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Kaposiform Hemangioendothelioma of the Sublingual Gland in an Adult: Resection is the Key.

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Abstract

Introduction: Kaposiform haemangioendotheliomas (KHE) are extremely rare, borderline malignant, locally aggressive vascular tumours. Although more commonly seen in childhood and adolescents, some very rare reports in adults do exist. KHE is usually found in the retroperitoneum, over the extremities and the soft tissues of the trunk, mediastinum and the head and neck regions. Prior published reports have shown a strong association with the Kasabach-Merritt phenomenon (KMP). We present a very rare case of KHE of the sublingual gland in an adult, which was not associated with KMP and was resected completely without any sequelae.

Case report: A 42-year-old female presented with a painful swelling over the floor of the mouth on the right for a year. Clinical examination revealed a bi-digitally palpable, non-transilluminant lesion on the right side of the lingual frenulum. Radiological investigations suggested the possibility of a benign soft tissue tumour arising from the sublingual gland. The patient underwent an intraoral excision of the lesion. The biopsy revealed spindle-shaped tumour cells in fascicles, surrounded by vascular spaces, suggestive of a KHE. The patient was offered radiation therapy, which she declined and continued to be on follow-up for two years. She remains symptom-free to date.

Conclusion: Excision of a KHE of the floor of the mouth proved to be sufficient, without the evidence of any residual lesion or progression of symptoms. To the best of our knowledge, our case represents the first reported case in the literature of a KHE arising from the salivary glands in an adult.

Introduction

Kaposiform haemangioendotheliomas (KHE) are very rare, locally aggressive vascular neoplasms occurring in childhood and adolescence. Classified as a borderline malignant tumour with a cutaneous distribution, it has inherent invasive properties into deeper soft tissues, without causing distant metastases. KHE is typically described to arise in the paediatric population, similar to infantile haemangiomas, without the tendency of spontaneous involution. KHE is often seen in association with the Kasabach-Merritt phenomenon (KMP), comprising of the spectrum of lymphangiomatosis and life-threatening haemorrhage secondary to severe thrombocytopenia. The prevalence of KHE is not widely reported due to the extremely limited literature available on the subject. An estimate puts the incidence at less than 1 per 100,000 cases of KHE in children (1). It has rarely been reported in adults, with descriptions existing for KHE arising from the tonsil, internal auditory meatus, chest wall, scalp and neck, although all patients lay in the age range of infancy to the second decade. This report describes the case of a spontaneously arising KHE of the sublingual gland in an adult, which was cured completely with local excision.

Case Report

A 42-year-old woman was referred to our otolaryngology centre with complaints of a painful swelling over the right side of her floor of the mouth for the past year. She did not complain of any restriction in the mobility of the tongue and did not have hindered swallowing. There was no bleeding from the lesion or from elsewhere. The lesion was smooth, firm, non-transilluminant and extended till the frenulum, displacing the tongue upwards **(Fig. 1)**. There was no associated cervical lymphadenopathy and other general and systemic examination were unremarkable. No such lesions were observed in other members of her family.

Routine blood workup did not reveal any abnormalities, particularly concerning the platelet count and the bleeding parameters. A fine-needle aspiration cytology (FNAC) study from the lesion indicated features suggestive of a benign mesenchymal tumour. No obvious vascular component was initially detected. Hence a contrast-enhanced computed tomography (CECT) of the neck was undertaken, which showed a moderately enhancing lesion with tiny non-enhancing areas arising from the floor of the mouth in the right sublingual gland, abutting the inner mandibular cortex without any bone erosion. It displaced the midline raphe to the left and was situated above the mylohyoid muscle. The right submandibular gland was normal, although the lesion was compressing the duct of the gland **(Fig. 2)**. We decided to proceed with our provisional diagnosis of a benign soft tissue tumour. Unfortunately, an MRI or an angiogram was not suggested before the surgery due to the tentative nature of the symptoms and lack of any suggestive involvement of blood vessels.

The patient underwent intraoral excision of the well-circumscribed mass under general anaesthesia. The lesion was approached via a transverse incision at the level of the lingual papillae and was delivered in toto after blunt dissection from the surrounding soft tissues. Given the benign nature of the lesion which was suspected pre-operatively, no attempt was made to obtain wide surgical margins. No unusual bleeding was noted. The tumour surface was bosselated and had areas of minimal haemorrhage and necrosis. The postoperative period was uneventful and the patient was discharged the next day on oral feeds.

The postoperative histopathology result was reported as a well-circumscribed lesion comprising of spindle cells with lobular architecture separated by fibrous septa. The tumour cells were arranged in fascicles with intervening curved slit-like vascular spaces. The stromal network was strongly positive for reticulin **(Fig. 3a and 3b)**. Further immunohistochemical evaluation revealed endothelial cell positivity for CD34 and CD31 **(Fig. 4a and 4b)**. The Ki67 index was 1%, thus ruling out a rapidly proliferating neoplasm. The tumour cells were negative for S-100 and EMA **(Fig. 5a and 5b).**

With a tissue diagnosis of KHE, the patient was counselled and advised about radiation therapy options according to the current literature. She declined further treatment and consented to follow-up regularly. She remains on a follow-up to date and there has been no evidence of any sequelae or reappearance of the lesion.

Discussion

KHE as a separate pathological entity, distinct from the more common haemangiomatous lesions, was described originally by Zukerberg et al in 1993, as a benign, locally aggressive, vascular tumour of childhood. A lack of both spontaneous involution and distant metastasis are features of all described KHE, though regional lymphadenopathy and local invasion into deeper subcutaneous and muscle planes are also seen (2). It commonly presents as a rapidly enlarging, bluish-red, subcutaneous mass in infants and children, with a known and consistent association with the Kasabach-Merritt syndrome or phenomenon (KMP), characterised by severe thrombocytopenia due to intralesional platelet trapping. In an extensive review of 107 cases by Croteau et al (3), the common presenting features were an enlarging cutaneous lesion, musculoskeletal pain associated with decreased function and thrombocytopenia along with its manifestations. A cutaneous vascular lesion is the commonest symptom, confusing with entities such as tufted angioma, pyogenic granuloma, juvenile haemangioma, vascular malformations and Kaposi sarcoma(KS) as well. Older patients lacking thrombocytopenia were found to have musculoskeletal features in multiple reports, as in our case.

Although widely reported in children, it was first reported in adults by Mentzel et al (4). Several atypical cases of KHE have been since seen in adults, with lesions arising from the thoracic cavity, lateral neck, buttock region (4), tongue (5), tonsil (6), spleen, gastrointestinal tract and the extremities. According to published reports, many features of KHE are vastly different in children and adults. KMP in children with KHE tend to be large, and because of intralesional platelet trapping, cause widespread thrombocytopenic manifestations. A cascade of consumption coagulopathy follows from the interaction of abnormally proliferating endothelium within the KHE and the platelets, secondarily activating the clotting cascade (7). It is inherently refractory to transfused platelets, thus is considered to be a potentially life-threatening disorder. In contrast, lesions in adults tend to be smaller and do not present with KMP presumably due to the size and lack of abnormal epithelium. An empirical size of 8cm has been designated in a review of KHE (8), below which KMP in KHE is usually not observed.

No obvious aetiology for the abnormal angiogenesis and lymph-angiogenesis has been identified (9). KHE is not related to HHV-8 or the more ominous KS. Biopsies are usually not recommended in KHE, given the risk of KMP, but are advised in cases where the diagnosis is doubtful or unusual sites are involved. KHE consists of irregularly infiltrating, compressed vascular spaces, intervening between spindle-shaped endothelial cells. Occasionally the vessels contain erythrocyte and platelet thrombi (10). Dilated discrete lymphatic vessels may also be found. Nuclear atypia and abnormal mitoses are rare. The spindle cells are positive for endothelial cell markers such as CD31, CD34 and ERG but negative for GLUT-1, which is found in infantile haemangiomatous endothelium. The most specific IHC marker, however, is podoplanin, found on the endothelial cells, which harbours co-receptors for platelets (1).

Ultrasound is the modality of choice for small subcutaneous lesions, though MRI is more sensitive. KHE appears ill-defined on MRI, involving multiple tissue planes, with hemosiderin deposits, prominent vessels, fat stranding and remodelling of the underlying bone, with high T2 signal intensity and diffuse early enhancement (11). Osteolytic destruction of surrounding bone, spiculations and flow voids are suggestive, but not characteristic.

A major clinical concern is a differentiation from the more sinister Kaposi sarcoma (KS), which is suspected in the setting of an immunocompromised patient. Periodic acid Schiff (PAS) positivity and better histologic differentiation, in a background of HHV-8 positivity, points to a diagnosis of KS rather than KHE (12).

Aggressive treatment is indicated in cases with catastrophic bleeding, especially when associated with KMP. A host of treatment modalities have been proposed, with fairly consistent success. Surgical excision with a safe margin, embolization, radiation therapy and pharmacologic therapy have all been tried in KHE, with radical surgery generally deemed adequate and definitive (13). Lasers, high dose systemic corticosteroids, interferon-alpha therapy, cryotherapy, vincristine, sirolimus, antiplatelet-antifibrinolytics and propranolol are all indicated, either in combination with surgery or alone, depending upon clinical practice and availability. The long duration of response to medical therapy and lack of reliable treatment guidelines precludes consistent pharmacotherapy in all cases of KHE.

In the case of a first, a sublingual gland KHE without KMP is an atypical diagnosis obtained at an unusual site. The routine excision of the sublingual gland was sufficient in our case without any histopathological evidence of positive margins. However, it is prudent to excise the gland along with an empirical margin for oncological safety, as KHE is considered a potential malignancy of intermediate grade.

Conclusions

KHE is an extremely rare cause of sublingual gland enlargement. Adequate surgical excision usually suffices for uncomplicated lesions. Heterogeneity in presentation and lack of treatment guidelines make the management challenging. The prognosis is based on the size and anatomical site. To the best of our knowledge, ours is the first case of a salivary gland KHE being reported in an otherwise healthy adult. There is a need for wider dissemination of reports about KHE to obtain definitive data for decision making and cure. All vascular intraoral masses should be viewed with suspicion and the diagnosis of KHE should be kept in mind.

Declarations

Conflicts of interest

All authors have declared that there is no conflict of interest among them.

Ethical approval

All procedures performed in studies involving human participants were by the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all the individuals involved and included in the study.

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References

1. Ji Y, Chen S, Yang K, Xia C, Li L. Kaposiform hemangioendothelioma: current knowledge and future perspectives. Orphanet Journal of Rare Diseases. 2020 Feb 3;15(1):39.
2. Zukerberg LR, Nickoloff BJ, Weiss SW. Kaposiform Hemangioendothelioma of Infancy and Childhood: An Aggressive Neoplasm Associated with Kasabach-Merritt Syndrome and Lymphangiomatosis. The American Journal of Surgical Pathology. 1993 Apr;17(4):321–8.
3. Croteau SE, Liang MG, Kozakewich HP, Alomari AI, Fishman SJ, Mulliken JB, et al. Kaposiform hemangioendothelioma: atypical features and risks of Kasabach-Merritt phenomenon in 107 referrals. J Pediatr. 2013 Jan;162(1):142–7.
4. Mentzel T, Mazzoleni G, Dei Tos AP, Fletcher CD. Kaposiform hemangioendothelioma in adults. Clinicopathologic and immunohistochemical analysis of three cases. Am J Clin Pathol. 1997 Oct;108(4):450–5.
5. Vashi P, Abboud E, Bier-Laning C, Gupta D. Adult-onset Kaposiform hemangioendothelioma of the tongue: case report and review of the literature. Curr Oncol. 2016 Oct;23(5):e517–20.
6. Rekhi B, Sethi S, Kulkarni S, Jambhekar N. Kaposiform hemangioendothelioma in tonsil of a child associated with cervical lymphangioma: A rare case report. World journal of surgical oncology. 2011 May 23;9:57.
7. Ribag Y, Khalfi L, Fiqhi K, Ouardi A, MokfiI I, Elkhatib K. ADULT KAPOSIFORM HEMANGIOENDOTHELIOMA OF THE LEG COMPLICATED BY KASABAKH MERITT PHENOMENON.:8.
8. Gruman A, Liang MG, Mulliken JB, Fishman SJ, Burrows PE, Kozakewich HPW, et al. Kaposiform hemangioendothelioma without Kasabach-Merritt phenomenon. J Am Acad Dermatol. 2005 Apr;52(4):616–22.
9. Aguirre LE, Ali RA, Kerr DA, Khanlari M, Lopes G. Kaposiform Hemangioendothelioma of the GI Tract: An Exception to Occam's Principle in an Adult with SBO [Internet]. Vol. 2019, Case Reports in Oncological Medicine. Hindawi; 2019 [cited 2021 Feb 24]. p. e3269326. Available from: https://www.hindawi.com/journals/crionm/2019/3269326/.

10. Flucke U, Karanian M, Broek RW ten, Thway K. Soft Tissue Special Issue: Perivascular and Vascular Tumors of the Head and Neck. Head and Neck Pathol. 2020 Mar 1;14(1):21–32.
11. Navarro OM, Laffan EE, Ngan B-Y Pediatric Soft-Tissue Tumors and Pseudo-tumors: MR Imaging Features with Pathologic Correlation. RadioGraphics. 2009 May 1;29(3):887–906.
12. White JB, Pullman J, Wenig B, Smith RV. Kaposiform Hemangioendothelioma of the Tongue in an Adult. Arch Otolaryngol Head Neck Surg. 2009 Aug 17;135(8):824.
13. Vetter-Kauczok CS, Ströbel P, Bröcker EB, Becker JC. Kaposiform hemangioendothelioma with distant lymphangiomatosis without an association to Kasabach-Merritt-Syndrome in a female adult! [Internet]. Vascular Health and Risk Management. 2008 [cited 2021 Feb 24]. Available from: https://www.dovepress.com/kaposiform-hemangioendothelioma-with-distant-lymphangiomatosis-without-peer-reviewed-article-VHRM.

Figures

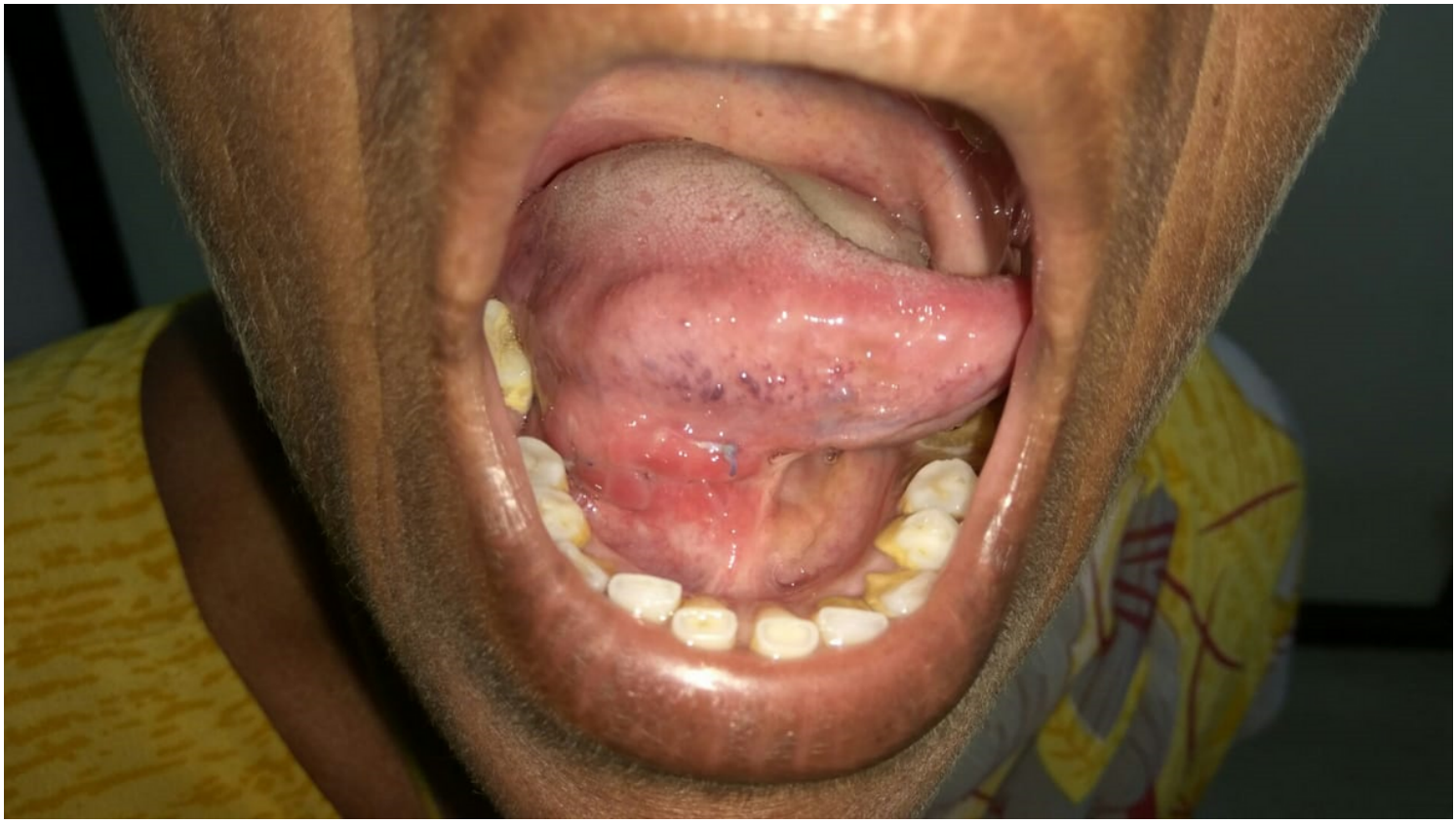

Figure 1

Clinical photograph showing the lesion arising from the floor of the mouth on the right. The mass appears to have a mixed consistency.

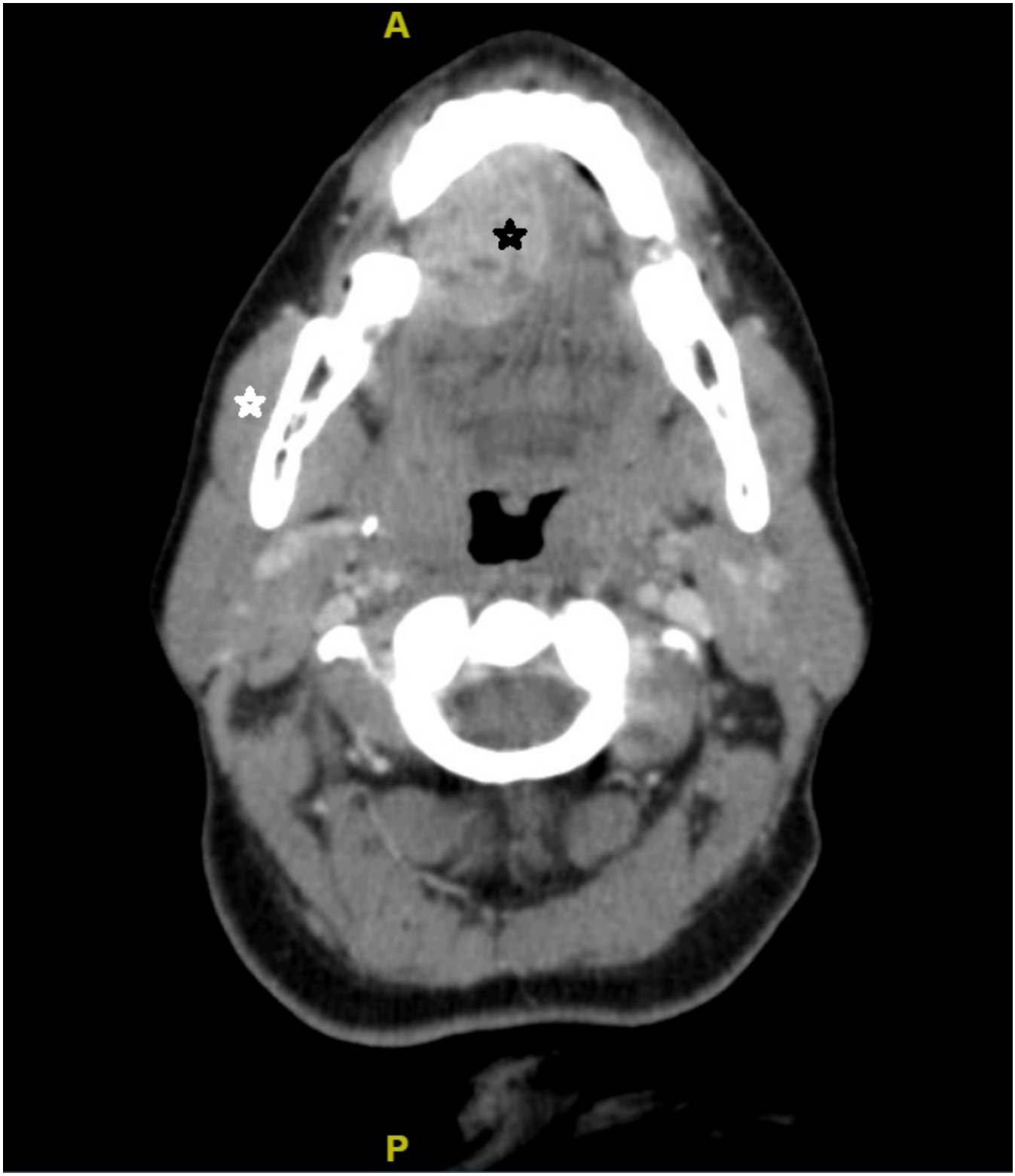

Figure 2

Contrast-enhanced CT scan (axial section) depicting the heterogeneously enhancing mass abutting the right mandibular cortex (black asterisk). The white asterisk depicts the normal-appearing submandibular gland.

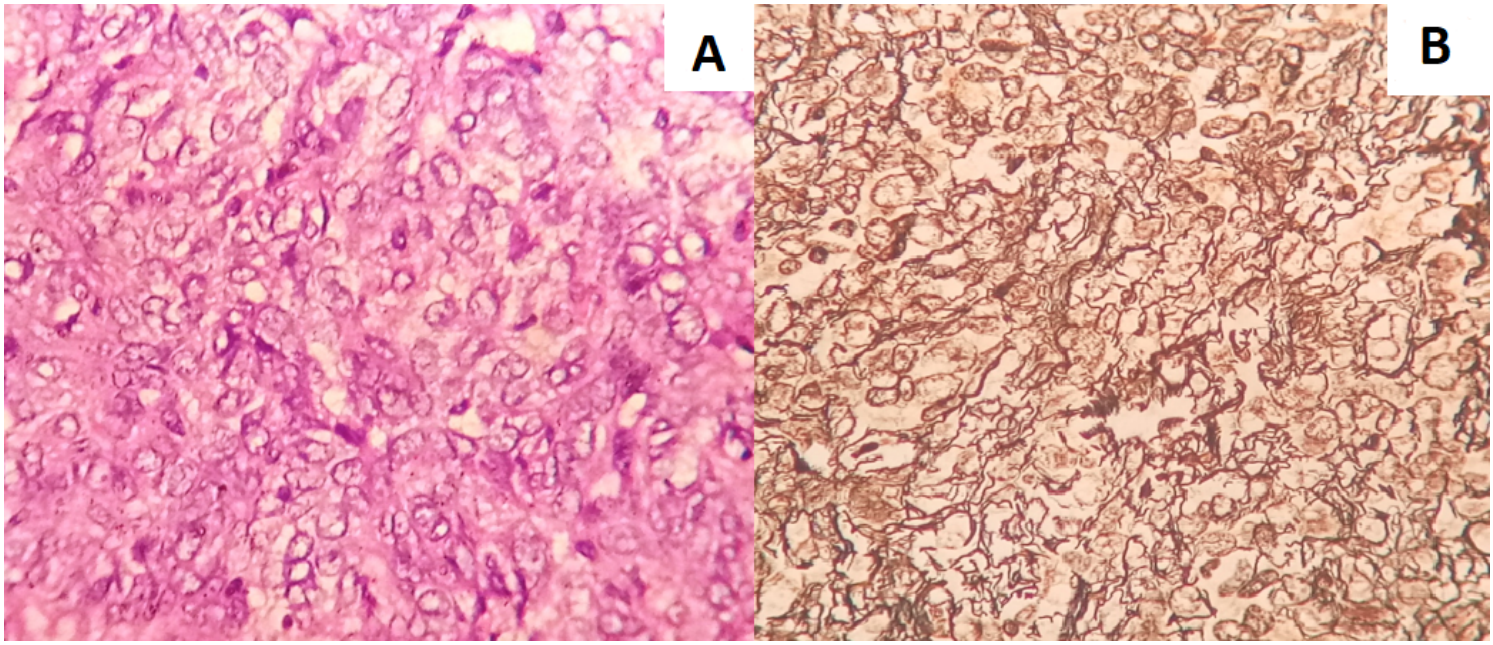

Figure 3

Photomicrograph of the histopathological examination of the specimen depicting tumour cells arranged in fascicles with slit-like vascular spaces (Figure 3a: Haematoxylin and eosin, 40X magnification). The lesion has a rich reticulin network, confirming the presence of true blood vessels (Figure 3b: Reticulin, 40X magnification).

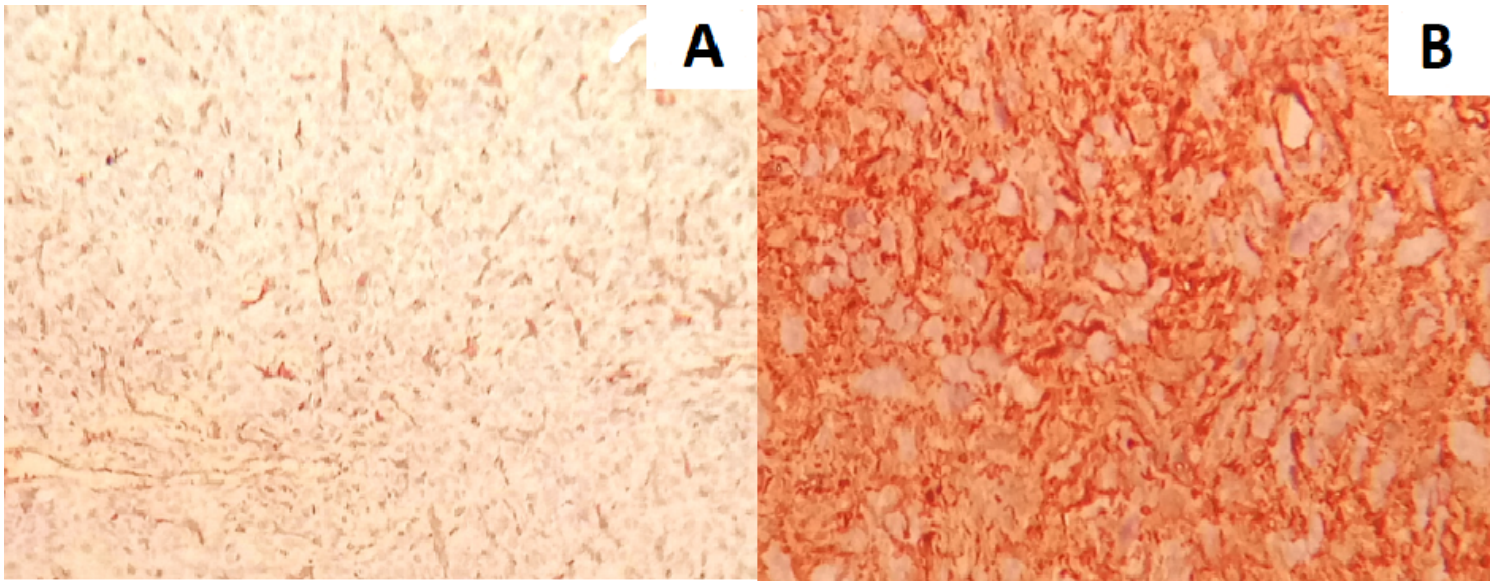

Figure 4

Photomicrograph depicting the endothelial cells positive for CD31 (Figure 4a: Diaminobenzidine, 10X magnification). Photomicrograph depicting the endothelial cells positive for CD34 (Figure 4b: Diaminobenzidine, 10X magnification).

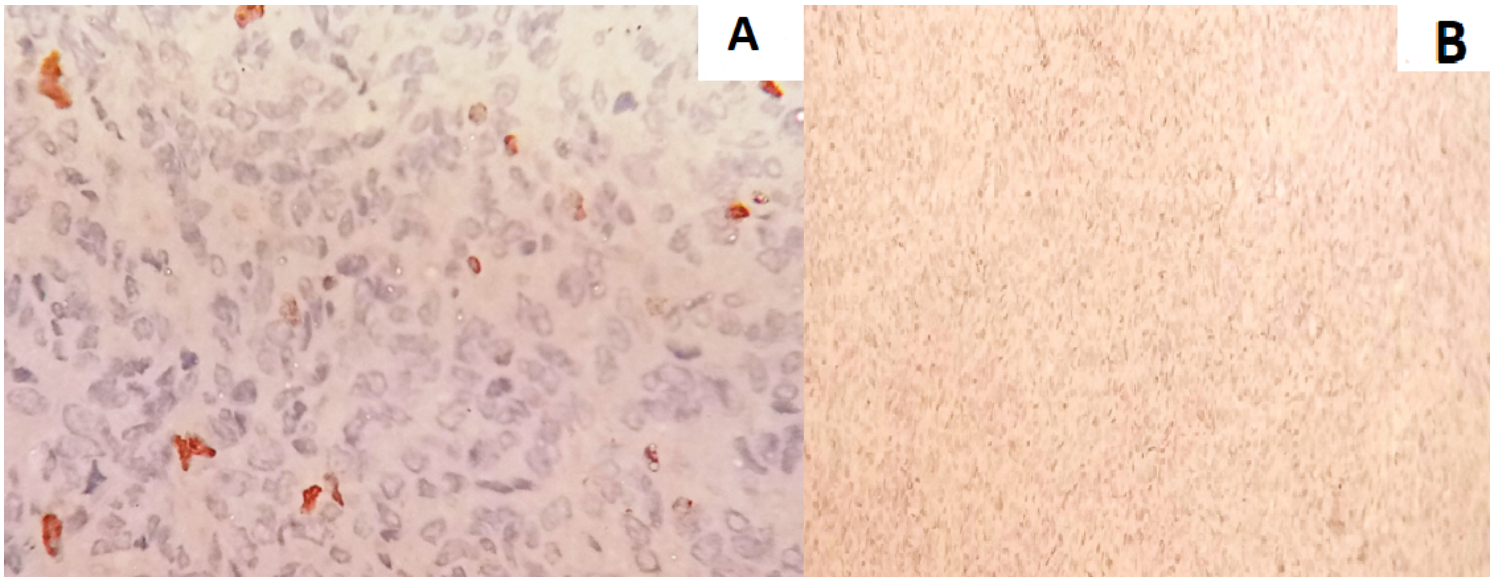

Figure 5

Photomicrograph depicting 1% Ki67 staining (Figure 5a) and tumour cells negative for SMA (Figure 5b: Diaminobenzidine, 10X magnification).

Supplementary Files

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- CAREchecklistEnglish2013.pdf