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Cytokeratin expression in palatal and marginal mucosa of cleft palate patients

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Summary

Objective: The margin of a palatal cleft is a unique anatomical site since the palatal mucosa is continuous with the nasal or nasopharyngeal mucosa. The aim of this study was to compare the expression patterns of cytokeratins and basal membrane components of the mucosa in the area of the cleft.
Design: Biopsies from the mucosa of the hard palate and from the cleft margin in the soft palate were obtained from five patients during the primary surgical closure of the cleft. The tissues were processed for haematoxylin—eosin staining and for immunohistochemistry. Antibodies against the cytokeratins (CK) 4, 7, 8, 10, 13, 16 and 18, and the basal membrane components heparan sulphate (HS) and collagen type IV (CIV) were used for immunostaining.
Results: The nasopharyngeal epithelium was thinner than the epithelium of the soft palatal mucosa, and showed less interpapillary ridges. The nasopharyngeal epithelium was stratified but expressed the keratins of a simple epithelium (CK 7, 8 and 18). The

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expression pattern abruptly changed into that of a typical non-keratinized stratified epithelium (CK 4, 13) at the transition to the soft palatal epithelium. The epithelium of the hard palate was a fully differentiated, keratinized and stratified epithelium (CK 10, 16). The basal membrane was thinner in the nasopharyngeal epithelium, which might be related to the presence of abundant inflammatory cells.
Conclusion: The area around the palatal cleft showed three different types of epithelium. There was an abrupt transition in phenotype of the epithelium from the oral side to the nasopharyngeal side.

Introduction

A cleft palate causes severe physiological problems. The complex mechanisms of normal sucking, breathing, hearing and speech are impaired because the secondary palate has not closed.[1] The embryonic development of the secondary palate is divided into three phases, which are characterized respectively by the formation of the palatal shelves from the maxillary processes, the elevation of the palatal shelves, and the fusion and subsequent degradation of the medial edge epithelium covering the paired palatal shelves.[2] The complete fusion of the palatal shelves is important for the normal function of both the oral and the nasal cavities. A deviation at any stage of the formation of the secondary palate can lead to a cleft.[3]

At the cleft margin, the anterior palatal mucosa is continuous with the nasal mucosa and the posterior mucosa with the nasopharyngeal mucosa. Normal oral mucosa can be classified into three types: (1) the oral lining mucosa, which is found on the soft palate, the ventral and lateral sides of the tongue, the floor of the mouth and the cheeks. All of these are covered by non-keratinized stratified epithelium; (2) the masticatory mucosa which occurs on the hard palate and the gingiva, and is covered by a keratinized stratified epithelium; (3) a specialized type of mucosa that covers the dorsum of the tongue and may be keratinized locally.[4,5] The nasopharynx, on the other hand, is lined by a pseudostratified ciliated columnar epithelium or a stratified epithelium in the more posterior region.[6] It has been described that, at the margin of the cleft, the mucosa of the soft palate is paler than the nasal mucosa.[1] The demarcation line is said to be clinically visible as the so-called "white line". However, only little is known about the histological and immunohistochemical characteristics of the marginal mucosa within the cleft.

Epithelial cells are characterized by intermediate filaments that consist of different combinations of cytokeratins.[4] The profile of suprabasal cytokeratin expression in a particular epithelium is indicative for its degree of differentiation.[5,7] Keratinized epithelium like that from skin is highly differentiated and expresses the larger cytokeratins 1 and 10. In contrast, the simple and glandular epithelia express the smaller cytokeratins 7, 8 and 18. The cytokeratin expression in skin epithelium, normal oral epithelia and respiratory epithelia has been well investigated.[5,7–12] The basal layers of these epithelia usually express the cytokeratins 5 and 14. In the suprabasal layers of the masticatory mucosa the cytokeratins 1 and 10 are found (like in skin) but also 6 and 16. The lining mucosa of the oral cavity is characterized by suprabasal expression of the cytokeratins 4 and 13, which is also typical for the oropharyngeal mucosa. In contrast, little is known about the specific cytokeratin expression of the epithelia in the region of the palatal cleft. An epithelium can further be characterized by the structure and composition of its basement membrane (BM). The thickness and the composition of the BM can differ from normal during wound healing and under inflammatory conditions.[13–16]

In the present study, the general histology and the expression of cytokeratins and BM components in the marginal epithelium from the cleft region were compared with that of the hard palate epithelium. To our knowledge, this is the first time that the transitional epithelium from the cleft margin of children with a cleft palate is described in detail.

Materials and methods

Patients

This study was carried out at the Radboud University Medical Centre Nijmegen in The Netherlands. For this study, five patients in the age of 1–2-years old with a non-syndromic cleft palate, with or without cleft lip and alveolus (CLA)P were selected. These patients were scheduled for primary surgical closure of the soft palate. All patients were routinely screened on contra-indications for surgical procedures (e.g. haemostasis problems). Normal mucosal samples from the hard palate were obtained using a 3 mm biopsy punch and samples from the cleft margin in the soft palate were excised during the closure of the cleft (Fig. 1). Samples of the cleft