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CLINICAL REPORT

Tonsillar Epithelioid Haemangioendothelioma: Description of a Rare Clinical Case

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Abstract We present a rare case of tonsillar EHE with local recurrence and neck metastasis 30 months after surgery, as well as further neck recurrence 27 months later. We describe clinical, immunohistopathological, and therapeutic aspects of the tumor highlighting the diagnostic difficulties, lack of therapeutic guidelines and need for long-term follow-up.

Keywords Epithelioid haemangioendotelioma · Haemangioendotelioma · Palatine tonsil · Oropharynx

Introduction

The term "haemangioendothelioma" was introduced for the first time by Borrmann, who proposed the concept of "vascular neoplasm with intermediate or low malignant potential" over a century ago. Three histological types of haemangioendothelioma are described: kaposiform, hobnail (or Dabska-retiform), and epithelioid [1]. Epithelioid haemangioendothelioma (EHE) was first described by Weiss and Enzinger in 1982 as an uncommon angiocentric vascular neoplasm with biological, clinical, and histological features between those of hemangioma and angiosarcoma. It is specifically characterized by neoplastic proliferation of endothelial cells around the vascular lumen [2]. This is an extremely rare neoplasm and can occur in both men and women in the age range of 20–40 years.

In 2002, the WHO included EHE in the category of local aggressive tumors with rare metastatic potential. EHE usually develops in soft tissues and internal organs such as the lungs, liver, bone, and musculoskeletal system3. In particular, it is extremely rare in the head and neck region, and even more so in the oral cavity, with only 31 cases having been described in the literature since 19,753. To the best of our knowledge, no cases of oropharyngeal EHE have been described previously.

Case Report

A 76-year-old female patient came for observation due to a history of a foreign body sensation in her throat and mild dysphagia. The ENT physical examination revealed a swelling of the right palatine tonsil with a regular and not ulcerated surface. There was no evidence of cervical lymphadenopathies.

A computed tomography (CT) scan of the head and neck with contrast showed an ovoid expansive lesion of the right tonsillar fossa that was 24 mm × 17 mm. The lesion involved the glosso-tonsillar sulcus, and there was no clear cleavage plane with the oral floor and the posterior margin of the tongue (Fig. 1a). A diagnostic biopsy was performed, and the result was positive for mesenchymal neoplasia. The patient underwent a right enlarged tonsillectomy, and the definitive histological examination was positive for EHE of the palatine tonsil (pT1 TNM 8th ed. for soft tissue sarcoma).

Microscopically, the lesion consisted of a widespread proliferation of neoplastic elements with a hyperchromic

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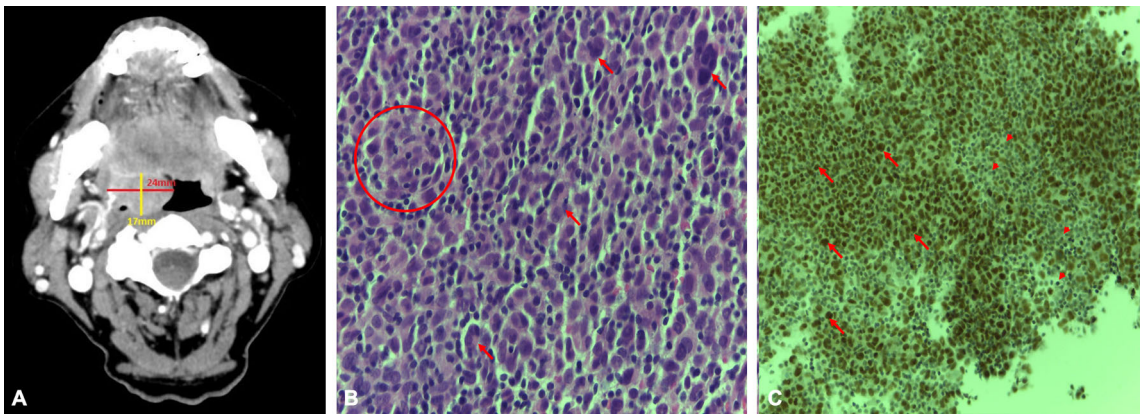

Fig. 1 **a** CT scan with contrast, axial view: a 24-mm lesion of the right tonsillar fossa is visible, the lesion involves the glosso-tonsillar sulcus, and a clear cleavage plane with the oral floor and the posterior margin of the tongue can't be found; **b** Hematoxylin–eosin 20x: markedly atypical neoplastic cells (arrows) gathered with syncytial aspect (circle); **c** Immunohistochemical positivity for Fly-1 (arrows), lymphocytes of the residual tonsillar parenchyma are visible (arrow heads)

nucleus and vacuolated clear cytoplasm (Fig. 1b). The lesion diffusely infiltrated the tonsillar parenchyma, and resection margins were clear. The immunohistochemical investigation was positive for vimentin, CD34, CD31, FLY-1 (Fig. 1c), and factor VIII, while the results were negative for cytokeratins, melan A, CD20, and CD30. The Ki67 score was 5%. No adjuvant therapy was performed after considering the wide clear resection margins.

The patient underwent regular clinical and radiological follow up. At 30 months after surgery, a 24-mm right cervical lymphadenopathy was observed at the right IIa level. Ultrasounds, CT scan, and a cytological study with needle aspiration raised suspicions of lymph node metastasis of EHE. Moreover, a biopsy of a suspicious area at the level of the glosso-tonsillar sulcus revealed recurrence of the EHE in histology. The patient underwent surgical resection of the local recurrence and a modified radical neck dissection type III.

The histological examination confirmed the local recurrence of EHE with lymph node metastasis (rpT1 N1). The microscopic examination was consistent and comparable to the first diagnosis, with immunohistochemical positivity for CD31, CD34, vimentin, anti-INI-1, FLY-1, PD-L1, and factor VIII, as well as negativity for ALK, p63, TTF-1, CD99, cytokeratins, CK20, CK7, and S100. Ki67 was expressed in 80% of neoplastic cells for both T and N.

After a multidisciplinary discussion, an adjuvant radiotherapy treatment was performed on T and N. After 27 months of negative clinical and radiological follow-up, a 15-mm ipsilateral neck node appeared at level V with cytology suggestive for EHE metastasis. The patient underwent neck dissection revision. Definitive histology results confirmed the occurrence of EHE metastasis (rpN1).

Discussion

EHE is a rare vascular tumor with intermediate malignancy. It is often asymptomatic and rarely involves the head and neck. Only 31 cases of EHE of the oral cavity have been described in the literature since 1975 [3].

A total of 5 papers were identified in literature which reported other histological types of oropharyngeal hemangioendothelioma. However, no cases of oropharyngeal EHE have been described. The first case of hemangioendothelioma described dates back to 1975, and the histological type was not specified [4]. More recently, two studies focused on kaposiform hemangioendothelioma (KHE) [5, 6]. One reported a case of a spindle-cell hemangioendothelioma of the posterior pharyngeal wall [7], and a single case was reported involving a papillary intralymphatic angioendothelioma (Dabska's tumor) of the tonsil [8]. The complete report is shown in Table 1.

Because of its heterogeneous presentation, representing less than 1% of all vascular tumors, EHE is often misdiagnosed and inadequately treated, leading to a poor prognosis in some cases. Imaging is necessary to determine the extent of the lesion, while immunohistochemical analysis allows us to recognize the microscopic evidence of vascular differentiation of the tumor and helps in the differential diagnosis from hemangiomas and squamous cell carcinoma [3]. According to previous reports, the majority of intraoral EHE lesions are positive for CD34, CD31, factor VIII, and vimentin, which was also the case in our patient.

Due to the rarity of the disease, there is no standardized treatment protocol. Surgery is recommended and, in patients with suspected local residues, radiotherapy should

Table 1 Papers' features in detail

References	Year of publication	No. of patient including	Age	Sex	Anatomical subsite	Country	Therapeutic approach	Hystological subtype
Kovacs et al	1975	1	n.a	n.a	Palatine tonsil	Hungary	Surgery	n.a
Lade et al	2005	1	25	Male	Posterior pharyngeal wall	India	Surgery	Spindle-cell
DeFatta et al	2005	1	3	Male	Soft palate	USA	Surgery	Kaposiform
Rekhi et al	2011	1	2	Male	Palatine tonsil	India	Surgery	Kaposiform
Mukherjee et al	2012	1	13	Female	Palatine tonsil	India	Surgery	Papillary intralymphatic angioendothelioma

n.a. = Not available

be considered as an option to prevent recurrence. Chemotherapy can be added to the treatment regimen for widespread disease, but its benefits are still unclear [9].

The risk of lymph node metastasis is low (8.3%) when globally considering EHE in the different head and neck sub-sites. This is different from local recurrence, which can happen in 25% of cases according to the literature [10]. However, we should emphasize that in previous reports, none of the lesions were located in the oropharynx. According to the observations of our patient, who experienced regional recurrence twice, we could infer that oropharyngeal EHE is characterized by a higher risk of loco-regional recurrence than other sub-sites. Thus, a more aggressive treatment should be considered ab initio. Recurrence can also happen several years after treatment [3]. Consequently, a long-term follow up (both clinical and radiological) should be considered.

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Compliance with Ethical Standards

Conflict of interest Authors declare they have not conflict of interest.

Informed Consent The patient gave her consent for the publication of this case.

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