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Review Article

Oral Mucosal Manifestations of Autoimmune Disorders: A Review

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Abstract: Immunity is the ability of the body to defend itself against infectious diseases. The immune system has developed to protect the host from a continually evolving universe of dangerous bacteria. In addition, the immune system aids the host in the elimination of hazardous substances or allergenic chemicals that enter the body through the mucosal membranes. Autoimmunity is characterised by disruptions in the immune system's control at multiple levels. To avoid the onset of autoimmunity, self-tolerance and discrimination between self and non- self work together. Tolerance is produced and maintained via a combination between negative selection in the thymus, the transcription factor AIRE, CD4+CD25+ regulatory T cells, and dendritic cells. Autoimmune disease occurs when the adaptive immune system pedestals an attack counter to healthy tissue. When the adaptive immune system attacks healthy tissue, autoimmune disease develops.

Keywords: Innate immunity, Adaptive immunity, OLP, Malpighian epitheliocytes, EBA, Telengactasia.

INTRODUCTION

The Latin term immunis, which means "exempt," is the root of the English word immunity, which refers to the state of being immune to infectious disease. The immune system is a highly adaptable defense system that has developed to defend animals from harmful bacteria and cancer [1]. Nonspecific and specific components of the immune system exist; that is, some constituents act without precisely recognizing the target, while others show exquisite specificity [2]. Innate and adaptive immune system components, each with a distinct purpose and role, have historically been separated from one another. The first time bacteria or other microbes enter the body through its epithelial surfaces, cells and substances that can elicit an innate immune response are triggered. According to the theory of adaptive immunity, each person creates a whoppingly different repertoire of receptors that match the antigen/pathogen on an entirely individual basis [5]. The innate and adaptive immune system plays an important role in autoimmunity [6]. Autoimmunity is characterised by disruptions in the immune system's control at multiple levels. Autoimmune disorders are defined as a situation in which the immune system of the host assaults itself by mistake [7]. Various autoimmune disorders express themselves in the oral cavity in their earliest stages, and early detection by a dental examination can be the key to improved outcomes, since it is claimed that the "mouth is the mirror that can reflect the general health of your body [8]." As a result, the goal of this review is to highlight the most recent trends and concepts in autoimmune illnesses that affect the orofacial region [9].

Classification [10]

- Lichen planus
- Recurrent Apthous Stomatitis
- Pemphigus vulgaris
- Paraneoplastic pemphigus
- Cutaneous, bullous pemphigoid
- Epidermolysisbullosa

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- Erythemamultiforme
- Discoid lupus erythematosus
- Scleroderma
- Bechets syndrome

1. Lichen Planus

Lichen planus (LP) is derived from the Greek words lichen, which means tree moss, and planus, which means flat. In 1869, Erasmus Wilson characterised LP as a chronic disease affecting the skin, scalp, nails, and mucosa, with the possibility of rare malignant change. Oral lichen planus (OLP), a chronic inflammatory disease affecting the oral mucosa with relapses and remissions, is the oral version.

The precise etiology of OLP is unknown and only few predisposing factors are contributing to the pathogenesis of lichen planus like stress, anxiety, and increased cortisol levels, genetic background, trauma, systemic medication & dental materials.

Treatment:

In general, treatment should focus on symptomatic relief and a reduction in the risk of malignant transformation. Topical drug treatment is preferable since it has fewer side effects. Corticosteroids for topical application are available in adhesive vehicles or as mouth rinses. Higher potency corticosteroids, such as clobetasol, appear to be more effective, according to the research [11].

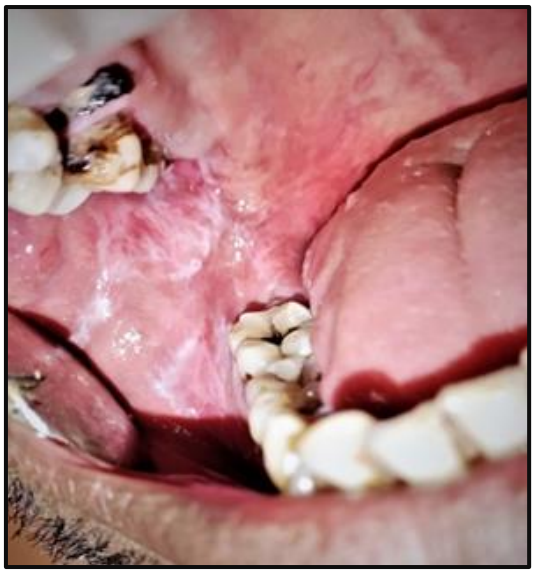

Fig 1: Reticular OLP on Right Buccal Mucosa

2. Recurrent Apthous Stomatitis:

Recurrent oral ulcers, recurrent aphthous ulcers, or simple or complicated aphthosis have all been recorded as symptoms of RECURRENT APHTHOUS STOMATITIS (RAS), often known as canker sores. RAS lesions are small, painful, shallow, round to oval ulcers surrounded by an erythematous halo and covered by a grey to tan fibromembranous slough. RAS lesions usually affect the oral cavity's non-masticatory soft mucosa, sparing the masticatory mucosa of the hard palate and the maxillary and mandibular alveolar ridges. RAS lesions are self-limited, lasting between one and two weeks, healing with or without scarring, and reoccurring after periods of remission.

Classification: Cooke classified the lesions of RAS into three groups. These are:

1) Minor aphthous ulcers,
2) Major aphthous ulcers, and
3) Herpetiform ulcers.

Causes: The exact cause of RAS lesions is unknown, however it is very likely multifactorial and influenced by a variety of predisposing factors. Sircus *et al*., found in 1957 that emotional or environmental stress predicted the onset of the first episode of RAS in 60% of patients and the onset of recurring episodes in 21% of patients [12].

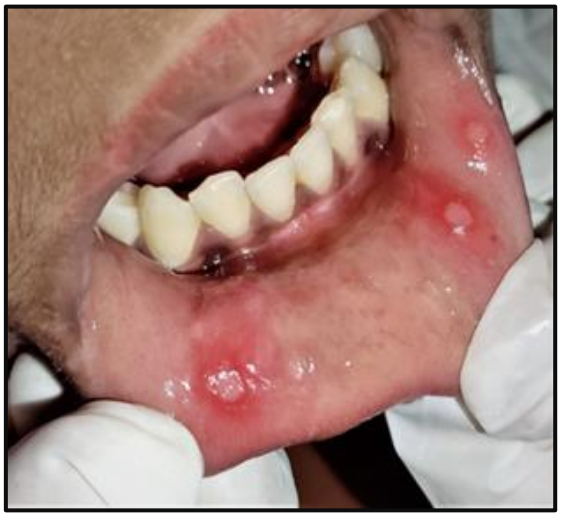

Fig 2: Apthous Ulcer on Lower Labial Mucosa

Treatment:

Recurrent aphthous stomatitis (RAS) treatment has remained empirical and non-specific to date. Topical anaesthetics and analgesics, antiseptic and anti-phlogistic preparations, topical steroids as creams, pastes, or lotions, antacids such as sucralfate, chemically stable tetracycline suspension, medicated toothpaste containing the enzymes amyloglucosidase and glucoseoxidase, and the well-known silver nitrate application are just a few examples [13].

3. Pemphigus

Pemphigus Vulgaris is an immune-mediated chronic disease. The skin and mucosa are both affected by this condition. Immune globulin G autoantibodies against desmosomal components such as desmoglein-1 and desmoglein-3 are found in pemphigus patients. The characteristics of adhesion cell molecules are altered as a result, resulting in intraepithelial blisters between Malpighian epitheliocytes. Suprabasilar keratinocyte acantolysis is the name for this condition [14].

Disease	Clinical characteristics	Histopathology	Diagnosis
Paraneoplastic	Autoimmune syndromes associated with lympho-prolifeartive neoplasm of B-cells autoantibody production of desmoplakin .1 and 2, BP antigen.	Intraepidermal acantholysis, necrotic keratinocyte, vascular interface dermatitis.	Mucocutaneous eruptions, direct immunofluorescence IgG, complement deposits, immunoprecipitation, indirect presence of circulating antibodies
Cicatrical pemphigoid	Oral and ocular mucosa can be affected. Oral lesions present with erythematous patches, blister erosion, scarring absent, BP 1 and 2, laminin, BP 180 involved	Separation of mucosal epithelium from underlying tissue at the level of lamina lucida between basal cell layer and lamina densa	Direct immunoflourescence demonstrating linear IgG, IgA or C3
Bullosa pemphigoid	Effective with elderly aged individuals with morbidity.Itchy excoriated eczematosalpapular, utricarial lesions persist for several weeks or months.	Subepidermal cleft with presence of eosinophils in the dermis and bulbous regions.	Skin biopsy, direct immunoflourescence, indirect immunofluorescence BP-180, ELISA

Oral lesions can range from microscopic vesicles or blisters to rather superficial ulcers. When a small amount of pressure is applied to the epithelium of these patients, a considerable section of the surface detaches, resulting in the production of blisters. The Nikolsky phenomenon is the name given to this event [15]. Diagnosis is on three major criteria, that is, clinical features, histology and immunological [10].

Treatment:

The mainstay of systemic treatment in pemphigus is a combination of high-dose systemic corticosteroids (1.0–1.5 mg/kg/d prednisolone) and an adjuvant steroid-sparing immunosuppressant, usually azathioprine (1.5–2.5 mg/kg/d according to thiopurine methyltransferase activity) or mycophenolate mofetil (2 g/d)/mycophenolic.

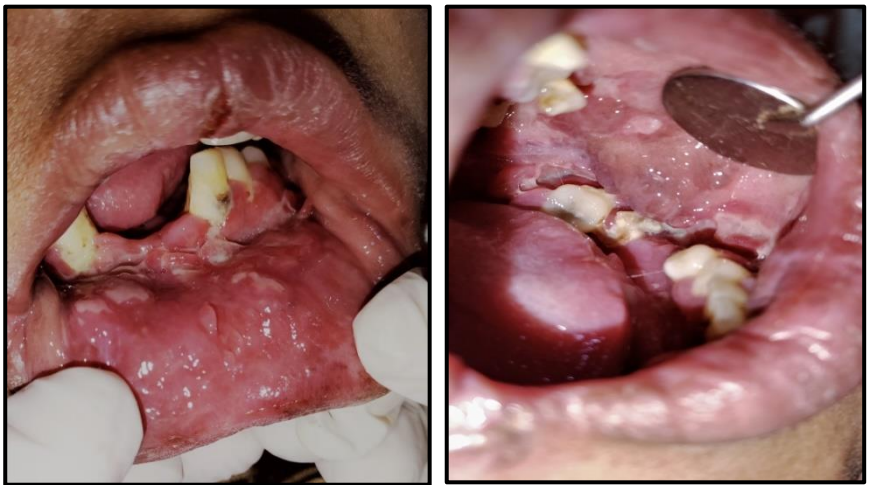

Fig 3: The image shows the affected gingiva with mixed desquamative, vesicular, and hypertrophic/hyperplastic features of Pemphigus

4. EPIDERMOLYSIS BULLOSA

Epidermolysis bullosa acquisita (EBA) is a prototypical autoimmune illness in which the auto antigen (self-protein) is recognised and extensively defined, as well as the autoantibody. EB is a chronic, subepidermal blistering illness caused by autoimmunity to the collagen (type VII collagen) within the dermal–epidermal junction's anchoring fibril structures. Roenigk *et al*., proposed the following initial diagnostic criteria for EBA:

1) No previous blistering disorder in the family or personal history
2) Adult onset of the eruption
3) Spontaneous or trauma-induced blisters that resemble those of hereditary dystrophic EB
4) Exclusion of all other bullous diseases.

Although EBA is not a Mendelian disease, it is possible that certain EBA patients have a hereditary susceptibility to autoimmunity. The non-inflammatory form of epidermolysis bullosa acquisita, also known as the classic, mechanobullous variety, affects around one-third of patients and is characterised by skin fragility and the development of tight blisters. [(16)]

Diagnosis: By using direct IF microscopy to find linear IgG autoantibody deposits at the basement membrane and indirect IF microscopy to find serum autoantibodies, a diagnosis can be made.

Treatment

All patients with EBA require supportive care. This involves wound care teaching as well as trauma prevention methods. Cyclosporine, a type of immunosuppressive drug commonly used in organ transplantation, has been proven to help with EBA. Large group of EBA patients respond to colchicine also. In some EBA patients, intravenous immunoglobulin has been shown to be effective.

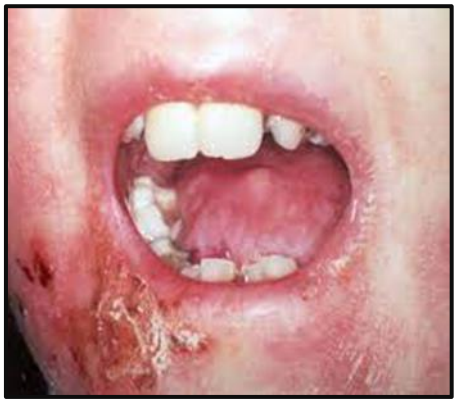

Fig 4: Crustation on Lips in Epidermolysis Bullosa

5. Erythema Multiforme

The target or iris lesions of the skin and mucous membranes are characteristic of this common, self-limiting, and recurrent mucocutaneous reaction. An immune-mediated condition called erythema multiforme causes a hypersensitivity to both infections and medicines. The aetiology is thought to include the herpes simplex virus, fungi, and medications such barbiturates, nonsteroidal anti-inflammatory medicines, pencillins, etc. The Steven Johnson syndrome variant starts out mildly self-limiting with minimal oral involvement and progresses to a fulminating state. In erythema multiforme patients, oral lesions are observed as vesicles or bullae that rupture and produce a white or yellow discharge. Lip ulcerations that are painful, bleeding, crusty, and oozing are seen [17].

Fig 5: Erythema Multiforme

6. Discoid Lupus Erythematosus

It is a collagen vascular lesion. Scarring results from the chronic dermatological condition. Vermilion margins, buccal mucosa, and labial mucosa all exhibit oral lesions. Clinical manifestations include a border-forming radiating white striae, a centre white papular erythema, and peripheral telengactasia [18].

Treatment

Steroid ointments, such as fluocinolone acetonide or hydrocortisone butyrate, lower inflammation and decrease swelling. Anti-inflammatory drugs such as dapsone or low-dose methotrexate reduce pain and swelling. Treatment with antimalarial drugs constitutes first-line systemic therapy for DLE.

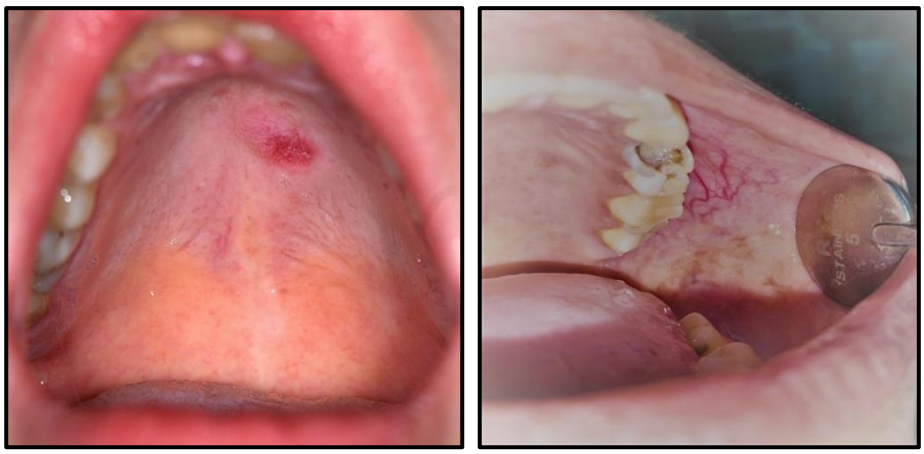

Fig 6: Discoid Lupus Erythematosus with Peripheral Telengactasia

Scleroderma:

It is a multisystem disease affecting the connective tissue, blood vessels, and immune system. Clinical signs and symptoms, a barium swallow, and an endoscopy can all be used to make the diagnosis. There is no consensus on the treatment protocol. Although

being controversial, penicillamine has been used to inhibit collagen deposition. Dysphagia and gastroesophageal reflux are frequently reported complaints in this group of patients. Trismus, widening of the periodontal space, decrease in facial wrinkles owing to fibrosis of skin, orofacial telengiectasia, resorption of mandibular angle are some of the changes which may occur in the oral and maxillofacial region [17].

Treatment:

Immunosuppressing drugs include methotrexate, cyclosporine, antithymocyte globulin, mycophenolate mofetil and cyclophosphamide. Vasospasm is best treated with vasodilator therapy, the most effective continues to be the calcium channel blockers (e.g., nifedipine). Several drugs are used that have in vitro (in the tissue culture) ability to reduce collagen production include colchicine, para-aminobenzoic acid (PABA), dimethyl sulfoxide, and D-penicillamine. Treatment with antimalarial drugs should start with hydroxychloroquine at a dose of 200 mg per day for an adult.

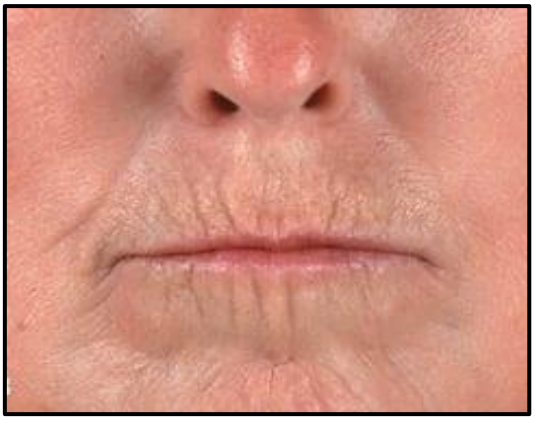

Fig 7: Scleroderma

Behcet's Disease: Behcet's disease, commonly known as Silk

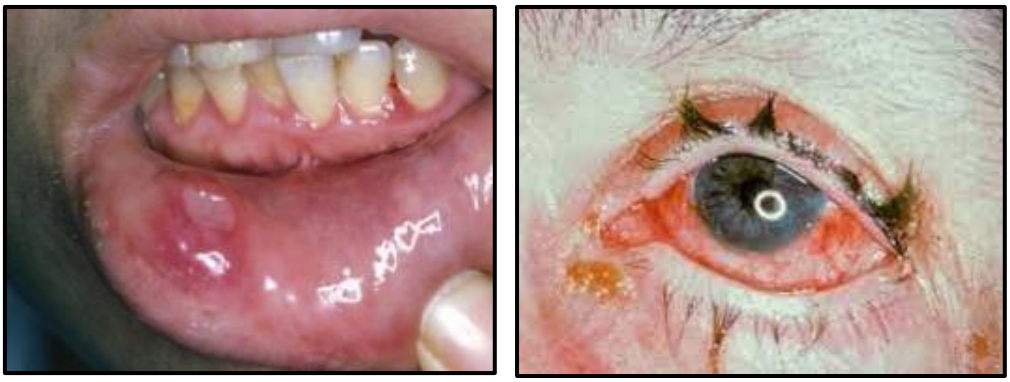

Fig 8: Oral Ulcers in Behcet's Disease Ocular Involvement showing Posterior Uveitis

Road Disease, is a rare etiologically unknown systemic vasculitis ailment. Recurrent attacks of oral aphthous ulcers, vaginal sores, and ocular lesions characterise Behcet's Disease (BD), a rare systemic vasculitis disorder with an unclear cause (triple-symptom complex). The existence of antimucous autoantibodies, as well as the disease's relationship with the HLA configurations B5 and B51, demonstrate an autoimmune aetiology [7]. The mucocutaneous lesions are frequently the first indication that Behcet syndrome is present. The oral lesions are oral mucosal ulcers that look just like regular oral mucosal aphthae. They are restricted to the tongue, soft palate, lips, and buccal mucosa [19]. The genital ulcers are smaller and can be found on the labia majora, near the base of the penis, or at the level of the scrotum. The eye lesions initially manifest as photophobia, then develop uveitis and conjunctivitis [20].

Treatment:

The use of local and systemic cortisones alone or in combination with immunosuppressant medications is the basis for the treatment of Behcet syndrome. The fundamental goal of Behcet syndrome patient care is to treat oral mucocutaneous lesions as soon as possible in order to halt the disease's progression and to avoid irreparable organ involvement, especially during the active period.

CONCLUSION

Many concerns about the specific genesis of the bulk of autoimmune diseases remain unanswered. The identity and mechanism of action of genes that predispose or accelerate autoimmunity, the regulatory mechanisms that govern the onset and extent of the autoimmune response, the mechanisms by which spontaneous remissions and flare-ups occur, the role of environmental factors and how they initiate and perpetuate autoimmune responses, and the identity and mechanism of action of genes that predispose or accelerate autoimmunity, all remain a mystery to scientists in the field. Future research efforts will be focused on these essential topics.

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