



Clinical management of oral fordyce granules: A narrative review

Dr. M Saranya¹, Dr. V Ilayaraja², Dr. T Maheswaran^{3*}, Dr. B Adhithya⁴, Dr. Manisha Kumar⁵, Dr. G Jisha⁶

¹ Associate Professor, Department of Oral Pathology and Microbiology, Vivekanandha Dental College for Women, Tamil Nadu, India

² Professor, Department of Oral Pathology and Microbiology, Vivekanandha Dental College for Women, Tamil Nadu, India

³ Professor, Department of Oral Pathology and Microbiology, Adhiparasakthi Dental College and Hospital, Tamil Nadu, India

Corresponding Author Email: Maheswaranmds@Gmail.Com

⁴ Associate Professor, Department of Oral Pathology and Microbiology, Adhiparasakthi Dental College and Hospital, Tamil Nadu, India

⁵ Assistant Professor, Department of Oral Pathology and Microbiology, Adhiparasakthi Dental College and Hospital, Tamil Nadu, India

⁶ Assistant Professor, Department of Oral Pathology and Microbiology, Nandha Dental College and Hospital, Erode, Tamil Nadu, India

Abstract

Fordyce's granules represent ectopic sebaceous glands commonly observed on oral mucosa, manifesting as asymptomatic yellowish-white papules predominantly on the buccal mucosa and vermilion border. These benign developmental variations affect approximately 70-95% of adults, with increased visibility during puberty due to hormonal influences. While typically requiring no treatment, recognition is essential for differential diagnosis and identifying potential associations with systemic conditions. This review synthesizes current evidence on clinical presentation, histopathology, diagnostic approaches, and management strategies for dental clinicians.

Keywords: Fordyce's granules, ectopic sebaceous glands, oral mucosa variation, yellow lesion, hyperlipidemia

Introduction

First described by John Addison Fordyce in 1896, these sebaceous glands without hair follicles represent a common physiological variant rather than pathological lesions ^[1]. The prevalence ranges from 57% to 95% across different populations, with male predominance and increasing visibility with age ^[2-3]. Understanding their clinical significance is crucial for appropriate patient counseling, distinguishing them from pathological conditions, and recognizing potential systemic associations ^[4-5]. This review attempts to provide a comprehensive clinical overview for dental practitioners.

Clinical Features and Epidemiology

Fordyce's granules typically present as multiple, discrete, pinhead-sized papules measuring 1-3 mm in diameter, appearing yellowish-white to creamy yellow ^[6]. The most common locations include the buccal mucosa, particularly near the commissure region, followed by the vermilion border of the upper lip, retromolar area, and labial mucosa ^[1-2]. Lesions are characteristically bilateral and symmetrical, appearing as clusters that may occasionally coalesce into larger plaques. The condition affects both genders, with studies reporting male-to-female ratios ranging from 11:5 to 2:1 ^[6]. Although sebaceous glands are present since birth, they become clinically apparent during puberty due to androgenic hormonal stimulation ^[3]. Patients are typically asymptomatic, with lesions discovered incidentally during routine oral examinations ^[6]. Prevalence studies demonstrate significant variation across populations, with one South African study reporting 62% in males and 57% in females ^[2], while Israeli population studies showed prevalence up to 95% ^[1].

Histopathological Characteristics

Microscopic examination reveals normal sebaceous gland architecture consisting of mature sebaceous lobules located in the lamina propria beneath the epithelium. The glands typically measure 1.62 ± 0.55 mm in diameter and are predominantly situated in the upper dermis, with some extending to the lower dermis. A distinguishing histological feature is the absence of associated hair follicles, differentiating them from typical cutaneous sebaceous glands. The sebaceous ducts open directly onto the mucosal surface in approximately 81% of cases, creating the characteristic central opacity visible on clinical examination ^[6]. The overlying epithelium shows parakeratotic stratified squamous epithelium with mild spongiosis in some cases ^[7]. Individual sebocytes demonstrate characteristic features including central dark nuclei and abundant foamy cytoplasm containing lipid droplets ^[1].

Diagnostic Approaches and Differential Diagnosis

Clinical diagnosis is typically straightforward based on characteristic appearance and anatomical distribution, obviating the need for biopsy in most cases ^[1]. Dermoscopy and mucoscopy have emerged as valuable non-invasive diagnostic tools, revealing whitish-to-yellowish discrete ovoid structures with central opacity surrounded by linear and branching vessels ^[8]. Ultraviolet-induced fluorescence dermatoscopy demonstrates a novel pattern of regularly distributed bright dots over yellowish-greenish clods, helping differentiate Fordyce's spots from clinical simulators ^[9]. The differential diagnosis includes several conditions presenting as yellowish oral mucosal lesions, as outlined in Table 1. Important differentials include sebaceous hyperplasia, sebaceous adenoma, lipoma,

lymphoepithelial cyst, mucosal xanthoma, and early oral squamous cell carcinoma [1]. Milia can be distinguished by their keratinous content rather than sebaceous material, while mucosal

warts typically show papillomatous architecture [8]. When diagnostic uncertainty exists, biopsy remains the gold standard, revealing normal sebaceous gland architecture without atypia or malignant features [6].

Table 1: Differential Diagnosis of Fordyce's Granules

Condition	Key Distinguishing Features	Clinical Appearance
Fordyce's Granules	Ectopic sebaceous glands, no hair follicles	Yellow-white papules, 1-3mm
Sebaceous Hyperplasia	Larger lobulated lesions	Yellowish nodules with central dell
Milia	Keratinous cysts	White, dome-shaped papules
Lipoma	Deeper soft tissue mass	Soft, mobile submucosal nodule
Mucosal Warts	HPV-induced, papillomatous	Irregular surface projections
Lymphoepithelial Cyst	Subepithelial lymphoid tissue	Yellowish nodule, movable

Associations with Systemic Conditions

Recent evidence suggests potential associations between Fordyce's granules and systemic conditions warranting clinical attention. A significant correlation exists with hereditary non-polyposis colorectal cancer syndrome, with one study demonstrating Fordyce's granules in 87% of gene carriers compared to 0.95% of controls, yielding a relative risk of 91.0 [4]. Similarly, association with Muir-Torre syndrome has been documented, with 100% of mismatch repair gene mutation carriers displaying Fordyce's granules versus 6.4% of controls [5]. However, mismatch repair protein expression studies show preservation of MLH1, MSH2, MSH6, and PMS2 in Fordyce's granules biopsies, suggesting their presence serves as a clinical marker rather than harboring the same genetic defects [10]. Metabolic associations have also been investigated, with studies indicating individuals with elevated lipid profiles tend to demonstrate higher density of Fordyce's granules. One cross-sectional study of 350 patients found 90% had detectable Fordyce's granules, with those exhibiting hyperlipidemia showing significantly higher granule scores [11]. These associations suggest potential utility as clinical markers for systemic screening, though further validation is required [4].

The primary management approach for Fordyce's granules involves patient education and reassurance regarding their benign nature [1]. Treatment is rarely medically indicated but may be pursued for aesthetic concerns, particularly when lesions are extensive or cause patient distress. Carbon dioxide (CO₂) laser ablation has emerged as the most effective treatment modality, with studies demonstrating excellent cosmetic outcomes and minimal recurrence. The pinhole ablation technique using superpulsed CO₂ laser at 2-4 watts power settings achieves complete re-epithelialization within two weeks with no residual papules or scarring [7]. Alternative treatment approaches are summarized in Table 2. Electrodesiccation and curettage provide alternative destructive options with comparable outcomes [6]. Chemical cauterization with bichloroacetic acid or trichloroacetic acid offers less expensive alternatives with reasonable efficacy. Systemic isotretinoin has shown variable results, with temporary reduction noted during treatment but recurrence common upon discontinuation [1]. Photodynamic therapy with 5-aminolevulinic acid has been attempted but is associated with significant adverse effects including pain, vesiculation, and post-inflammatory hyperpigmentation, limiting clinical utility. Surgical excision remains an option for localized lesions but carries higher risk of scarring [6].

Management and Treatment Options

Table 2: Management Options for Fordyce's Granules

Treatment Modality	Efficacy	Advantages	Disadvantages
CO ₂ Laser	High	Precise ablation, minimal scarring, rapid healing	Requires specialized equipment, cost
Electrodesiccation	Moderate	Widely available, cost-effective	Potential scarring, longer healing
Chemical Cauterization	Moderate	Inexpensive, simple application	Multiple sessions, variable outcomes
Isotretinoin	Variable	Systemic approach	Temporary effect, systemic side effects
Surgical Excision	High	Definitive removal	Scarring risk, invasive
Observation	N/A	No intervention risks, no cost	No aesthetic improvement

Conclusion

Fordyce's granules represent common benign sebaceous ectopia requiring recognition by dental clinicians for accurate diagnosis and appropriate patient management. While typically asymptomatic and requiring only reassurance, awareness of potential systemic associations necessitates appropriate screening consideration, particularly for hereditary cancer syndromes. For patients seeking treatment for cosmetic concerns, CO₂ laser ablation offers optimal outcomes with minimal complications. Future research should focus on standardizing diagnostic criteria and validating systemic screening protocols.

References

- Schafer DR, Glass SH. A Guide to Yellow Oral Mucosal Entities: Etiology and Pathology. Head and Neck Pathology,2019;13(1):33–46. doi: 10.1007/s12105-018-0977-4. Epub 2019 Jan 31. PMID: 30693453, PMCID: PMC6405798.
- Olivier JH. Fordyce granules on the prolabial and oral mucous membranes of a selected population. South African Dental Journal,2006;61(2):072–074. PMID: 16711559.
- Alamri N, Alotaiby F. Association of Fordyce Granules with Skin Types, A Cross-Sectional Study. Journal of Pharmacy and Bioallied Sciences,2024;16(Suppl 2):S1633–S1636. doi: 10.4103/jpbs.jpbs_1170_23.

- Epub 2024 Apr 16. PMID: 38882851, PMCID: PMC11174180.
4. De Felice C, Parrini S, Chitano G, Gentile M, Dipaola L, Latini G. Fordyce granules and hereditary non-polyposis colorectal cancer syndrome. *Gut*,2005;54(9):1279–1282. doi: 10.1136/gut.2005.064881. Epub 2005 May 6. PMID: 15879014, PMCID: PMC1774669.
 5. Ponti G, Meschieri A, Pollio A, Ruini C, Manfredini M, Longo C, *et al.* Fordyce granules and hyperplastic mucosal sebaceous glands as distinctive stigmata in Muir-Torre syndrome patients: characterization with reflectance confocal microscopy. *Journal of Oral Pathology and Medicine*,2015;44(7):552–557. doi: 10.1111/jop.12256. Epub 2014 Sep 12. PMID: 25213213.
 6. Lee JH, Lee JH, Kwon NH, Yu DS, Kim GM, Park CJ, *et al.* Clinicopathologic Manifestations of Patients with Fordyce's Spots. *Annals of Dermatology*,2012;24(1):103–106. doi: 10.5021/ad.2012.24.1.103. Epub 2012 Feb 2. PMID: 22363169, PMCID: PMC3283840.
 7. Bhingradia YM, Patokar AS, Moradiya N. Treatment of Fordyce Spots with CO2 Laser: A Case Series of Three Patients. *Journal of Cutaneous and Aesthetic Surgery*,2024;17(1):78–80. doi: 10.4103/JCAS.JCAS_159_22. PMID: 38736855, PMCID: PMC11086941.
 8. Jakhar D, Kaur I. Mucoscopy of Fordyce's Spots on Lips. *Indian Dermatology Online Journal*,2019;10(4):498–499. doi: 10.4103/idoj.IDOJ_185_18. PMID: 31334087, PMCID: PMC6615395.
 9. Pietkiewicz P, Navarrete-Dechent C, Goldust M, Korecka K, Todorovska V, Errichetti E, *et al.* Differentiating Fordyce Spots from Their Common Simulators Using Ultraviolet-Induced Fluorescence Dermatoscopy, Retrospective Study. *Diagnostics*,2023;13(5):985. doi: 10.3390/diagnostics13050985. PMID: 36900129, PMCID: PMC10000991.
 10. Fernandez-Flores A, Rodríguez Peralto JL. Mismatch Repair Protein Expression in Fordyce Granules. *Applied Immunohistochemistry and Molecular Morphology*,2017;25(3):209–212. doi: 10.1097/PAI.0000000000000339. PMID: 26894645.
 11. Gaballah KY, Rahimi I. Can presence of oral Fordyce's granules serve as a marker for hyperlipidemia? *Dental Research Journal*,2014;11(5):553–558. PMID: 25426145, PMCID: PMC4241607.