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ORIGINAL ARTICLE

Dermoid and epidermoid cysts of the mouth: Clinicopathological and cytokeratin profile

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Abstract:

Introduction: The mechanisms of cell differentiation and pathogenesis in oral epidermoid cysts and dermoid cyst is poorly know. **Objective:** To report clinicopathological features and investigate cytokeratin profile of oral epidermoid cysts and dermoid cyst. **Material and Methods:** Eight cases of epidermoid cysts, 4 of dermoid cyst, and 2 Fordyce granules were included. For analysis of the immunohistochemical expression of cytokeratins (6, 7, 8, 10, 13, 14, 18 and 19), brown staining in the sections examined were defined as positive considering three layers: superficial, intermediate and basal. **Results:** In dermoid cyst, cytokeratins 7, 8, 9 and 19 were expressed in one case. Cytokeratin 6 was detected in six cases of epidermoid cysts. Cytokeratins 10, 13 and 14 were expressed in all cysts. Cytokeratin 18 was absent in all cysts. Cytokeratins 10 and 14 was observed in Fordyce granules. Cytokeratin 10 was more expressed in peripheral cells and immature sebaceous glands. As these glands became more differentiated, cytokeratin 10 was not detected, while cytokeratin 14 was expressed in mature sebocytes. Cytokeratins 10, 13 and 14 were expressed in the lining mucosa adjacent to Fordyce granules, similar to normal oral mucosal lining. **Conclusion:** cytokeratin profile is altered in dermoid cyst and epidermoid cysts compared to lining oral mucosa.

Keywords: Dermoid Cyst; Epidermal Cyst; Keratins.

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INTRODUCTION

Dermoid (DCs) and epidermoid cysts (ECs) are considered histological variants of a developing cystic lesion. These cysts arise from entrapment of ectodermal remnants in areas of fusion during embryogenesis[1,2] and from ectodermal differentiation of multipotent stem cells[1,3]. However, the molecular factors related to the histogenesis and pathogenesis of these lesions have been little studied and are not fully elucidated[4–7].

DCs and ECs occur at almost any site of the body, including the head and neck where they account for 1.6 to 6.9% of all cysts[1,8]. In the oral cavity, these cysts are rare, corresponding to less than 0.01% of all cysts[9], and can be found in the palate, tongue and, more commonly, in the floor of the mouth[1,9,10].

Microscopically, DCs are blined with squamous epithelium resembling the epidermis and contain cutaneous appendages such as sebaceous glands, sweat glands and hair follicles. In the absence of appendages, these cysts are called epidermoid[9].

Each epithelial tissue exhibits a profile of cytokeratins (CKs) that contributes to its identification and immunophenotypic characterization. For this reason, the study of the CK profile is one of the most widely used methods to identify lesions of epithelial origin and to characterize the process of epithelial maturation, which may be disordered in a certain tissue[11,12].

To our knowledge, there is only two studies that describes the expression of CKs in oral DC[6,7]. Therefore, the aim of this study was to report the clinicopathological features and to investigate the mechanisms of cell differentiation and pathogenesis in oral ECs and DCs by evaluating the profile of CKs 6, 7, 8, 10, 13, 14, 18 and 19. Fordyce granules and adjacent lining mucosa were used for comparison.

MATERIAL AND METHODS

This is a retrospective study, whose approval number on the Research Ethics Committee was 1309.308. Fifty-two cases of DCs and ECs were obtained from the archives of the School of Dentistry, Federal University of Bahia, the Department of Dentistry, Federal University of Rio Grande do Norte, and the Department of Health, Feira de Santana State University.

Fourteen cases were selected, including 10 cases of ECs and 4 cases of DCs. The other cases were excluded because of the lack of information about their location and/or because they were located at extraoral sites. Twelve cases had preserved and sufficient biological material for immunohistochemistry and were therefore included (8 ECs and 4 DCs). For comparison, two cases of Fordyce granules were also selected. Clinical data such as sex, age, location, color and size of the lesion and clinical diagnosis were obtained from the biopsy request forms.

For histopathological analysis, the 10% formalin-fixed and paraffin-embedded material was cut into 5-µm thick sections. The slides of each case were stained with hematoxylin and eosin (HE) and submitted to new histopathological analysis under a light microscope by an experienced pathologist.

For immunohistochemistry, 3-µm thick histological sections were obtained from 10% formalin-fixed and paraffin-embedded material. The sections were deparaffinized and rehydrated. After antigen retrieval, endogenous peroxidase was blocked using a solution of 3% hydrogen peroxide and distilled water for 10 minutes. The sections were immersed in a solution of 1% Tris-HCl/BSA, Tris-HCl/Triton and distilled water for 5 minutes each. Next, nonspecific background staining was blocked with Protein Block (Dako Corporation, Carpinteria, CA, USA) for 10 minutes.

The EnVision Polymeric system (Dako Corporation, Carpinteria, CA, USA) was used following the protocol in Table 1. The sections were incubated with the primary antibodies. Table 1 shows the specificity, clone, antigen retrieval solution, dilution, and time of incubation for the antibodies used. The reaction was developed with 3,3'-diaminobenzidine (Dako Corporation, Carpinteria, CA, USA) and counterstained with Harris hematoxylin. The positive controls of the reactions consisted of keratocyst tissues known to be positive for these antibodies. Sections in which the primary antibodies were replaced with non-immune serum served as negative controls.

For analysis of the immunohistochemical expression of CKs, cases showing brown staining in the sections examined were defined as positive. Immunostaining in the cystic epithelial lining was evaluated considering they three layers: superficial, intermediate and basal. The slides were examined under a light microscope by an experienced pathologist.

RESULTS

In general, all DCs and ECs were nodular. There was a predominance of female patients and age ranged from 14 to 82 years. The buccal mucosa was the most

affected site, followed by the floor of the mouth. The size of the cysts ranged from 0.5 to 5 cm, with a duration of 2 to 25 years. The mean age of patients with DCs was 49.5 years and that of patients with ECs was 39.55 years. Although the cheek mucosa was the most commonly affected site, this location corresponded only to cases of ECs, while the floor of the mouth was involved in both ECs and DCs. Table 2 shows the clinical features of the lesions.

Microscopic features

The lesions generally exhibited a cystic formation of the thin fibrous wall lined with atrophic stratified squamous epithelium resembling the epidermis, with hyper-orthokeratinization and hypergranulosis (Figure 1A and Figure 2A). In addition, cutaneous appendages such as sebaceous glands were observed in DCs (Figure 2A). The other morphological findings observed were chronic inflammation, melanin pigmentation in the basal layer of four ECs, and granulation tissue associated with a xanthomatous macrophage reaction in two other cases of ECs. Fordyce granules were represented by oral mucosa lined by stratified squamous epithelium with sebaceous glands well differentiated.

Immunohistochemical expression of cytokeratins in dermoid and epidermoid cysts

Some CKs were expressed differently in ECs (Figure 1B-1E) and DCs (Figures 2B-2H). In DCs, the expression of CKs 7, 8, 9 and 19 was observed in only one case. Positive staining for CK6 was detected in six cases of ECs. CKs 10, 13 and 14 were expressed in all cases of DC and EC. CK18 was absent in all DCs and ECs. Table 3 shows the immunostaining in the different epithelial layers of DCs and ECs.

Immunohistochemical expression of cytokeratins in Fordyce granules and adjacent lining mucosa

Only staining for CKs 10 and 14 was observed in Fordyce granules. CK10 was more expressed in peripheral cells and immature sebocytes. As these glands became more differentiated, CK10 was no longer detected, while CK14 was still expressed, including in mature sebocytes. CKs 10, 13 and 14 were expressed in the lining mucosa adjacent to Fordyce granules, similar to the normal oral mucosal lining.

DISCUSSION

Dermoid and epidermoid cysts are benign lesions that arise from the entrapment of epithelial remnants during embryogenesis[2], with a duration of months to many years as observed in the present study[5,13,14]. In general, DCs and ECs are well circumscribed and slow growing, but are often diagnosed only when they reach a considerable size. Complications in swallowing, phonation and eating resulting from these lesions have been reported, as well as displacement of organs and structures[13].

In the oral cavity, the floor of the mouth is the most affected site[15]. However, there was only one case of DC at this site in our series, while ECs more commonly involved the cheek mucosa. With respect to gender and age, in this study, DCs and ECs were more common in female patients and affected a broad age range, although other authors reported these lesions to occur in young patients and no gender predilection was found[16]. In our series, the diameter of the cysts ranged from 0.5 to 5.0 cm, with the upper limit being similar to that reported by Teszler et al.[17].

The cases of DCs and ECs described here fulfilled the histopathological criteria proposed for the diagnosis of these lesions[17]. However, four cases of EC exhibited melanin pigmentation in the basal layer, a feature also observed by Ueda et al.[18] but in a DC located in the ovary.

The present study shows that epithelial maturation is altered in DCs and ECs, especially when these cysts were compared to lining mucosa adjacent to Fordyce granules. In general, ECs were positive for CKs 6, 10, 13 and 14, while DCs expressed CKs 10, 13 and 14. Marked staining differences were observed between the epithelial layers as discussed below.

The expression of CK6, together with CKs 16 and 17, is directly related to situations of cell hyperproliferation[17,19]. In the present study, no CK6 immunostaining was observed in the lining mucosa adjacent to Fordyce granules. Expression of CK6 was also absent in cases of DCs, while most ECs exhibited positive staining for this CK in the superficial and intermediate layers, in agreement with the findings of Tomková et al. [20] who also found hyperproliferation and negative staining for CK17. Although the CK6 profile differed between DCs and ECs in this study, suggesting a hyperproliferative feature of ECs compared to DCs, further studies are needed to clarify this aspect since the presence of other cytokeratins such as CKs 16 and 17 also indicates hyperproliferation.

Furthermore, although DCs and ECs share the same clinical features, malignant alterations in DCs, including those arising in the head and neck, have been reported. In this respect, Jayasuriya et al.[21] described a

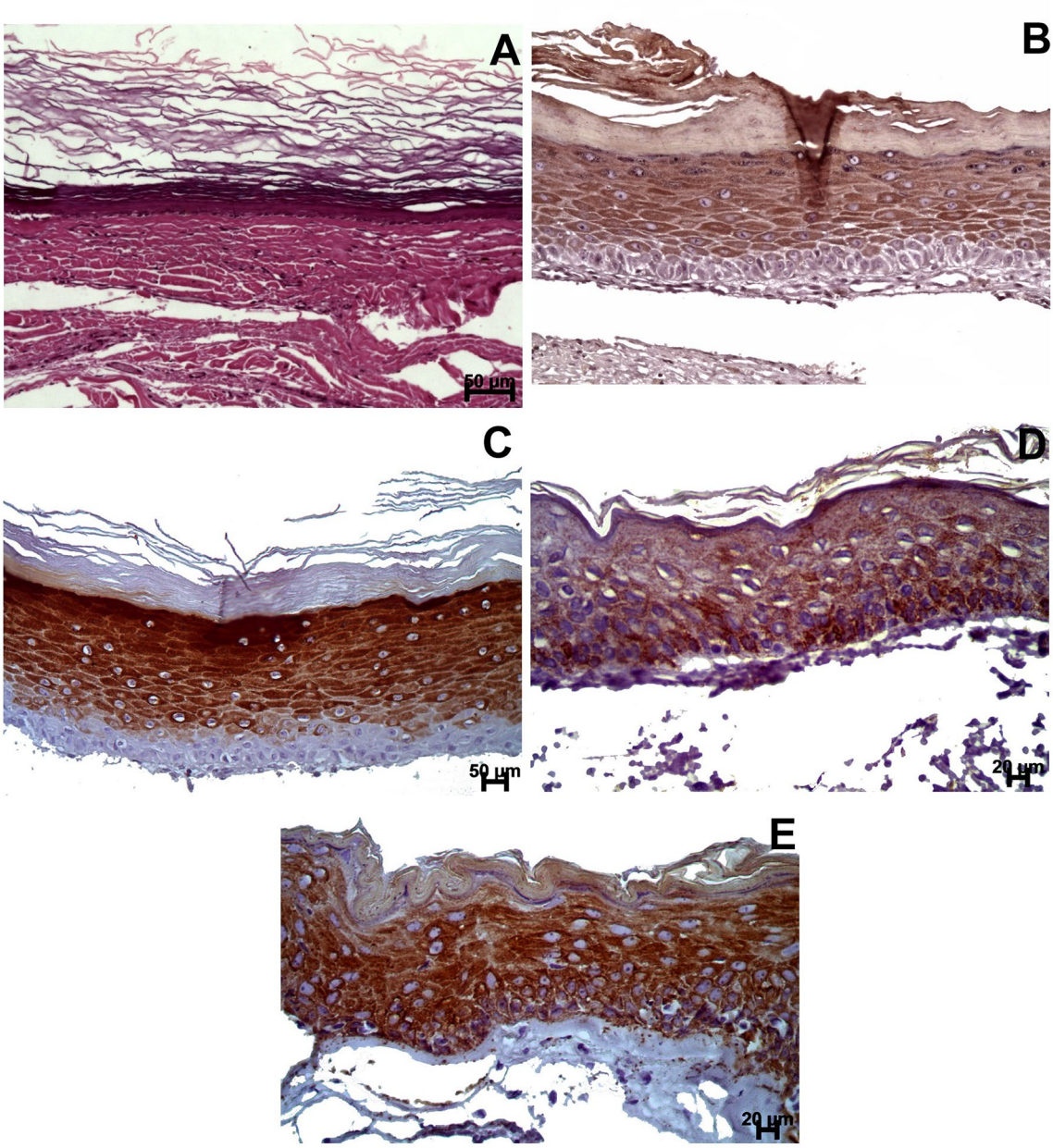

Figure 1. Epidermoid cyst: A - Intra-oral cyst represented by a fibrous wall lined by queratinized stratified squamous epithelium exhibiting hyperkeratosis. B – Suprabasal epithelial cells, intermediate and superficial layers immunopositive for CK 6. C - Suprabasal epithelial cells and intermediate layer immunopositive for CK 10. D – Basal, intermediate and superficial layers immunopositive for CK 13. E - Basal, intermediate and superficial layers immunopositive for CK 14.

case of malignant transformation in a submental DC. Thus, hyperproliferation may occur in DCs, although some authors suggest the opposite[5,6].

CK7 and CK8 were expressed in only one case each of DC, a fact that makes interpretation of this result difficult. Obviously, CKs 7 and 8 were absent in the lining mucosa adjacent to Fordyce granules. According to Valach et al.[22], these CKs are present in simple and glandular epithelia, but are absent in DCs[6]. Furthermore, no expression of CK18 or CK19 was detected. However, marked staining for the latter was observed in the intermediate layer of one case of DC in the form of focal accumulations. The absence of immunostaining for CK19 in oral DCs has also been reported by Tsuji et al.[6] Investigation of a larger number of cases may clarify this matter.

Positive staining for CK10 was observed in the present study, especially in the intermediate layers of

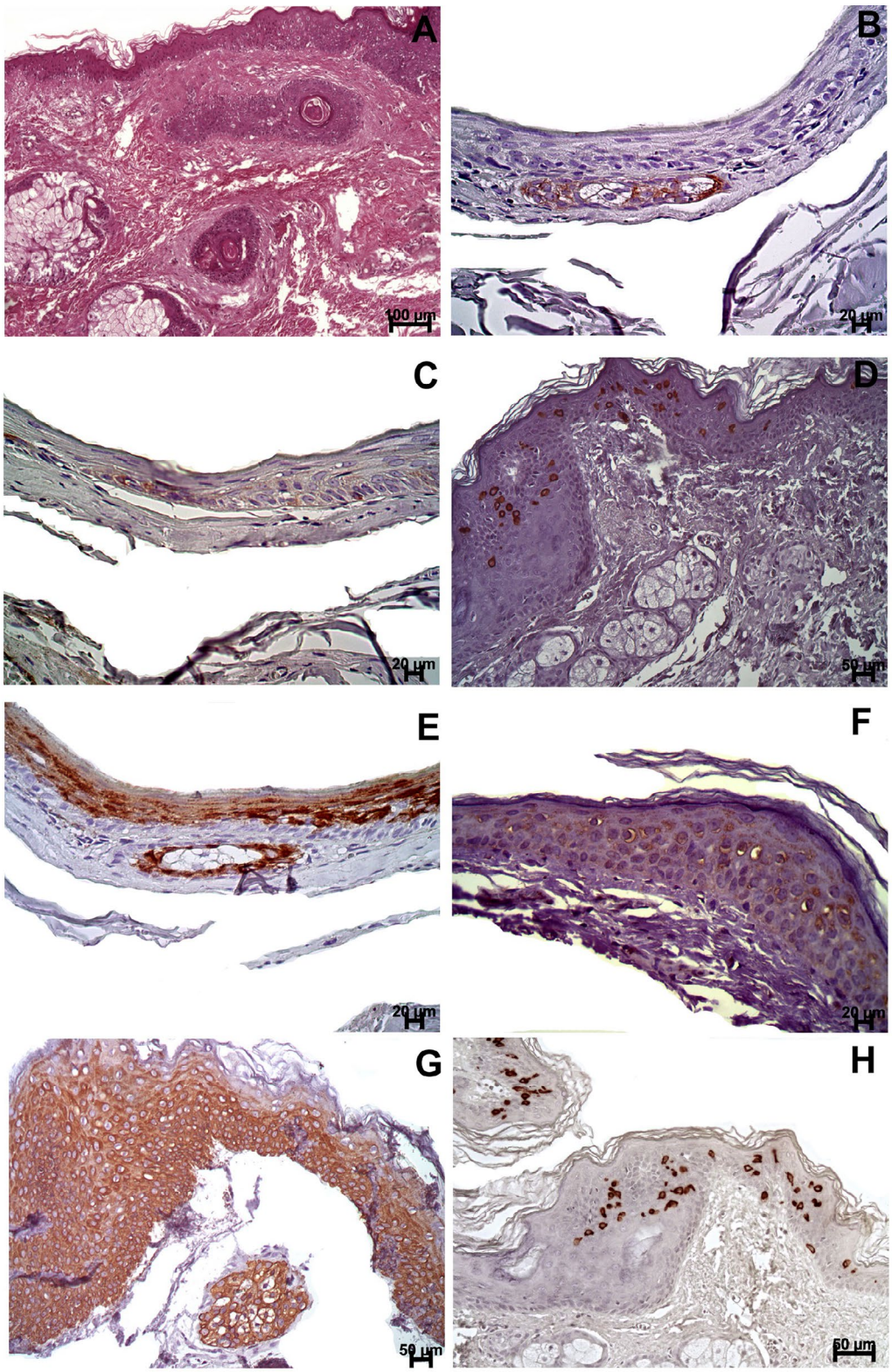

Figure 2. Dermoid cyst: A - Intra-oral cyst lined by queratinized stratified squamous epithelium exhibiting pilosebaceous units in the fibrous wall. B – Sebaceous gland immunopositive for CK 7. C – Basal layer immunopositive for CK 7. D – Clusters of keratinocytes are immunopositive for CK 8. E – Cystic epithelial lining and sebaceous gland immunopositives for CK 10. F – Basal and intermediate layers immunopositive for CK 13. G - Cystic epithelial lining and sebaceous gland immunopositives for CK 14. H - Clusters of keratinocytes are immunopositive for CK 19.

DCs and ECs, similar to the findings of Kurokawa et al.[5], Tsuji et al.[6] and Hoshino et al.[7], as well as in the epithelial lining adjacent to Fordyce granules. Although related to keratinized epithelia and terminal epithelial differentiation[23,24], CK10 staining was also detected in the basal layer of one case of DC and one case of EC. Together with the immunostaining in the intermediate and superficial layers, this finding suggests heterogeneity in the maturation process of these cysts.

CK13 is an intermediate filament protein found in non-keratinized epithelia[24]. However, in the present study, this CK was mainly detected in the intermediate layer of DCs and ECs, although in some cases immunostaining was also observed in the basal and superficial layers. Exceptionally, Hoshino et al.[7] also found immunostaining in the basal layer of one DC and in two ECs. These results show that, although altered, the maturation process is occurring since the epithelial lining of these cysts is orthokeratinized, even considering the similar immunostaining of the intermediate layer compared to the lining mucosa adjacent to Fordyce granules. In contrast, Tsuji et al.[6] found no CK13 immunostaining in oral DCs.

In the present study, CK14 was mainly detected in the basal and intermediate layers of the epithelial lining of the cysts, although in some cases immunostaining was observed in the superficial layer. Similar findings have been reported by Kurokawa et al.[5] for cutaneous DC. However, Hoshino et al.[7] demonstrated that all cases of oral and cutaneous DCs were immunostained for CK14 in the basal and intermediary layers, whereas there was no immunostaining in the superficial layers.

Although CK14 is a marker of the basal epithelium[25], the immunostaining observed in other epithelial layers demonstrates the complexity of epithelial maturation in these cysts. It should be noted that there was only one case of EC in which CK14 immunostaining was absent, suggesting that this CK is important for the attachment of ECs. On the other hand, in DCs, CK14 seems to be important for the differentiation of cutaneous appendages. Expression of this CK in epithelial layers other than the basal layer has been described for other oral cysts of different origin[12].

Immunostaining of CK10 and CK14 in the sebaceous glands of DCs was similar to that seen in Fordyce granules, demonstrating that CK14 is an important protein for cell differentiation in sebaceous glands. Kurokawa et al.[5] also found CK14 immunostaining in sebaceous glands of cutaneous DC. With respect to CK13, although immunostaining in DCs was similar to that of CK14, the absence of immunostaining in the sebaceous glands of Fordyce granules does not permit to infer that this CK contributed to the differentiation of sebaceous glands in these cysts, but reinforces the fact that the maturation process is altered and complex.

CONCLUSION

Although oral DCs and ECs are uncommon in this region in Brazil, they should be included in the differential diagnosis of swellings found in the cheek mucosa and floor of the mouth. Furthermore, the CK profile is altered in DCs and ECs when compared to the lining oral mucosa.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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