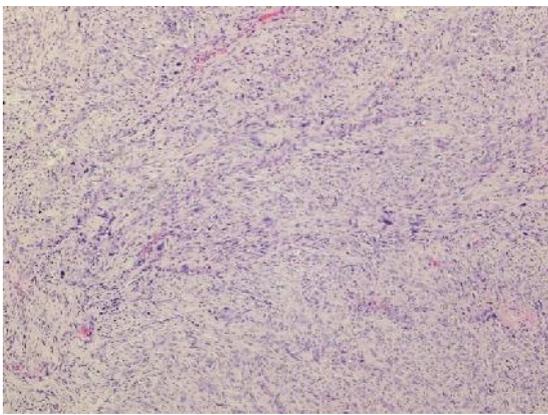


Fig.3.

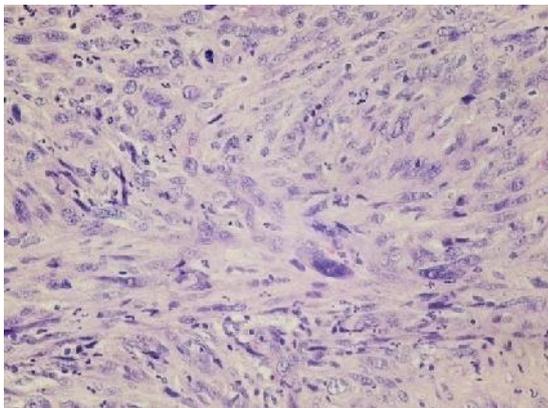


Fig.4.

Figures 3 showing low power view and 4 showing high power view of a malignant spindle cell tumour of the larynx with overlying normal appearing mucosa

Immunostains for pancytokeratin, desmin, CD34 and S-100 were all negative. A second opinion was obtained from another histopathologist who tested for immunostains to CK5, CAM5.2, p63 and CD34, which were all negative. Tests were also done for MDM2 and CDK4 which showed a multifocal strong nuclear positivity (consistent for gene amplification) for these markers. A diagnosis of dedifferentiated liposarcoma, high grade was thus made. It was noted in the report that "well-differentiated/dedifferentiated liposarcoma probably

represents the single most common type of soft tissue sarcoma in the larynx or pharynx. Careful radiologic correlation may help to demonstrate the presence of a well differentiated fatty component nearby. Lesions of this type at this site often pose greatest problems in terms of local control." A CT Scan of the patient's Head, Neck and Chest was also done which showed a subglottic lesion with a few sub centimetre lymph nodes (Figure 5).

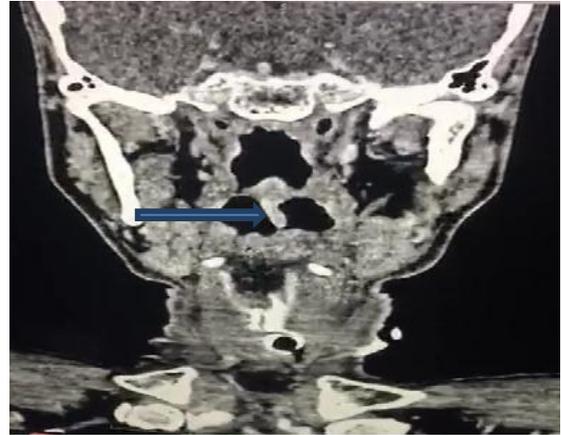


Figure 5. Coronal view of the CT scan of the neck showing mass on the left vocal cord extending into the subglottic region

After consultation with the patient and his family, a decision was made for the patient to undergo a total laryngectomy (Figures 6 and 7). The relatives agreed that with the high risk of recurrence this option was the best one presented to them.

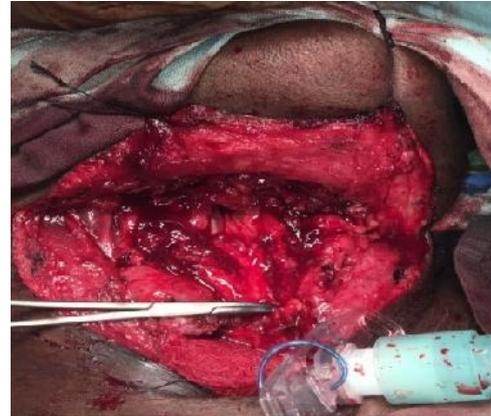


Fig.6.



Fig. 7.

Figure 6. The patient after resection of the larynx before repair of the pharyngeal defect to create the neo-pharynx. Figure 7 shows the resected larynx

The total laryngectomy was successfully performed with the patient commencing oral diet on day 10 post surgery. He suffered no complications (Figure 8) and was discharged by day 13 post surgery.



Figure 8. The patient on Day 7 post-op

Follow up visits to clinic so far have shown no complications or recurrence of tumour and the patient was also referred to our Oncology department for a consultation.

DISCUSSION

Laryngeal liposarcomas are a rare type of tumour with limited data available in terms of the management of the condition. As there are no clear guidelines available up to this time for the best management of this condition, it was thought best to treat this tumour as aggressively as possible. Voice sparing procedures were a large part of our counselling and consent, but the patient opted for total removal of the tumour. In light of the experiences with recurrence noted in limited case reports we totally agreed with this decision. Of the 40 cases of primary laryngeal liposarcoma (LLP) described in the literature, the most common histologic subtype are the well differentiated liposarcomas/atypical lipomatous tumours. Conversely, only 5 have been diagnosed as dedifferentiated, representing an exceedingly rare variant. LLPs have only been documented in adults and occur predominantly in males (Barnes *et al.*, 2007; Han *et al.*, 2015). These tumours most commonly arise in the supraglottic larynx. Dedifferentiated liposarcomas (DDLPSs) are characterized by the development of a high grade non-lipogenic sarcoma arising within a well differentiated liposarcoma (WDLPS) (Fletcher *et al.*, 2002) and are most commonly described in the retro-peritoneum and extremities, with only rare cases of laryngeal occurrences described in the literature (Giodano *et al.*, 2006) These tumours can at times pose a diagnostic challenge to pathologists, and thorough sampling may be crucial to detect the well differentiated component to these tumours, as the dedifferentiated areas can otherwise closely resemble other malignant sarcomas including high grade myxofibrosarcoma and pleomorphic sarcoma (Fletcher *et al.*, 2002). Cytogenetics have identified ring and giant marker chromosomes within DDLPS comprised of the amplified material of chromosome sub-region 12q13-15 (Fletcher *et al.*, 2002). This locus includes the oncogene *MDM2* which serves as a repressor of the tumour suppressor *p53*, and thus its amplification and overexpression is a key step in the tumorigenesis of these lesions. While this abnormality on its own can be seen in other sarcomas, a panel including *CDK4*, another oncogene in the 12q13-15 amplicon, and possibly *p16* (Kammerer-Jacquet *et al.*, 2017) has proved

reproducibly sensitive and specific for both well differentiated liposarcoma (WDLPS) as well as DDLPS (Binh *et al.*, 2005; Kashima *et al.*, 2012). Techniques to demonstrate *MDM2* gene amplification or protein overexpression have thus proved a useful ancillary tool in the diagnosis of these biphasic soft tissue sarcomas (Kimura *et al.*, 2013; Ben Salha *et al.*, 2016).

Like all sarcomas, these tumours tend to spread haematogenously and not by lymphatic spread. Wide local excision is thus the treatment of choice, but current management does not include neck dissection due to the rarity of lymph node metastases. In a minority of cases patients have also re-presented with metastases at distant locations (Han *et al.*, 2015). Our patient underwent a total laryngectomy which was performed the following week after confirmation of the diagnosis by immunohistochemistry. Two lymph nodes were also found: 1) located to the right of the neck at level III measuring approximately 2 cm and 2) located to the right of the neck in level VI measuring approximately 0.5cm. Both were removed and sent separate from the specimen and showed no evidence of infiltration by tumour. No neck dissection was performed on the patient in keeping with the management reported in the literature. As reported by Brockstein *et al* (2017), when adjuvant radiation therapy (RT) is used for head and neck sarcomas, it is usually administered postoperatively and not prior to an operation, as is commonly done in extremity sarcomas. The benefit of adjuvant RT for most histologic subtypes is controversial. There are no randomized trials proving benefit for RT in head and neck sarcomas, and results from retrospective reports are mixed. However, extrapolation of experience in extremity sarcomas strongly argues in favour of adjuvant RT for soft tissue sarcomas of the head and neck that are large and high-grade, or low-grade with positive and/or close (often defined as <1 mm) margins. Our patient was also referred to the Oncology department for a consultation re: further management. So far our patient has undergone an uneventful period post-operatively and is being kept in our clinic for life long monitoring.

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Author's declaration: The authors have nothing to disclose

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