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Original Research Paper

Oral Medicine

SYNDROMES ASSOCIATED WITH ORAL ULCERATIONS: A SHORT REVIEW AND AN UPDATE

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ABSTRACT

Oral Ulcerations are common and are routinely encountered by dentists in their practice. A thorough knowledge about the features of oral ulcerations and the systemic conditions associated with them is very crucial for treatment of the condition. This review aims to provide an update about various syndromes associated with oral ulcerations.

KEYWORDS :

INTRODUCTION

Ulcers in oral mucosa often presents as a breach of the epithelium in turn exposing the lamina propria.[1] A common oral condition associated with formation of multiple recurrent painful oval or round ulcers, with a clean edge, erythematous halo, white – yellow fibrinous exudate without any underlying diseases is termed as Recurrent Aphthous Stomatitis (RAS) or canker sore.[2,3,4,5] RAS is the commonest oral ulcer affecting oral mucosa, commonly during 2nd to 3rd decade, which is diagnosed on the basis of history and clinical examoination.[2,3] Oral ulcers including RAS may also be associated with some syndromes which should be always considered during differential diagnosis.[2] A short review of such conditions has been described below.

1. Behcet's Syndrome

Behcet's Syndrome was first described in 1937 by Turkish dermatologist Huluci Behcet, as a triad of genital ulcers, oral ulcers and iridocyclitis.[2,6] This condition is a chronic inflammatory disorder without any confirmed aetiology and has a higher incidence in the area near Mediterranean Sea, far east and middle east, in adults under the age group 30 – 40 years.[2,6,7] Apart from the above-mentioned triad, this condition may also present with ocular lesions, skin lesions, positive pathergy test, thrombophlebitis, Gastro-Intestinal lesions and central nervous system disease.[2,8] Currently Behcet's Syndrome has been considered under major histo-compatibility complex pathologies.[6] This condition may be characterised by various periods of exacerbations and remissions which also can lead to stroke and loss of vision.[6] Management for the condition depends on severity which includes corticosteroids, pentoxifylline, cyclosporine, azathioprine and colchicine.[2,6]

2. MAGIC Syndrome

First described by Firestein et al in 1985, as an overlap of Behcet's disease and relapsing polychondritis, led to the discovery of mouth and genital Ulcers with inflamed cartilage (MAGIC) syndrome.[9,10] Along with the typical features patients may also present with uveitis, keratitis, conjunctivitis, iritis, scleritis, erythema nodosum, urticaria, pseudo-folliculitis, cutaneous vasculitis, acne vulgaris, skin ulcers, pustules, positive pathergy test, arthralgia, arthritis and aortic aneurysm.[10] Treatment consists of managing symptoms and immunosuppression.[9] Drugs such as corticosteroids, colchicine, azathioprine and methotrexate are considered for management.[9]

3. PFAPA Syndrome

A periodic disease involving children, particularly in non-Mediterranean countries with unknown aetiology, characterised by Periodic Fever, Aphthous Stomatitis, Pharyngitis and cervical Adenitis (PFAPA) Syndrome or Marshall Syndrome was first described in 1987 by Marshall.[2,11,12] The syndrome is characterised by episodes of recurrent fever which lasts for 3-7 days, every 2 – 8 weeks.[11,12,13,14] In addition to the main symptoms, headache, myalgia and abdominal pain has also been reported.[11] 60% of patients has also been reported to experience fatigue before the onset of fever.[11] The main aim of treatment is to reduce inflammation by controlling fever and reducing the severity and frequency of attacks, which in turn improve the life quality of the child.[11] Options for symptomatic management includes Corticosteroids, non-steroidal anti-inflammatory drugs (NSAID's), Colchicine, Probiotics, Histamine Receptor antagonists, Tonsillectomy and Cimetidine.[11,12,13]

4. SWEET Syndrome

Sweet syndrome (Gomm Button disease) was first described by Robert Douglas Sweet in 1964, as an acute febrile neutrophilic dermatosis.[2,15,16,17] Sweet Syndrome shows clinical polymorphism with symptoms including fever, neutrophilia, painful cutaneous erythematous lesions (including papules, nodules and plaques) and poly morphonuclear neutrophilic infiltrate.[2,15] Three different clinical variants of sweet's syndrome reported includes Classical(Idiopathic), Malignancy associated and Drug Induced.[16,17] Even though exact aetiology of this syndrome in unknown, an unusual hypersensitivity reaction due to viral, bacterial or neoplasm antigens has been proposed.[2,17] Oral manifestations of this disease includes RAS, Bullae and vesicles, gingival hyperplasia, necrotising ulcerative periodontitis, papules, nodules and pustules.[2,16] Management includes both topical and systemic corticosteroids, Potassium Iodide, Colchicine, Indomethacin, Cyclosporin and Dapsone.[2,16]

5. VEXAS Syndrome

VEXAS (Vacuoles, E1 enzyme, X-linked, Auto-inflammatory, Somatic) Syndrome is a systemic auto-inflammatory adult-onset disease characterised by systemic inflammation, cutaneous lesions, hematologic abnormalities and acquired pathologic genetic alterations.[18,19,20] A systematic review by Al Hakkimi;2025 reported a cluster of manifestations including cutaneous, musculoskeletal, vascular and thrombotic, neurologic, ophthalmic, cardiac, genitourinary and renal, oropharyngeal and audio vestibular, chondritis and lymphoid system.[18] RAS also has been reported in many cases of VEXAS Syndrome during the course or at the onset pf the disease.[21] No definite treatment protocol exist for this newly established disease.[19] The disease is also associated with high mortality rates and resistance to many therapeutic agents.[19]

6. Cyclic Neutropenia

Cyclic Neutropenia is a rare congenital autosomal dominant disease, characterised by periodic failure of bone marrow stem cells causing decrease in the total amount of circulating neutrophils, which occurs every 21 days, and each episode lasting for 3 – 6 days.[2,22] The severity and the recurrence pattern of Major RAS and Cyclic neutropenia are similar, in which the ulcers will be deep and self-limiting measuring more than 10 mm in diameter.[22] Other clinical features include malaise, fever, Periodontitis, infections of the mucous membrane and lumphadenopathy.[2] Antibiotics, Antipyretics, Glucocorticoids

and Lithium are used for the management of the condition.[2] For severe patients, hematopoietic stem cel transplantation may also be considered.[2]

7. Steven Johnson Syndrome

First described by Hebra in 1866, Stevens-Johnson syndrome (SJS) is an acute life-threatening mucocutaneous disease resulting in destruction of skin epithelium which occur due to an aggressive immune response.[23,24,25] SJS belongs to a spectrum of Erythema Multiforme (EM) complex involving, oral, ocular and genital mucosa.[23,25] If the disease involves <10% of skin, it is called SJS and if it involves >30%, its is called Toxic Epidermal Necrolysis (TEN).If the extent of skin involvement is between 10 – 30%, it is called TEN – SJS Overlapping disease.[23,25] SJS may be precipitated by numerous factors namely drugs, vaccinations, viral infections, food, or physical agents.[24] Iqbal;2016, has reported a case of SJS which presented with oral ulcers resembling candidiasis.[25] Management of SJS involves antibiotics, analgesics, intravenous fluids and proper nutritional support.[25]

8. Lesch Nyhan Syndrome (LNS)

In 1964, doctors named Micheal Lesch and Bill Nyhan reported this condition in 2 brothers with neurological and motor disorder, self-mutilation and hyperuricemia.[26] The syndrome occurs due to defect in the enzyme Hypoxanthine-Guanine Phosphoribosyl Transferase (HGPRT) and occurs mostly in males.[26,27] As a result of this compulsive self-injurious behaviour, patient's bite on their own lips, tongue and fingers, which leads to tissue loss and amputations.[26] In a systematic review, ulceration of tongue and surrounding tissue in patients with LNS was reported in 20%.[28]

9. Basex Syndrome (Acrokeratosis Paraneoplastica)

Initially proposed by Basex et al, Basex Syndrome is a condition associated with dermatological disorders with an underlying malignancy.[29] With aetiology still unclear, this condition is usually reported in males more than 40 years of age.[29] In 2010, Santos-Silva AR et al reported a patient diagnosed with Basex syndrome presenting with oral ulcerations and suggested the importance of identifying persistent and specific oral ulcerations and its association with any paraneoplastic condition.[29]

10. Acquired Immuno-Deficiency Syndrome (AIDS)

RAS is a common manifestation of AIDS, but will be less responsive and long lasting than those in non-infected counterparts.[2] In patients with advanced disease, major aphthae can also be detected.[2]

CONCLUSION

Ulcers including RAS are a common presentation in the oral mucosa. Correctly understanding the features of the ulcers along with identifying any systemic diseases is important for differential diagnosis. Dentists should be well aware of the various syndromes which are associated with various oral ulcerations for an early intervention and also for referral to an appropriate specialist.

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