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Symptomatic Fordyce Granules of the Bilateral Buccal Mucosa: An Unusual Clinicopathological Case Report

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Abstract

Fordyce granules are ectopic sebaceous glands of the oral mucosa that represent a common developmental anatomical variant and are typically encountered as incidental, asymptomatic findings. Symptomatic presentations are exceedingly rare and may constitute a diagnostic challenge because of their clinical resemblance to a spectrum of papular lesions affecting the oral cavity. A 32-year-old male presented with a three-month history of persistent burning sensation associated with multiple yellowish-white papules involving the bilateral buccal mucosa. Clinical examination revealed innumerable discrete, round-to-ovoid papules measuring approximately 1–2 mm in diameter, diffusely distributed over both buccal mucosae, without ulceration or other surface alterations. Routine haematological investigations were within normal limits, whereas biochemical analysis incidentally demonstrated hyperlipidaemia. Histopathological examination confirmed the diagnosis by revealing multiple ectopic sebaceous gland lobules within the connective tissue stroma, composed of mature sebocytes with abundant lipid-rich vacuolated cytoplasm and centrally placed nuclei. Conservative management comprising systemic vitamin A supplementation, topical Benzocaine, Benzydamine mouth rinse, and appropriate medical referral for hyperlipidaemia resulted in marked symptomatic improvement at the three-month follow-up.

This case broadens the recognized clinicopathological spectrum of Fordyce granules by documenting an uncommon symptomatic presentation and underscores the pivotal role of meticulous clinicopathological correlation in establishing a definitive diagnosis while excluding clinically significant mimickers. The incidental coexistence of hyperlipidaemia represents an intriguing observation that, although insufficient to establish causality, warrants further investigation to clarify its potential association with the clinical expression of ectopic sebaceous glands.

Keywords: Developmental disorder, Hyperlipidemia, Oral mucosa, Pathology, Sebaceous gland

Introduction

Fordyce's granules represent ectopic sebaceous glands or sebaceous choristoma. This condition is regarded as developmental and can be considered a variation of normal[1]. Because sebaceous glands are typically considered to be dermal adnexal structures, those found in the oral cavity often have been considered to be ectopic. However, because Fordyce granules have been reported in more than 80% of the population, their presence must be considered a normal anatomic variation[2]. It has been postulated that the occurrence of sebaceous glands in the mouth may result from inclusion in the oral cavity of ectoderm having some of the potentialities of skin in the course of development of the maxillary and mandibular processes during embryonic life[3]. Fordyce's granules are multiple and often are seen in aggregates or in confluent arrangements. Sites of predilection include the buccal mucosa and the vermilion of the upper lip. Occasionally, these glands also may appear in the retromolar area and anterior tonsillar pillar. Lesions generally are symmetrically distributed and tend to become obvious after puberty, with maximal expression occurring between twenty to thirty years of age [1]. These glands are characterized by their tiny size, lack of discomfort, elevated appearance, and yellowish or white hue. They typically measure from 1 to 3 mm in diameter [4]. These are generally asymptomatic but occasionally presented with burning sensation.

Therefore, a rare case of symptomatic Fordyce granules in bilateral buccal mucosa is documented here with histopathological corroboration.

Case History

A thirty-two years male patient visited the Oral and Maxillofacial Pathology Out Patient Department with a chief complaint of multiple, small, whitish granular lesions with burning sensation inspite of having any kind of food and beverages presented in both buccal mucosa since last almost three months. Intra-oral examination revealed multiple, discrete, minute dimensioned, yellowish white, round to ovoid, milia like papular lesions, throughout his buccal mucosa bilaterally. They are innumerable and haphazardly distributed over buccal mucosa. There are no surface changes (like ulceration, tooth indentation and vascular prominence) and overlying mucosa are slightly stretched. On palpation, the papules were firm, non-compressible, non-tender in nature. No pulsation was felt and surface temperature felt normal. The average size measured is 1mm x 1.5mm x 1.2mm (Figure-1). Lesion was associated with stomatodynia. No significant systemic comorbidity was reported. On general physical examination, the patient was well built and nourished. Body weight and body mass index were within the normal range for age, and all vital signs were stable and within normal physiological limits. He had no oral deleterious habit or any history of known drug allergy. After investigating routine hematological values, all parameters were within reference range, but his serum lipid profile yielded abnormal findings (Table-1).

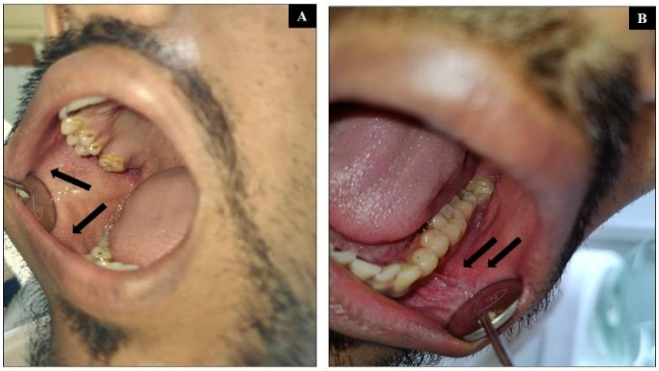

Figure 1(A&B): Intra-oral photographs of the patient, A) Right buccal mucosa showing haphazardly distributed multiple, small, whitish yellow granular lesions (Black arrow marked), B) Innumerable, discrete, minute dimensioned, yellowish white, round to ovoid, milia like papular lesions throughout left buccal mucosa (Black arrow marked)

Table 1: Distribution of routine hematological and biochemical laboratory investigations result of the patient in tabular format

Test description	Result
Haemoglobin	14.5gm/dl
Red Blood Cell count	4.96 million/cu mm
Total Leukocyte Count	4,900/cu mm
Platelet Count	2.29 lakh/cu mm
Erythrocyte Sedimentation Rare	10mm/ 1st hour
Bleeding time	2min 10sec
Clotting time	4min 45sec
Prothrombin Time	13.5 sec
Activate partial Prothrombin time	29.8 sec
International Normalized Ratio	1
Fasting Blood sugar	71mg/dL
Post Prandial Blood sugar	98mg/dL
Serum Cholesterol	224mg/dl
Triglycerides	351mg/dl
VLDL Cholesterol	69mg/dl

Based on the clinical appearance of the patient provisional diagnosis made as Fordyce granules and differential diagnoses as Papular Lichen Planus, Verruciform xanthoma of oral mucosa. Lichen planus was ruled out because there is no basal cell degeneration, juxta-epithelial chronic inflammatory cell infiltration also absence of acanthosis along with “saw-tooth” rete ridges. Verruciform xanthoma was excluded owing to the lack of lipid-laden foamy macrophages (xanthoma cells) also it predominantly occurs on lateral border of tongue and gingiva.

To corroborate clinical diagnosis, incisional biopsy from representative site of buccal mucosa was performed. Hematoxylin and Eosin (H&E) stained sections revealed

para-keratinized stratified squamous epithelium with irregular rete pegs and underlying loose fibrovascular connective tissue stroma. Epithelium demonstrated spongiosis in spinous cell layer. The striking feature was inclusion of multiple sebaceous glands with varying size could be appreciated in the stroma. The glands were composed of one to five lobules. Sparse peri-glandular infiltration of chronic inflammatory cells around the sebaceous glands and areas of extravasated RBCs was noted. Large ovoid sebaceous cells were with lipid filled vacuoles and a centrally placed nucleus (Figure-2).

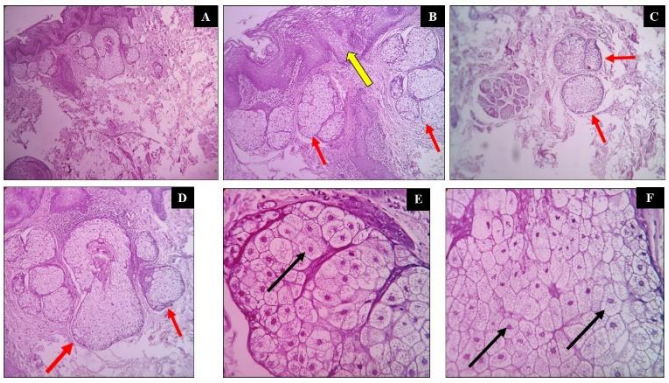

Figure-2(A-F): Hematoxylin-Eosin(H&E) stained photomicrographs of the tissue section obtained from representative site through incisional biopsy, A) Scanner view(4X) of H&E stained histopathogical section showing para-keratinized stratified squamous epithelium with irregular rete pegs and underlying sebaceous gland in the loose fibrovascular connective tissue stroma, B-D) Low magnification view(10X) of H&E stained histopathogical section showing spongiosis in spinous cell layer (Yellow arrow marked), inclusion of multiple sebaceous acinar glands composed of 1-5 lobules of varying size just beneath the epithelium (Red arrow marked), E&F) High magnification view (40X) of H&E stained histopathogical section showing Large ovoid sebaceous cells were with lipid filled vacuoles and a centrally placed nucleus (Black arrow marked)

For treatment, Vitamin-A supplement (25,000 International Unit) was prescribed twice daily with food for two months then tapered down to once daily for another one month. Ideally Oral Retinol should be prescribed, but Intra-oral Retinol or Tretinoin cream is not easily available in India, therefore, Vitamin-A was the drug of choice, as Retinol is the alcohol form Vitamin-A. Additionally, locally applicable anesthetic ointment containing Benzocaine 20% w/w and Anti-inflammatory mouth rinse containing Benzydamine 0.15% w/v was advised for three weeks to alleviate patient discomfort. Also, he was referred to medicine expert as he was incidentally diagnosed with hyperlipidemia. He was recalled after three months for follow-up and demonstrated a favourable clinical response to the treatment.

Discussion

Fordyce granules, also described as Fordyce dots, are ectopic sebaceous glands. These glands are characterized by their tiny size, lack of discomfort, elevated appearance, and yellowish or white hue. They typically measure from 1 to 3 mm in diameter and are seen inside the oral cavity [5]. Likewise, similar granules may be seen in the genital region, often manifesting as yellowish-white patches or milky spots. Fordyce granules are often seen along the vermillion border and lips, which are well recognized as prominent locations for their occurrence [6]. The granules were initially described by Kölliker in 1861, but are named after Fordyce who reported on the same problem in 1896[7]. The Chemical composition of Fordyce's spots was found to be identical to that of sebaceous glands on the skin and about 50% of sebum composition is triglycerides [8,9]. It has more female predilection, ratio 2:1[10]. Histologically these heterotopic collections of sebaceous glands are identical with those seen normally in the skin, but are un-associated with hair

follicles, although a single hair follicle and hair shaft growing from the gingiva, an extremely rare occurrence. The glands are usually superficial and may consist of only a few or a great many lobules, all grouped around one or more ducts which open on the surface of the mucosa[3]. Acinar lobules can be seen immediately beneath the epithelial surface, often communicating with the surface through a central duct. The sebaceous cells in these lobules are polygonal in shape, containing centrally located nuclei and abundant foamy cytoplasm. These ducts may show keratin plugging [2].

These glands are innocuous, have no clinical or functional significance, and require no treatment when asymptomatic. However, very rarely a benign sebaceous gland adenoma may develop from these intraoral structures, also occasional development of keratin-filled pseudocysts from the ducts of these sebaceous glands are reported [3]. For treatment, CO2 laser and oral isotretinoin are some options for treatment available but are not suitable as CO2 laser leave scar marks & isotretinoin is poisonous and therefore cannot be applied for a longer time period. Chemical cauterization 5-aminolevulinic acid Photodynamic therapy, trichloroacetic acid/ bi-chloroacetic acid are also implied in such cases. Photodynamic therapy reported vesiculation, hyperpigmentation & burning sensation after treatment [10,11].

The relationship between the elevated lipid and the increase in the density of Fordyce granules has not been reported and may not be easy to explain. The elevated lipid levels may contribute to the appearance of the Fordyce granules either by the increase in the fat content of clinical undetectable glands making them easily visible during the oral examination or de novo differentiation of cells leading to more Fordyce granules present in oral mucosa [12].

Conclusion

Although Fordyce granules are widely recognized as a benign developmental variant of the oral mucosa, symptomatic presentations remain distinctly uncommon and may pose a diagnostic challenge owing to their resemblance to a variety of papular oral lesions. The present case underscores the importance of meticulous clinicopathological correlation, with histopathological evaluation serving as the cornerstone for definitive diagnosis and exclusion of clinically significant mimickers. The coexistence of hyperlipidaemia in this patient represents an intriguing observation that, while insufficient to infer causality, may merit further investigation into the potential interplay between systemic lipid metabolism and the clinical expression of ectopic sebaceous glands. This report broadens the existing spectrum of Fordyce granules by highlighting their rare symptomatic manifestation, reinforces the value of conservative management in appropriately selected cases, and emphasizes the need for heightened clinical awareness to avoid unnecessary diagnostic and therapeutic interventions.

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