Tubulopapillary Hidradenoma-like Tumour of the Mandible: A Case Report and Literature Review

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Abstract Tubulopapillary hidradenoma is an uncommon benign sweat gland tumour which appears as a well-defined superficially located dermal nodule, most commonly occurring in the head or of the extremities. Its occurrence is extremely rare in the mandible, as there are only two cases of tubulopapillary hidradenoma-like tumour of the mandible reported in the literature. Microscopically, the lesion appears as a well circumscribed but unencapsulated neoplasm composed of numerous irregularly shaped tubular structures that have a double to several layered epithelial lining. The outer layer consists of flat to cuboidal myoepithelial cells and inner layer contains cuboidal to columnar cells that demonstrate decapitation secretions. We report an unusual case of tubulopapillary hidradenoma-like tumour presented as a nodular growth in the right retromolar region of the mandible in a 67-year-old man. The light microscopic features along with immunohistochemical findings of this unusual neoplasm are discussed.

Keywords Tubulopapillary hidradenoma · Mandible · Sweat glands · Immunohistochemistry

Introduction

Tubulopapillary hidradenoma (TPH) is a rare benign tumour of the sweat glands usually presenting as a well-circumscribed superficially located dermal nodule with wide age distribution (18–78 years) and a female predominance. The scalp is the most affected site however other sites involving the face or the skin of the extremities are also involved [1, 2].

Histologically, these tumours have a well circumscribed lobular architecture. The lobules consist of numerous irregularly shaped tubular structures lined by an outer layer of flattened myoepithelial cells, and inner (luminal) layer composed of cuboidal or columnar cells demonstrating decapitation secretions. A few tubules can show pseudopapillary cellular extension lacking a fibrovascular core [3, 4].

We recently had the opportunity to study this rare neoplasm with the purpose of characterizing the light microscopic features and immunohistochemical findings that may be useful in differentiating TPH from other sweat gland neoplasms. We report an unusual case of a TPH in the right mandible of a 67-year-old man. To our knowledge, this is the third report of a central (intraosseous) tubulopapillary hidradenoma of the mandible.

Case Presentation

A 67 years old apparently healthy edentulous man was referred to the Department of Oral Pathology with a

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complaint of painless mass in the right mandibular posterior region. The patients medical, social and family history was non-contributory. The patient was unaware of the lesion until it was brought to his notice by the prosthodontist, whom he visited for the construction of dentures. Intra-oral examination revealed nodular growth in the right retromolar region of the mandible measuring about 1 cm × 1 cm. The surface of the lesion was smooth and non-ulcerated (Fig. 1). On palpation, the growth was non-tender, immobile, sessile and firm in consistency. No cervical lymphadenopathy or draining extra-oral sinus was observed. Based on the clinical examination, a differential diagnosis of a reactive lesion like a pyogenic granuloma, peripheral giant cell granuloma, traumatic fibroma, benign neoplasm like a lipoma and malignancy of epithelial or non-epithelial origin were considered. An orthopantomogram revealed a well-defined, saucer-shaped radiolucency in the right retromolar region of the mandible (Fig. 2). Radiographically, the differential diagnosis was broad, including an odontogenic cyst, giant cell lesions and tumours.

Surgical excision of the growth was performed under general anaesthesia. During surgical exploration the growth was found to be attached to the underlying bone. The cut surface of the lesion was smooth, white in colour and firm in consistency. A hematoxylin and eosin stained section of formalin-fixed paraffin embedded tissue showed a mandibular tumour mass primarily composed of parakeratinised stratified squamous epithelium-covered tubulopapillary processes projecting into cystic spaces. Two layers of epithelial cells lined the tubular structures: an outer layer of flat or spindle shaped myoepithelial cells with oval hyperchromatic nuclei and an inner (luminal) layer composed of cuboidal to columnar cells producing non-villous papillary projections devoid of connective tissue core (Fig. 3a). The luminal cells have round, pale nuclei with prominent nucleoli and bright

Fig. 1 Intra-oral view showing smooth surfaced sessile nodule in the right retromolar region of the edentulous mandible

Fig. 2 Orthopantomogram showing well-defined, large saucer-shaped radiolucency in the right retromolar region of the edentulous mandible

eosinophilic cytoplasm. Most of these cells have snout like apocrine luminal projections and features suggestive of decapitation secretion identical to tubulopapillary hidradenoma of the skin (Fig. 3b). Atypical mitoses, cellular atypia or signs of infiltrative growth were absent. The lumina of some of the tubules contained granular eosinophilic material that was periodic acid-Schiff (PAS) positive and diastase labile (Fig. 4). Histopathologically the

Fig. 3 Photomicrograph of TPH-like tumour of the mandible. **a** Multiple irregularly tubular glandular structures (H&E, ×25). **b** Higher magnification showing intratubular papillary projections and lumina filled with granular eosinophilic material (H&E, ×100)

Fig. 4 Photomicrograph showing PAS-positive granular material in the lumina of the tubular structures (PAS, ×50)

diagnosis of tubulopapillary hidradenoma-like tumour of the mandible was made. Post-operative recovery was uneventful. The patient was lost to follow-up.

Immunohistochemical Findings

The immunohistochemical profile of the mandibular tumour is shown in Table 1. Immunohistochemically, the inner (luminal) as well as the outer (myoepithelial) cells stained positive with pan-cytokeratin antibody (CK) (Fig. 5a) and smooth muscle actin (SMA) (Fig. 5b). However there was a difference in staining intensity of both the cells. The outer (myoepithelial) cells stains intensely with SMA than inner (luminal) cells, while CK was more intense in inner (luminal) cells than outer (myoepithelial) cells. The inner (luminal) cells were positive for both, the epithelial membrane antigen (EMA) (Fig. 5c) and carcinoembryonic antigen (CEA) (Fig. 5d). In contrast none of these antibodies was reactive in the outer (myoepithelial) cells. Both, the outer (myoepithelial) and inner (luminal) cells stained negative for S-100 protein (Fig. 5e). The proliferative activity Ki-67 was exclusively restricted to myoepithelial cells (Fig. 5f).

Discussion

TPH is a rare benign sweat gland tumour that presents as a well-defined asymptomatic, superficially located solitary nodule, demonstrating apocrine differentiation with a wide range of age distribution and a female preponderance [1, 2]. The scalp is the most commonly affected site followed by skin of the face and extremities. Its occurrence in the oral cavity is extremely rare. To the best of our knowledge, there are only two cases of intra-osseous TPH-like tumour

of the mandible reported in the literature (Table 1). Surprisingly, our case had similar clinical presentation of the lesion in the right retromolar region of the mandible affecting old males as reported in previous cases [4, 5], which is finding was contradictory to dermal TPH, which shows female predilection [1, 2].

The histogenesis of TPH of the mandible is still unknown. We believe that entrapment of the retromolar mucous glands or embryonic remnants of the submandibular and sublingual glands, or ectodermally derived odontogenic epithelium within the mandible during development could be the source of TPH of the mandible [4].

Tubular apocrine adenoma (TAA) was originally described by Landry and Winkelmann in 1972, believed to be a apocrine sweat gland origin [6, 7]. Papillary eccrine adenoma (PEA) was first reported by Rulon and Helwig in 1977 as a benign neoplasm of the eccrine sweat glands [7]. Microscopically TAA and PEA are difficult to differentiate as they show considerable histologic overlap. Since there is no clear ductal or glandular pattern of differentiation for these benign sweat gland tumours, the term tubulopapillary hidradenoma (TPH) has been used for the description, which encompasses ductal as well as eccrine and apocrine features [8–12].

Histologically, the TPH shows distinctive microscopic features. The lesion is well defined, composed of tubules or ducts that were lined by an outer layer of flattened or spindle-shaped myoepithelial cells and inner layer whose cells aggregate focally producing non-villous projections devoid of connective tissue cores. Absence of cytologic atypia and presence of myoepithelial cell surrounding irregularly shaped tubular structures suggest the benign nature of this lesion [4].

TPH must be differentiated from other sweat gland neoplasms like papillary eccrine adenoma (PEA) and apocrine adenocarcinoma. TPH resembles PEA in many aspects. However, PEA rarely communicate with the surface epithelium and lacks decapitation secretion microscopically [13, 14]. In contrast to apocrine adenocarcinoma, TPH lack cytologic atypia and possess a peripheral myoepithelial layer [5].

The results of the immunohistochemical stains were essentially the same as previously reported by El-Mofty et al. and Baumhoer D et al. [4, 5]. CEA and EMA are found in eccrine and apocrine structures of normal skin and of adnexal neoplasms with sweat gland differentiation, which was similar to our findings [15]. The proliferative activity (MIB-1) was almost restricted to myoepithelial cells, which also showed a positive reaction for CK and SMA. It is noteworthy that, unlike El-Mofty finding of S-100 positivity for myoepithelial cells, our case showed absence of S-100 protein reactivity. Since S-100 protein is found in eccrine secretory epithelium but not

Table 1 Previously reported TPH-like tumour of the mandible in the English-language literature

Case	Author	Age (years)	Sex	Site	Size	Immunohistochemistry										Management	Follow-up
						Antibody	CK	VIM	SMA	S-100 protein	EMA	CEA	LYS	A-1-AT			
1	EL-Mofty et al. [4]	73	Male	Right Posterior Mandible	–	Myoepithelial cells	++	++	+++	–	–	–	–	–		Curettage	5 y (R)
						Luminal cells	+++	–	–	++	++	++	++	++			
						Antibody	Pan-CK	CEA	GCDFP-15	MIB-1	SMA						
2	Baumhoer et al. [5]	80	Male	Right Posterior Mandible	4 cm	Myoepithelial cells	–	–	–	+	++					Curettage, Combined intraoral & extraoral en-bloc resection	17 m (R)
						Luminal cells	++	++	+	–	–						
						Antibody	Pan-CK	SMA	EMA	CEA	S-100 protein	Ki-67				Surgical excision	Absent
3	Desai R S et al. (present case)	67	Male	Right Posterior Mandible	1 cm × 1 cm	Myoepithelial cells	++	+++	–	–	–	+					
						Luminal cells	+++	+	++	++	–	–					

CK cytokeratin, VIM vimentin, LYS lysozyme, A-1-AT α_1 -antitrypsin, GCDFP-15 gross cystic disease fluid protein 15, MIB-1 molecular immunology borstal number 1, SMA smooth muscle actin, EMA epithelial membrane antigen, CEA carcinoembryonic antigen, y Year, m Month, R Recurrence

+++ strongly positive, ++ moderately positive, + mildly positive, – negative staining

Fig. 5 Photomicrographs of immunostained sections of all study markers in TPH-like tumour of the mandible. Original images taken at $\times 100$ magnification and *insets* at $\times 400$ magnification. **a** CK-positive expression stronger in *inner* (luminal) cells than *outer* (myoepithelial) cells; **b** strong SMA-positive expression in *outer* (myoepithelial) cells

than *inner* (luminal) cells; **c** exclusive EMA-positive-expression in *inner* (luminal) cells; **d** CEA-positive-expression in *inner* (luminal) cells; **e** S-100-negative-expression in both, *inner* (luminal) and *outer* (myoepithelial) cells; **f** Ki-67-positive-expression exclusively in *outer* (myoepithelial) cells

in apocrine secretory epithelium, its absence in the present case strongly suggests apocrine differentiation. Thus the immunohistochemical findings reported in the present case confirm its eccrine and apocrine phenotypic differentiation similar to that of dermal TPH. Thus the lesion under discussion showed benign TPH-like tumour of the mandible showing both, eccrine and apocrine differentiation, as indicated by its clinical course, radiographic

appearance, microscopic and immunohistochemical features.

Although TPH of the mandible is benign in nature, local recurrence after several years has been seen in both the previous case reports, therefore wide surgical excision with clear margins and long term follow up is advised [4, 5].

In conclusion, we present the third case of an intra-osseous tubulopapillary hidradenoma-like tumour of the

mandible, which should be considered in differential diagnosis for unusual tumours of the jaw.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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