PHILIPPINE JOURNAL OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY VOL. 30 NO. 1 JANUARY – JUNE 2015

Peter Ranjit, FEBORL-HNS, MS (ORL), DNB (ORL),
Parekh Nayan Madhusudan, MS (ORL), DNB (ORL), FRCS (ORL)
Dayangku Norsuhazenah Pengiran Suhaili, MS (ORL-HNS), MRCS (Edin)
Bickle Ian Christopher, MB, BCh, BAO, FRCR

Epitheloid Hemangioendothelioma of the Submandibular Region

ABSTRACT

Objectives: To present an uncommon cause for a submandibular mass and review of the literature.

Methods:

Design: Case Report
Setting: Tertiary Government Hospital
Patient: One

Results: A 25-year-old lady presented with a painless chronic submandibular swelling. Ultrasound identified a solid mass following which an uncomplicated core biopsy was performed obtaining an accurate pre-operative histopathological diagnosis. Pre-operative arterial embolization of this vascular mass led to a relatively bloodless wide local excision. Radiological imaging for distant metastases was negative.

Conclusion: Epitheloid Hemangioendothelioma is an uncommon cause for a submandibular mass. A malignant vascular soft tissue tumor with morphologic characteristics similar to carcinomas, melanomas and epitheloid sarcomas, it has a high rate of metastasis and morbidity when it affects the soft tissues and viscera. Immunohistochemistry provides clues to differentiation and recommended treatment consists of a surgical wide local excision with regional lymph node resection. As there are no established standard therapeutic protocols for this disease due to its rarity, an individual case-by-case approach and follow-up needs to be undertaken.

Keywords: *epitheloid hemangioendothelioma, malignant vascular tumor, submandibular mass*

Epitheloid hemangioendothelioma (EHE) is an uncommon vascular soft tissue tumor with intermediate malignancy risk and was first reported by Weiss & Enzinger in 1982.[1] EHE is known to be the most aggressive of hemangioendotheliomas and carries a high rate of metastasis (20-30%) and mortality (10-20%). [2-5] We report an uncommon case of EHE in the submandibular region

Correspondence: Dr. Ranjit Peter
Department of ORL, Level 3, Specialist Building I
RIPAS Hospital
Bandar Seri Begawan, Negara BA1710
Brunei Darussalam
Phone: +(673) 862 8007
Fax: +(673) 222 1085
Email: drranjitpeter@gmail.com
Reprints will not be available from the author.

The authors declared that this represents original material that is not being considered for publication or has not been published or accepted for publication elsewhere, in full or in part, in print or electronic media; that the manuscript has been read and approved by the authors, that the requirements for authorship have been met by the authors, and that the authors believe that the manuscript represents honest work.

Disclosures: The authors signed disclosures that there are no financial or other (including personal) relationships, intellectual passion, political or religious beliefs, and institutional affiliations that might lead to a conflict of interest.

Philipp J Otolaryngol Head Neck Surg 2015; 30 (1): 47-50

CASE REPORT

A 25-year-old lady presented to the Otorhinolaryngology clinic of RIPAS Hospital, Bandar Seri Begawan, Negara Brunei Darussalam with a large painless right submandibular swelling which had grown very slowly over a 6-year period. The submandibular mass was non-inflammatory, non-pulsatile, non-tender, lobulated and soft in consistency measuring approximately 4x4 cm in dimension. It exhibited an element of mobility with respect to the adjacent mandible with no fixation to the overlying skin. There were no palpable neck nodes and minimal movement on tongue protrusion. There were no significant ear, nose or throat findings on clinical examination. *(Figure 1)*

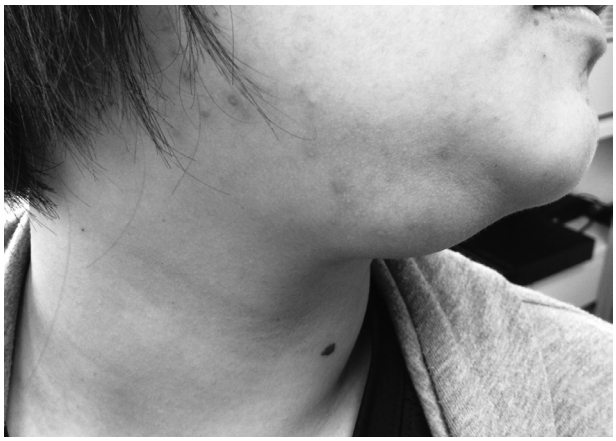

Figure1. Lateral view of the right submandibular swelling

Hematological evaluation was normal. An ultrasound scan (USS) of the neck revealed a 3.3cm well defined, mildly heterogeneous mass in the right submandibular region, separate from the submandibular gland. Minimal internal Doppler flow was elicited. A USS guided 18G core biopsy was performed. *(Figure 2)* Histopathological examination revealed fibro-vascular tissue containing large numbers of prominent endothelial lined capillaries along with a moderate number of veins around the lesion. *(Figure 3)* A proportion of the cells showed intra-cytoplasmic lumina with the pleomorphic nuclei. *(Figure 4)* Tumor cells stained for CD 34. However, S100 was negative. Reticulin stain highlighted the vascular nature of the tumor. The appearance was consistent with EHE.

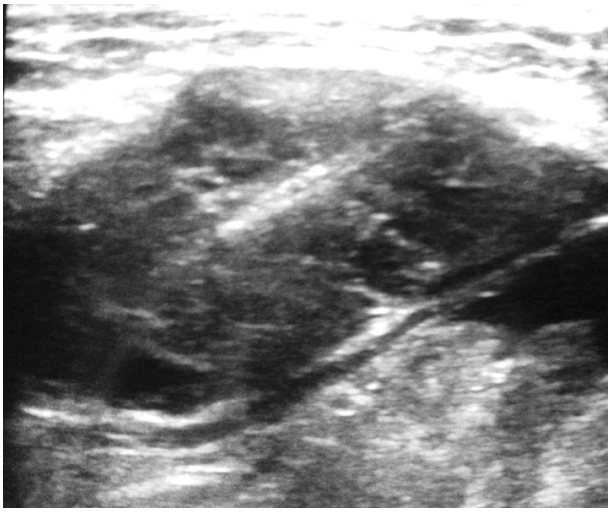

Figure 2. Longitudinal ultrasound: well defined, solid heterogeneous submental mass, with needle core biopsy in situ

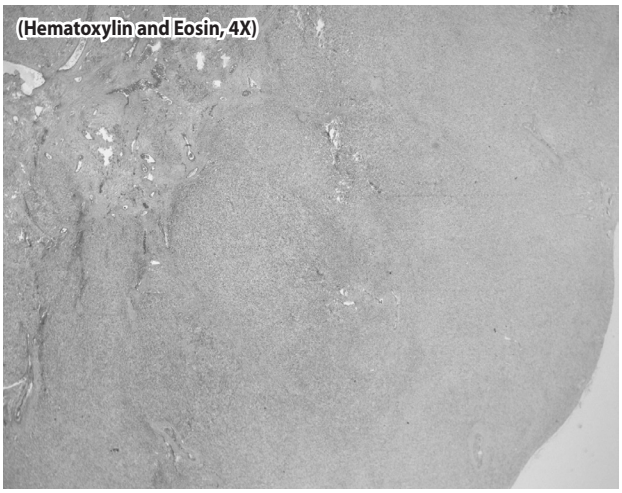

Figure 3. Photomicrograph, scanner view, Magnification 4X, H&E. Fibrovascular tissue containing large numbers of prominent endothelial lined capillaries along with a moderate number of veins around the lesion.

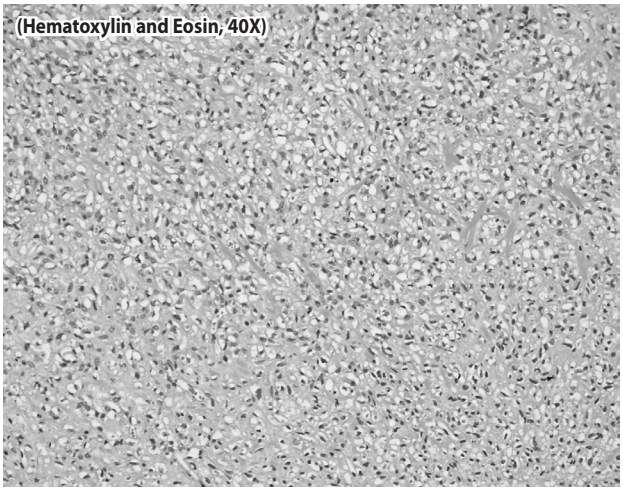

Figure 4. Photomicrograph, high power view, Magnification 40X, H&E. Cells showed intra-cytoplasmic lumina with the nuclei of the cells being pleomorphic.

An arterial phase CT scan of the neck was performed which revealed a 4 x 2.9 cm well-defined avidly enhancing mass in the right submandibular space with the vascular supply from an engorged retromandibular vein and facial artery lying on the medial aspect of the mass. Immediately adjacent to the mass on the anteromedial aspect

was an apparent separate identical 1.1cm lesion recruiting its vascular supply from the right lingual artery. In view of histopathological diagnosis, CT of the chest and abdomen was performed for staging purposes but was negative.

Pre-operative catheter angiography and embolization was performed 24 hours prior to surgery which revealed a vascular mass in the right submandibular region being supplied by a large feeder vessel from the lingual branch of the facial artery. *(Figure 5)* This was embolized with Surgicel.

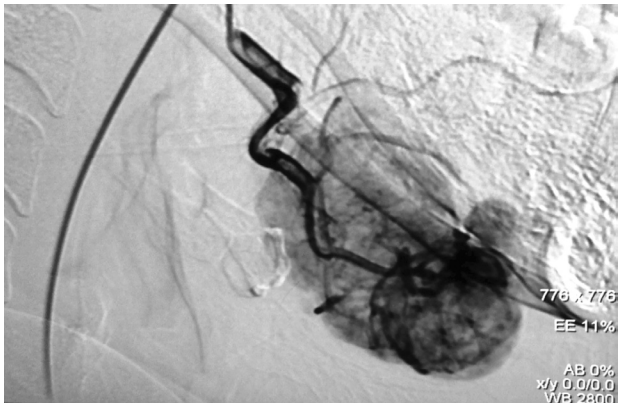

Figure 5. Longitudinal Angiographic Image: highly vascular submandibular mass, recruiting its arterial supply from branches of the facial artery

Wide local excision of the tumor was performed under general anesthesia via a horizontal curvilinear incision, 4 cm inferior to the horizontal lower border of mandible. Sub-platysmal wide dissection around the tumor mass was undertaken. The arterial branch from the facial artery and a feeding vessel from the deeper surface of the gland were ligated and divided. The venous branches were electro-cauterized. The tumor mass was anatomically located in the right submandibular region with the mylohyoid muscle and the right anterior belly of digastric muscle forming the surgical floor of the resected mass. It was distinct from the submandibular salivary gland located posteriorly. The excised surgical specimen was 6 X 4 X 2.5 cm in dimension. *(Figure 6)*

The right marginal mandibular nerve function was intact post-operatively. A vacuum lantern drain was placed for 48 hours.

Histopathology of the resected specimen revealed a tumor consisting of thin walled capillaries arranged in a lobular pattern situated in a hyalinized stroma. It contained prominent endothelial cells with eosinophilic cytoplasm and hyperchromatic, pleomorphic nuclei with indistinct nucleoli. There were 2-3 mitotic figures per 10 high power field. The margins were free of the tumor. The findings were consistent with EHE.

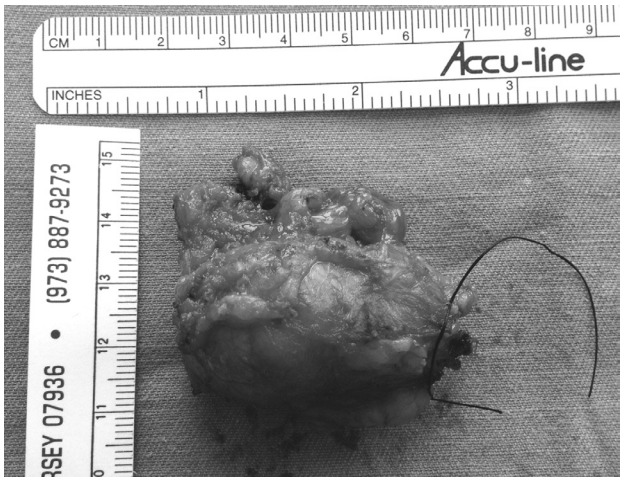

Figure 6. Excised tumor - gross specimen measuring 6x4x2.5 cm with suture marking on its superior-medial aspect

DISCUSSION

EHE has been documented to occur at several anatomical sites such as the liver, lung, pleura, bone, lymph nodes, skin, brain, meninges and heart. EHE in the head and neck has been found to originate from the soft tissues with approximately 26% of cases exhibiting re-absorption and / or adjacent bone destruction. Tongue and gingival ridges are the most common sites of origin in the oral cavity with the upper gingivae and oral mucosa being the most common sites of relapse. Lesions in the nasal cavity, parotid gland, larynx and thyroid have also been reported.[6] In our case, there was no evidence of adjacent soft tissue or bone involvement. EHE has no age or sex predisposition. It is rare in children. [6,7]

These lesions are generally asymptomatic, painless and present as ill-defined solitary masses in the superficial or deep soft tissues. Enzinger and Weiss considered the biological behavior of EHE to be between a hemangioma and angiosarcoma.[1] The World Health Organization (WHO) has classified EHE as a malignant vascular soft tissue tumor.[8]

EHE has been reported to have a high rate of metastasis (20-30%) and mortality (10-20%) when it affects the soft tissues and viscera.[6] Deyrup *et al.* analyzed 49 cases of EHE in soft tissues and concluded that large tumors (Diameter > 3cm) with high mitotic activity (> 3 mitotic figures / 50 HPF) have an aggressive clinical course.[9] EHE has several morphological characteristics that are similar to carcinomas, melanomas and epitheloid sarcomas.[10] Immunohistochemistry provides reliable clues regarding differentiation.

Some surgeons advocate pre-operative embolization in order to prevent excessive intra-operative hemorrhage.[11] In our case, radiological evaluation with Doppler ultrasonography and contrast-enhanced CT was helpful in assessing the vascularity and pre-operative angiography

followed by embolization led to a relatively bloodless surgical excision.

The recommended treatment for EHE consists of a wide local excision with regional lymph node resection due to the high risk of lymphatic metastases.[12,13] However, there are no established standard therapeutic protocols for this disease due to its rarity. Therefore an individual case-by-case approach and follow-up needs to be undertaken. Unresectable invasive EHE may be subjected to radiotherapy.[14] Anti-angiogenic agents have been proposed as a possible future treatment option.[10]

ACKNOWLEDGEMENTS

We acknowledge Dr. Pemasiri Upali Telisinghe, FRC (Path) for histopathological reporting and photomicrographs and Dr. Zachariah Varkki, MS (ENT) for the intra-operative photographs.

REFERENCES

1. Weiss SW, Enzinger FM. Epitheloid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. *Cancer* 1982; 50:970-981
2. Chi AC, Weathers DR, Folpe AL, Dunlap DT, Rasenberger K, Neville BW. Epithelioid hemangioendothelioma of the oral cavity: report of two cases and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, v. 100, n. 6, p. 717-24, 2005.
3. Goh SGN, Calonje E. Cutaneous vascular tumours: an update. *Histopathology*, v. 52, p. 661-73, 2008.
4. Makhlouf HR, Ishak KG, Goodman ZD. Epithelioid hemangioendothelioma of the liver. A clinicopathologic study of 137 cases. *Cancer*, v. 85, p. 562-82, 1999.
5. Mentzel T, Beham A, Calonje E, Katenkamp D, Fletcher CD. Epithelioid hemangioendothelioma of skin and soft tissues: clinicopathologic and immunohistochemical study of 30 cases. Am J Surg Pathol, v. 21, p. 363-74, 1997.
6. Ana Karla AC, Sérgio de OR, Ana Lucia AE. Epithelioid hemangioendothelioma: 15 years at the National Cancer Institute. Literature review." *Jornal Brasileiro de Patologia e Medicina Laboratorial* 49.2 (2013): 119-125. URL: http://www.scielo.br/pdf/jbpml/v49n2/07.pdf
7. Tseng CC, Tsay SH, Tsai TL, Shu CH. Epitheloid Hemangioendothelioma of the Nasal Cavity. *J Chin Med Assoc* January 2005 Vol 68 No.1: 45-48
8. Fletcher CDM. The evolving classification of soft tissue tumours – an update based on the new 2013 WHO classification. *Histopathology* 2014, 64, 2–11. DOI: 10.1111/his.12267
9. Deyrup, AT, Tighiouart M, Montag AG, Weiss SW. Epithelioid hemangioendothelioma of soft tissue: a proposal for risk stratification based on 49 cases. *Am J Surg Pathol*, v. 32, n.6, p. 924-7, 2008.
10. Jabeen N, Nelson GO, Mario AL, Michelle DW, Randal SW, Adel KE. Epithelioid Hemangioendothelioma of the Head and Neck: Role of Podoplanin in the Differential Diagnosis. *Head and Neck Pathol* (2008) 2:25–30 . DOI 10.1007/s12105-007-0035-0
11. Phookan G, A. T. Davis AT, Holmes B. Hemangioendothelioma of the cavernous sinus: case report. *Neurosurgery*, vol.42, no. 5, pp. 1153–1156, 1998.
12. Enzinger FM, Weiss SW. Hemangioendothelioma: vascular tumors of intermediate malignancy. *Soft Tissue Tumors*, 4th edition. St.Louis: CV Mosby, 1995:891-900
13. Weiss SW, Ishak KG, Dail DH. Epethelioid hemangioendothelioma and related lesions. Seminars in Diagnostic Pathology, vol. 3, no. 4, pp. 259–287, 1986.
14. Aksoy EA, Atalar B, Beylergil V, Unal OF. Unresectable Epitheloid Hemangioendothelioma of the Neck Region Cured by Radiotherapy. *J Med Cases* 2011;2(4):147-150 DOI : 10.4021/jmc216w.