Review Article

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Dentistry Section

Diagnosis of Desquamative Gingivitis using Different Diagnostic Modalities: A Narrative Review

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ABSTRACT

The condition known as chronic Desquamative Gingivitis (DG) was first documented in 1894. In 1932, Prinz the term 'chronic diffuse desquamate gingivitis' to describe instances of chronic diffuse inflammation that were marked by significant shedding of the outer layer of cells in the marginal gingiva. In 1960, it was proposed that this was a non specific clinical response of the gingiva to various mucocutaneous conditions and not a diagnosis per se. To effectively diagnose mucocutaneous lesions, one must possess a thorough understanding of their genesis and clinical progression. Additionally, proficiency in various biopsy procedures using modern diagnostic technologies is essential. Accurate diagnosis is crucial in cases with DG, as the appropriate therapy and subsequent monitoring will be determined by the specific illness present. Nevertheless, the illnesses responsible for DG typically provide diagnostic challenges due to the clinical similarity of their lesions and the limited ability of conventional histological investigation to distinguish between them. Immunohistology, namely immunofluorescence, is now being used more often with standard histology to enhance the accuracy of diagnosing DG disorders. Direct immunoflourescence analysis is not only proving very useful for differential diagnosis, but also adds insight into possible pathogenic mechanisms of DG.

Keywords: Direct immunoflourescence, Indirect immunoflourescence, Mucocutaneous conditions

INTRODUCTION

Although most periodontal diseases are caused by plaque, there is a distinct and important subset of disorders that have no association with plaque. DG is a clinical sign often associated with several chronic conditions. It is characterised by red, blistering and erosive sores on the gingiva [1]. The condition known as chronic DG was first reported by Tomes J and Tomes G in 1894 [2]. However, it was not until the 1930s that Prinz H and Merrit first used the phrase "chronic diffuse DG" and made the first effort to provide a precise definition of the disease process [3]. The level and severity of gingival involvement differ. Some lesions have a predominance of erythema with little desquamation, while other lesions show extensive areas of epithelial denudation [4].

The DG may be caused by disorders that fall into two categories: immunological (autoimmune or autoimmune-like) and idiopathic. Immunological disorders that may cause DG include benign mucous membrane pemphigoid, erosive lichen planus, paraneoplastic pemphigus, lichenoid mucositis, pemphigus vulgaris and linear Immunoglobulin A (IgA) disease and bullous pemphigoid. Idiopathic lesions are likely not caused by autoimmune-mediated, but rather by persistent bacterial, fungal and viral infections, or other causes that might lead to chronic irritation and inflammation [4].

Accurate diagnosis is crucial in cases with desquamative gingivitis as the appropriate therapy and subsequent monitoring will be determined by the specific disease process involved [5,6]. It is crucial to consider that disorders producing desquamative gingivitis may vary in severity, ranging from mild symptoms to chronic debilitating conditions and in some cases, even life-threatening ones. Nevertheless, these conditions often provide diagnostic challenges due to the clinical similarity of their lesions and the limitations of conventional histological investigation in distinguishing between the many diseases producing desquamative gingivitis [7,8]. Immunohistology is now often used with standard histology to identify the specific disease responsible for desquamative gingivitis. Immunofluorescent investigations have shown the presence of several Immunoglobulins, complement components and other protein compounds in the affected tissues of desquamative gingivitis [4].

The immunoreactants are present in specific quantities and focuses within the tissue of desquamative gingivitis. The diagnostic utility of the immunoreactants' existence and placement may also indicate their potential mechanistic involvement in certain diseases.

Clinical Features: Desquamative gingivitis is defined by a distinct set of clinical features that primarily impact the gingival tissues. Patients often exhibit inflamed, red, shiny, easily damaged gums with severe blistering, peeling, erosion and ulceration. One characteristic feature of this illness is desquamation, which refers to the shedding of the outer layer of the gingiva, resulting in exposed and ulcerated regions. These sores might worsen due to physical injury, such as brushing or gnawing. Furthermore, desquamative gingivitis might be accompanied by systemic conditions such as lichen planus, mucous membrane pemphigoid, or pemphigus vulgaris. Gingival tissues may exhibit frequent bleeding and provide a sleek or lustrous appearance, oscillating between periods of deterioration and amelioration. Due to the persistent and repetitive nature of desquamative gingivitis, it is necessary to do a comprehensive clinical assessment and frequently perform a biopsy to accurately diagnose the condition and choose the most suitable treatment [9].

DISCUSSION

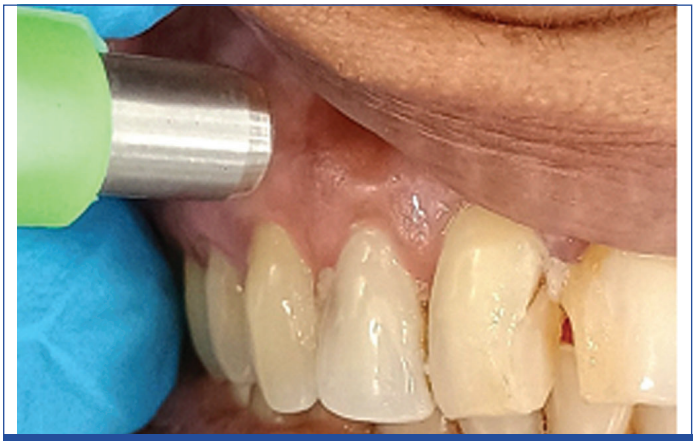
Different Types of Biopsy Procedures

Biopsies of gingival vesiculobullous lesions are taken at the periphery of the lesion to ensure that each specimen has the adhering epithelium, either in all aspects or to a large extent. Biopsies are performed at the periphery of erosive lesions to ensure that there is some intact epithelium available for optimal histology and immunofluorescent analysis. The biopsy specimens are bisected. One half of the sample is preserved in a solution of 10% buffered formalin, then embedded in paraffin, cut into sections measuring 5 µ, and finally stained with Haematoxylin and Eosin (H&E). The last

portion involves the procedure for immunofluorescence staining, where the sample is embedded in Optimal Cutting Temperature (OCT) compound and promptly frozen and preserved at a temperature of -86°C [10].

Punch biopsy: While identifying where to perform a biopsy, it is important to give priority to the spaces between the teeth and avoid the edge of the gingival margin. Avoid using topical anaesthesia, antiseptics, or iodine-based medicines that may contaminate the area. It is advisable to use infiltrative anaesthesia in the buccal fold to prevent the occurrence of bleeding caused by the leakage of injected substances into the surrounding tissues, as well as the formation of blisters and the development of vacuoles in the tissue. The incision is made by placing the handheld disposable punch at a right angle to the lesion and conducting simultaneous rotating motions with mild pressure. If there is difficulty accessing the punch in certain areas of the mouth (such as the lingual area of the mandibular symphysis, maxillary tuberosity, or retromolar pad), there are two methods. One option is to cut the handle of the punch at the desired level [Table/Fig-1,2] to allow for a better grip with the fingers. Another option is to use a 3 mm specific punch that is attached to a surgical motor with a contra-angle. This punch can be rotated at a speed of 20 rpm with gentle pressure until it reaches the bone surface. The mucoperiosteal cylinder is extracted from its osseous cavity via a periosteotome, without the need for forceps. The specimen is positioned on a filter paper with the mucosal side facing up to prevent any curling or twisting distortions and then immersed in a generous amount of fixing solution (at least ten times the volume of the tissue sample). Suturing is unnecessary and haemostasis may be readily established by applying pressure to the lesion or using a periodontal dressing [10].

[Table/Fig-1]: Handle of the punch can be cut at the desired level.



[Table/Fig-2]: A 5 mm specific punch handle.

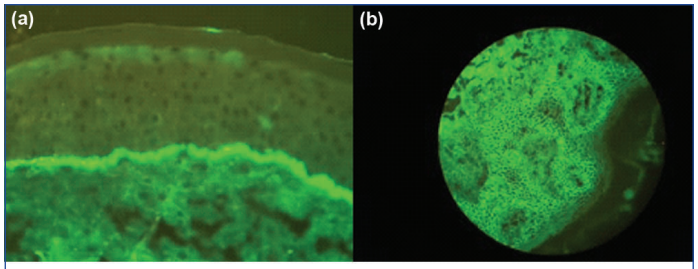
Stab-and-roll technique: The first administration of a local anaesthetic involves injecting it around the periphery of the tissue. Avoid direct infiltration into the biopsy site to prevent haemorrhage or artificial separation of the epithelium from its underlying connective tissue. This approach is specifically intended to inhibit the detachment of the epithelium from the biopsy material. This method focuses on internalising all cutting forces towards the bone. The operator carefully exerted down on the gingiva tissue with the tip of a no. 15 blade until they reached the surface of the bone. Then, the blade is smoothly slid from the tip to the complete cutting edge. This enables the cutting power to be focused exclusively in one internal direction, rather of being distributed both internally and laterally as is typical in a traditional cutting motion. If a larger specimen is needed, the technique is repeated by inserting the tip of the blade into the incision line and conducting a rolling stroke until the necessary length and angulation are achieved. The gingival sample is delicately extracted from the bone using tiny non serrated tissue forceps to prevent any tissue harm [11].

Nikolsky's test: The procedure involves the use of a syringe made of plastic that does not include a needle. This syringe is used to create a negative pressure on a specific area of the oral mucosa, which is located near an area that is experiencing desquamation or redness. Upon brief examination, the mucosa may exhibit a blister, shedding, or just redness with a small wound lining the contact with the syringe. After the negative pressure causes a blister or desquamation, an additional step is to use tweezers to remove the layer of peeled tissue, known as the "pellicle". This pellicle should then be placed on a rigid piece of paper before being transferred to a container containing formaldehyde (or Michel's transport if immunofluorescence is required) [12].

Immunofluorescence staining: As a periodontist, the importance of immunofluorescence staining in diagnosing desquamative gingivitis cannot be overstated. This advanced diagnostic tool is essential for identifying specific autoimmune disorders that manifest as gingival lesions, such as mucous membrane pemphigoid and pemphigus vulgaris. Immunofluorescence staining enables the precise detection of autoantibodies and immune complex deposits in the gingival tissue by using fluorescently labelled antibodies, which bind to specific target antigens. The resulting fluorescence under a microscope provides a detailed visual representation of the immunopathological processes occurring within the tissue. This level of diagnostic precision is crucial for differentiating desquamative gingivitis from other periodontal conditions, ensuring accurate diagnosis and enabling the development of targeted, effective treatment strategies. Consequently, immunofluorescence staining enhances patient care by facilitating early and accurate identification of the underlying autoimmune aetiology, thereby improving prognosis and guiding appropriate therapeutic interventions [5,13].

Direct Immunofluroscence (DIF): DIF entails the use of antibody-fluorophore conjugate molecules on patient tissue samples acquired from biopsies. The antibody-fluorophore conjugates specifically bind to aberrant protein deposits in the patient's tissue. When illuminated, the fluorophore produces light of a certain wavelength, which may be seen using a microscope. The specific pattern of staining and the kind of aberrant protein deposition seen in the tissue sample aid in the diagnosis of the condition [14]. The first set of slides consists of five or six slides, each designated for a distinct reagent. A single slide will be used for a standard Haematoxylin and Eosin (H&E) stain and a specialised pen is employed to delineate a boundary in order to contain the chemicals inside the slide. The slides have been cleaned and the reagents have been prepared. The antibody-fluorophore conjugates for IgG, IgM, IgA, complement protein C3 and fibrinogen (if needed) are applied onto the slides. The slides are then placed in darkness for a period of time. The slides are immersed once again in a solution and protective coverings are put on top of them [15-17]. The pathologist examines the immunofluorescence slides to identify the main locations of immune deposition, if any, the types of immunoglobulin or other immune deposits present and the patterns of deposition [Table/Fig-3]. Staining patterns can be classed into five groups [18]:

- Intercellular Surface Staining (ICS) pattern
- Linear Basement Membrane Zone (BMZ) pattern
- Granular BMZ pattern



A- Lichen Planus B- Pemphigus

[Table/Fig-3]: Immunofluorescence patterns in mucocutaneous diseases: (a) Fibrin deposits along the basement membrane of the epithelium exhibit a shaggy configuration; (b) C3 deposits confined along the basement membrane.

- Shaggy BMZ pattern
- Vascular and other patterns.

Indirect Immunofluroscence (IIF): The premise of Indirect Immunofluorescence (IIF) is based on the specific binding between antibodies and target antigens. This binding is then detected using secondary antibodies that are labelled with fluorescent markers. In this method, patient samples having specific antibodies are mixed with a substance containing the specific antigen(s) of interest and left to react. If the patient sample has antibodies that can identify these antigens, they will attach to them on the substrate. After a comprehensive washing process to eliminate any remaining components that are not bound, secondary antibodies that are labelled with fluorescent markers and are unique to the patient's antibodies are injected. The secondary antibodies adhere to the constant area of the patient's antibodies that are already bound to the antigens. This method enables the accurate and precise identification of antibodies in different clinical and research environments, assisting in the diagnosis and understanding of autoimmune disorders, infectious diseases and other medical situations [19] When seen with a fluorescence microscope, the appearance of fluorescence in regions where antibody-antigen complexes have formed reveals the existence and arrangement of particular antibodies in the patient sample [Table/Fig-4] [17,20,21].

Features	Direct Immunofluorescence (DIF)	Indirect Immunofluorescence (IIF)
Target	Single target antigen	Multiple target antigens
Primary antibodies	Fluorescently labelled primary antibodies	Unlabelled primary antibodies
Detection	Direct visualisation of target antigen	Secondary antibodies labelled with fluorophores bind to primary antibodies and facilitate detection
Sensitivity	Lower sensitivity due to direct labelling of primary antibodies	Higher sensitivity due to amplification through secondary antibodies
Specificity	Limited specificity due to direct labelling of primary antibodies	Enhanced specificity as secondary antibodies can be highly specific for primary antibodies
Background	Lower background fluorescence	Higher background fluorescence due to the presence of secondary antibodies
Time	Rapid turnaround time	Longer incubation times for primary and secondary antibody binding
Applications	Rapid screening assays	Detection of low-abundance antigens or antibodies in patient samples
Example	Direct detection of cell surface antigens in tissue sections	Detection of autoantibodies in patient sera

[Table/Fig-4]: Differences between direct and Indirect Immunofluorescence (IIF) techniques [17,20,21].

CONCLUSION(S)

Desquamative gingivitis that are usually a clinical manifestation or symptom of a variety of chronic diseases characterised by erythematous, vesiculobullous and erosive lesions of the gingiva. Correct diagnosis in desquamative gingivitis is critical since proper treatment and follow-up will depend on which disease process is involved. In periodontology, a comprehensive understanding of various biopsy techniques and immunofluorescence methods is indispensable, especially in diagnosing and managing conditions like desquamative gingivitis. These diagnostic tools serve as pillars in the foundation of periodontal care, offering vital insights into tissue pathology and immune responses within the oral cavity. By employing different biopsy methods- such as incisional, punch, or minimal invasive biopsies- periodontists can obtain essential tissue samples for thorough examination and accurate diagnosis. Moreover, direct and IIF techniques provide invaluable visualisations of immunological processes occurring in the gingiva, aiding in the identification of underlying causes and formulation of targeted treatment strategies. Through the adept utilisation of these diagnostic modalities, periodontists can deliver personalised care, ensuring optimal outcomes for patients and advancing the standards of periodontal practice.

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