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Extensive Sublingual Epidermoid Cyst – Diagnosis by Immunohistological Analysis and Proof by Podoplanin

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Abstract. *Aim: We present the case of a surgically treated 39-year-old man with diagnosis of a giant sublingual internal epidermoid cyst. Usually, such dermoid or epidermoid cysts are caused by aberrant ectodermal tissues or by acquired aberrant epithelial tissues arising from the foetal period, or from trauma or surgery. The incidence of oral dermoid or epidermoid cysts is about 1.6%; most occur at the mouth floor but they nevertheless are very rare. Case Report: The patient presented with a history of progressive swelling of the sublingual region with dysphagia, progressive snoring during sleep and occasional shortness of breath. The suspected clinical diagnosis of a giant sublingual dermoid or epidermoid cyst was supported by the radiological finding after performing magnetic resonance imaging. The cyst was surgically removed under general anaesthesia through an intraoral approach. The immunohistological analysis of the specimen with a monoclonal antibody against podoplanin (D2-40) showed a positive reaction in the basal epithelial layer, exclusively in areas with secondary inflammation, but not in the remaining cyst wall. Conclusion: Sublingually situated extensive epidermoid cysts are rare findings in the oral cavity. In such cases, surgical excision remains the only treatment. We demonstrated that cystic epithelia were normally not immunoreactive for D2-40 but strong immunoreactivity was observed in the basal epithelial cell layer, in areas of ruptured cyst wall associated with secondary inflammatory changes.*

Developmental cysts are rare, benign congenital tumours that can be divided into three histopathological subtypes, including dermoid, epidermoid and teratoid types. Dermoid and epidermoid cysts are developmental cysts, arising from ectodermal tissue lined by epidermis with skin appendages (dermoid cysts) or without appendages (epidermoid cysts) (1, 2). These cysts may occur in any region of the body, while they are found more often in ovaries or the sacral region compared to the head and neck region which has a frequency of 6.9% (1-3). Most of the oral dermoid or epidermoid cysts appear in the midline of the floor of the oral cavity or in the submental region (4). Reports concerning the incidence of dermoid and epidermoid cysts of the floor of mouth range from 1.6% to 19% depending on the sample of the analysed cases (3, 5, 6). The majority of oral dermoid and epidermoid cysts occur between the ages of 15-35 years, but they may also be present at the time of birth (7, 8). In most cases, dermoid and epidermoid cysts are small during childhood and enlarge during adolescence (9). When localized in the floor of the mouth, symptoms usually first occur when dermoid or epidermoid cysts have already grown to a significant size and hence cause dysphagia, reduced tongue movement, snoring or breathing difficulties. The cysts may feel fluctuant or doughy on palpation. The possibility of malignant transformation is rare, but such case have been reported (10).

Case Report

A 39-year-old male presented to the Department of Oral and Maxillofacial Surgery at the University Medical Center Hamburg Eppendorf with a history of progressive swelling of the sublingual region with dysphagia, progressive snoring during sleep and occasional shortness of breath. In addition, the patient reported speech disturbances and pain in the sublingual region. Clinical evaluation including physical examination of the extraoral region and the oral cavity showed a significant submental swelling of the right side, as well as a visible and palpable swelling of the right-side sublingual region, with no signs of an acute inflammation. At the time of examination, the patient did not report respiratory distress, however, swallowing was limited.

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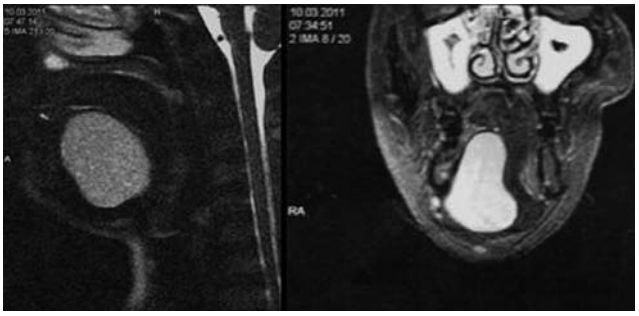

Figure 1. *Magnetic resonance imaging (sagittal and coronal view) of the patient after presentation, showing the midface and head and neck region, highlighting the giant epidermoid cyst located in the right sublingual region.*

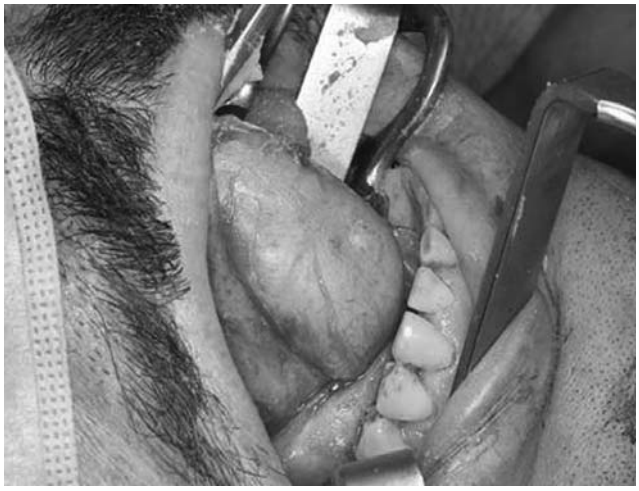

Figure 2. *Intraoperative view of the intraoral cavity showing the superior part of the epidermoid cyst after incision of the right sublingual region before rupture of the cyst body.*

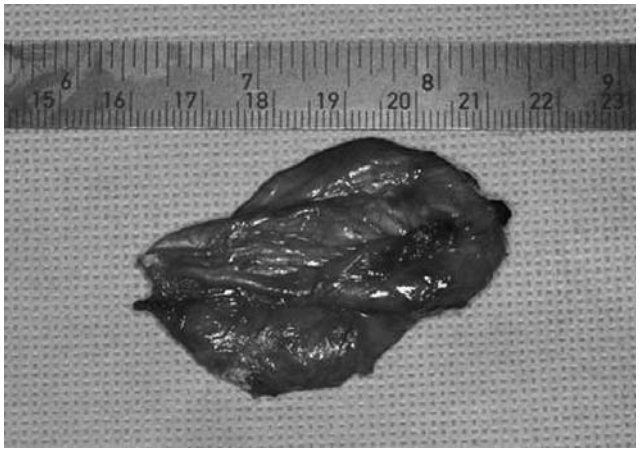

Figure 3. *Extension of the ruptured cyst body after total resection.*

Examination of the swelling showed a firm and hard mass that was non-pulsatile, movable, impressible, and with a discrete congestion of the overlying vessels. There was a minimal tongue displacement to the left side, tongue movement was limited anteriorly and to the right. Furthermore, intraoral examination did not show any mucosal abnormalities. Apart from the aforementioned findings, examination of the submental and neck region was inconspicuous. There were no swollen lymph nodes, no blood vessel congestion or opening of a possible median or lateral dermoid cyst of the neck region. The suspected diagnosis of a giant sublingual dermoid or epidermoid cyst was supported by radiological examination, by performance of magnetic resonance imaging (MRI) of the head and neck region (Figure 1).

Surgical removal of the cyst was carried out under general anaesthesia with oral intubation. The tongue was lateralized using a nylon suture. An initially planned resection of the whole cyst in total without opening the cyst body by using a single intraoral incision in the right side sublingual region became very difficult because of the huge size of the cyst (Figure 2). During preparation and mobilization of the cyst, the cyst body ruptured and the cyst contents were evacuated. However, an eventless total resection of the epidermoid cyst was performed with no injury to nearby structures (Figure 3). After total excision, the lateralised tongue returned to its physiological position and dysphagia, snoring and shortness of breath were gone.

Histopathological examination of the cyst was carried out by haematoxylin-eosin (H&E) staining. On H&E staining, typical structures of an epidermoid cyst wall were observed, such as keratinizing stratified squamous epithelium associated with focal inflammatory changes (Figure 4). Eccrine and apocrine glands were not present. Similarly, no salivary glands with typical pericystic connective tissue were found. Immunohistological analysis of the cystic tissue was carried out with monoclonal antibody against podoplanin (D2-40). Sections were deparaffinized and heated in the manufacturer's recommended unmasking solution at 95˚C for 20 min. Endogenous peroxidases were quenched with 0.3% H_2O_2 in phosphate buffered saline (PBS). Sections were incubated overnight at 4˚C using anti-podoplanin (clone D2-40, dilution 1:40; Signet, Dedham, MA, USA). Following this incubation, sections were incubated with Envision-system (Dako, Cytomation, Glostrup, Denmark) for 30 min at room temperature. D2-40 exhibited a positive reaction in the basal epithelial layer exclusively in areas with secondary inflammation, but not in the remaining cyst wall. Cellular atypia was not present. Furthermore, scattered subepithelial lymph vessels also had a positive reaction for D2-40.

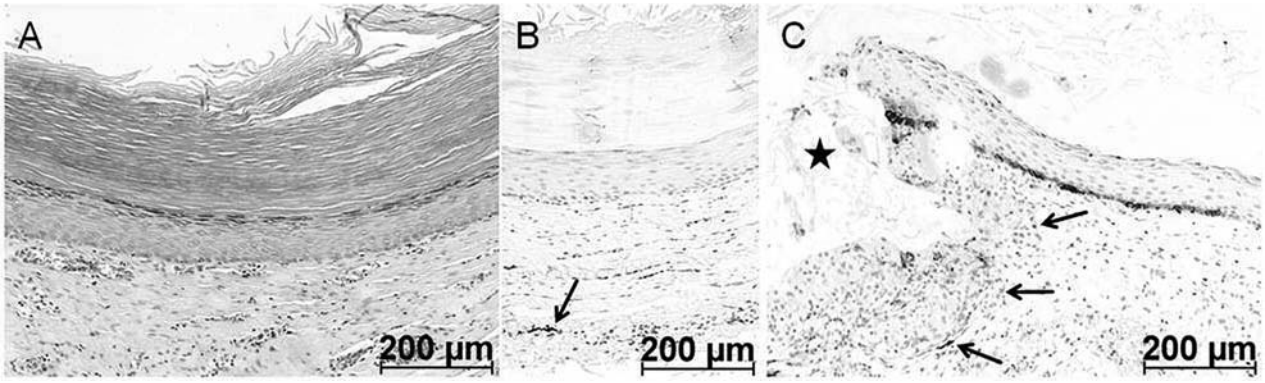

Figure 4. *Epidermoid cyst (histopathology). A: The cyst contained flattened keratin lamellae and the wall was lined with keratinizing stratified squamous epithelial surface without atypia (haematoxylin-eosin, original magnification: ×200). B: Although several lymph vessels were highlighted with D2-40 (arrow), the cyst wall showed no podoplanin positive cells in non-inflamed areas. C: Adjacent to the ruptured cyst wall with secondary inflammatory changes (asterix), the basal epithelial layer showed strong reaction for podoplanin (arrows) (monoclonal podoplanin antibody D2-40, original magnification: ×200).*

Discussion

Dermoid and epidermoid cysts of the head and neck region are very rare. The occurrence of both types of cysts in that region is nearly the same, about 50% each (9). A histopathological differentiation of dermoid and epidermoid cysts shows that epidermoid cysts are distinguished from dermoid cysts by the presence of an epidermoid lining which possibly contains adnexal structures, such as hair, hair follicles, sebaceous glands, and sweat glands (12, 13). Both types of cysts are lined by epidermis-like keratinized stratified squamous epithelium. The dermoid cysts are characterized by dermal appendages, while epidermoid cysts do not have such appendages (1, 2). Cases of teratoid cysts that contain elements derived from ectoderm, endoderm or mesoderm are extremely rare in the oral cavity (14).

The frequency of dermoid and epidermoid cysts in the head and neck region is around 6.9%, whereas only one third of those cysts occur at the mouth floor (1, 2, 5, 6). In a series of 76 cases with oral developmental cysts, 71% occurred up to the age of 30 years and 91% up to the age of 45 years (9). The male to female incidence is about 3:2 (5, 9). With reference to the study of Allard, dermoid and epidermoid cysts occur at approximately the same frequency (9). The most common location for oral lesions is the midline of the floor of the mouth (71%), merely one third is located in lateral parts. Next to the sublingual location (52%), cysts can be located submentally (26%), submandibularly (6%), or in more than one locations (16%) (5). Extraordinary cases of dermoid cysts located in the coronoid region of the mandible or in an intra osseous location have also been reported (15, 16).

In many cases, such cysts do not cause any symptoms. Nevertheless, when the cysts reach a significant size, symptoms such as breathing difficulties, snoring, reduced tongue movement, and difficulties in swallowing can occur (4). Usually, these types of cysts are benign, slow-growing, and cause no pain, but there are cases in which a malignant transformation has been reported after a long term during which dermoid or epidermoid cysts remain untreated (11).

Currently, surgical excision of dermoid and epidermoid cysts is still the only treatment (1). In cases of extreme extension, fine-needle aspiration can be helpful to reduce the mass of the cystic body before excision, but however, rupture of the cystic body may occur.

Histopathological examination of dermoid and epidermoid cysts is usually carried out using H&E. An attempt to examine the cystic lesion by immunohistological analysis was carried out here using podoplanin, a transmembrane sialomucin-like glycoprotein that has been categorized as a specific marker for lymphatic endothelial cells (17-20). Expression of podoplanin has been reported in basal epithelial keratinocytes of the skin, esophagus and the cervix (17), as well as in neoplastic tissues, particularly in oral cancer (20-24). Nonetheless, in basal cells of morphologically normal oral mucosal epithelium, a positive reaction for podoplanin was not detected (24). Formerly podoplanin was considered to be a typical marker of malignancy, particularly in leukoplakia and carcinoma (17-19). Podoplanin was also detected in inflammatory cells. Hence we were curious whether podoplanin could be detected in cystic epithelia or cystic lesions and it was shown, that there was no direct proof of its presence. However, in adjacent tissues with rupture or secondary inflammatory changes, podoplanin was demonstrated to be present.

Conclusion

Sublingual situated extensive epidermoid cysts are rare findings in the oral cavity. In such cases, surgical excision remains the only treatment. As well as histopathological

examination of the epidermoid cyst, we performed an immunohistological analysis of the cystic lesion using podoplanin (D2-40). We demonstrated that in this case of epidermoid cyst, the cystic epithelia were not immunoreactive for D2-40, but strong immunoreactivity was observed in the basal epithelial cell layer, in areas of ruptured cyst wall associated with secondary inflammatory changes.

Conflict of Interest

None declared. All Authors disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations that could inappropriately influence (bias) their work. There is no potential conflict of interest which should be disclosed, including employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/ registrations or grants and any other funding.

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