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Crohn's Disease And Its Oral Manifestations

Dr.L.Malathi, MDS[1], Dr T. Alamelu Mangai[2*], Dr.N.Anitha, MDS[1], Dr. E.Rajesh, MDS[1]

[1]*Reader, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Pallikaranai, Chennai.*

[2]*Post Graduate Student, Department of Oral Pathology and Microbiology, Sree Balaji Dental College And Hospital, Bharath Institute of Higher Education and Research, Pallikaranai, Chennai.*

[3]*Professor and Head, Department of Oral Pathology and Microbiology, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education and Research, Pallikaranai, Chennai.*

Abstract: Crohn's disease (CD) is a granulomatous inflammatory bowel disorder that was first reported in 1932 as a chronic granulomatous disease of the terminal ileum. It is currently recognized as a separate inflammatory bowel disease. It can affect any area of the gastrointestinal tract. Many patients, especially children appear with non-intestinal symptoms first, including mouth lesions. In children, oral symptoms of crohn's disease occur in roughly 50-80% of cases, and about 30% of CD cases in children begin in the mouth. The disease is marked by flares and remissions, which are driven by a complicated pathophysiology in which inflammation plays a crucial role. Crohn's disease could be caused by a complex interaction of genetic predisposition, environmental variables, and altered gut microbiota, resulting in dysregulated innate and adaptive immune responses. Oral Crohn's disease with or without intestinal signs, has been documented regularly in the previous three decades. It is recognized as one of the orofacial granulomatosis in the latter condition. There has been great debate about whether Crohn's disease intestinal signs may eventually appear in orofacial granulomatosis. Recognizing such oral lesions in children and seeking a biopsy may help to accelerate the diagnosis of CD.

Keywords: Crohn's Disease, Chronic granulomatous disease, orofacial granulomatosis, inflammatory bowel disease.

INTRODUCTION

Inflammatory bowel disease which include ulcerative colitis (UC) and Crohn's disease (CD) are characterized by persistent inflammation of the gastrointestinal tract in genetically prone people who are exposed to environmental risk factors[1]. Crohn's disease is a relapsing/remitting systemic inflammatory disease that mostly affects the intestines. Patients with Crohn's disease often have abdominal pain, fever, and bowel disturbances. Dalziel first defined the illness in 1913 as "transmural inflammation of both or either of the small and large intestines," and it was later reported as "regional or terminal ileitis" affecting mostly the ileum. Crohn's disease is the name given to this latter disorder, which can affect any region of the alimentary canal. The entire intestine is impacted by Crohn's disease inflammation, with the distal ileum being the most commonly affected region. During the course of their condition, patients with Crohn's disease go through flares and remissions. Current therapeutic options aim for profound and long-term remission in order to avoid complications and slow the progression of the disease[2].

PATHOGENESIS

The pathophysiology of Crohn's disease is based on tissue inflammation generated by an uncontrollable immunological response to luminal bacterial antigens. Immune cells such as CD4 T-Cells, CD8 T-Cells, B-Cells, CD14 monocytes, and natural killer cells invade the gut of crohn's disease patients and play a role in this process. Some intrinsic mechanisms of defense against infectious illnesses, including intestinal mucus secretion, have a role in immune-mediated susceptibility to Crohn's disease[3, 11]. Pathogenesis is caused by interactions between environmental stimuli, immune system, susceptibility genes, and changes in the micro biome of the host, resulting in intestinal mucosa disturbance [3]. Crohn's disease is characterized by excessive IL-12/IL-23 and IFN-/IL-17 production in the small intestine and colon, as well as discontinuous ulceration and full-thickness intestinal wall inflammation with granulomas[2, 4]. Gene mutations have been related to Crohn's disease with CARD15/NOD2 having the strongest connection. THE CARD15/Crohn's disease starts in the sub mucosa of the intestine and spreads over the intestinal wall, affecting the mucosa and serosa [2, 4]. Type 1 T helper -cells initiate a harmful inflammatory response and activate leucocytes, resulting in further damage. Leucocytes release prostaglandins, proteases, reactive oxygen species, leucotrienes, and nitric oxide, which perpetuate the inflammatory response and consequent damage. After neutrophils infiltrate and destroy the intestinal crypts, aphthoid lesions (shallow ulcers) develop[6]. Skip lesions are created when inflammation and lesions are interspersed with healthy mucosal tissue. The tissue on one side of the intestinal wall may be injured, whereas the tissue on the other side may be intact. Longitudinal and transverse fissures and crevices frequently extend into lymphoid tissue and are surrounded by edema in the sub mucosa, resulting in granuloma and a cobblestone appearance of the infected bowel (smith & haris 2014). Inflammation, edema, and fibrotic strictures can cause the intestinal lumen to constrict [3]. NOD2 genes code for a protein that aids in the identification of gram negative and gram positive bacteria. Crohn's disease could be the result of an overactive reaction to normal flora in the gut of individuals with a genetic predisposition[2,10].

CLINICAL MANIFESTATIONS

Patients report abdominal discomfort, diarrhea (greater than 5 stools per day), and rectal bleeding as well as weight loss, and exhaustion as gastrointestinal and systemic symptoms. These deficiencies may lead to anemia, hypoalbuminemia, and bone disease from low folic acid, vitamin –B12, vitamin-D and calcium levels. Patient may also experience extra intestinal manifestations including fever, gall stones, mouth ulcers ,erythema nodosum,primary sclerosing cholangitis of the liver,uveitis of the eye and migratory polyarthritis.30% of individuals experience fissures ,fistulas and /or perianal abscess(screenshot).there is an increased risk of intestinal adenocarcinoma for patients with a long duration of Crohn's disease[10]. Current therapeutic options aim for profound and long-term remission in order to avoid complications and slow the progression of the disease[2].

ORAL MANIFESTATIONS

The number of young individuals with oral signs of inflammatory bowel disease may be expanding as the frequency of the disease rises Any region of the oral cavity, including the buccal mucosa, lips, tongue, hard and soft palate, salivary glands, gingiva, and teeth, can be affected by oral crohn's disease. Alterations can be pathognomonic (occurring almost usually in association with inflammatory bowel disease), highly suspicious (occurring almost always in association with inflammatory bowel disease), or nonspecific Orofacial granulomatous cheilitis, and pyostomatitis vegetans are examples of pathognomonic oral changes. Up to 5-15 % of CD patients develop orofacial CD, which includes recurring or persistent lip swelling, cobblestone apperance of the oral mucosa, stomatitis, mucogingivitis, deep linear or serpiginous ulcerations surrounded by epithelial hyperplasia, tissue tags, or polyps, and is often linked to Candida-associated angular cheilitis[8]. This modification resembles the features present in the gastrointestinal tract macroscopically and histologically and can be related with pain on touching or while eating acidic or spicy meals, impairment of oral function, eating, speaking, and psychosocial stress[6,8]. Orofacial Crohn's disease on the other hand is indistinguishable from orofacial granulomatosis, a clinical condition seen in a variety of disorders such as sarcoidosis, Miescher's cheilitis granulomatosa, Melkersson-Rosenthal syndrome, foreign body granuloma, and many granulomatous infectious diseases[2,8].Crohn's disease can develop in up to 40-50 percent of young children with orofacial granulomatosis, and it can appear years after the first oral symptoms. Granulomatous cheilitis is a rare, subacute granulomatous disease that affects only the lips. A history of abrupt swelling of the lips, primarily the lower lip, that subsides within hours or days, followed by permanent edema and lumpy swelling is commonly observed. However, allergies, sarcoidosis, Melkersson-Rosenthal syndrome, relapsing herpes simplex, relapsing erysipelas, malignancies, and genetic illnesses can all manifest as granulomatous cheilitis[7, 8] Finally, pyostomatitis vegetans is an uncommon manifestation that has been related to inflammatory bowel illness. It's characterized by a swollen and erythematous oral mucosa with pustules and superficial erosions that seem like "snail tracks." In 75 % of patients, it's associated to inflammatory bowel disease[8.]

HISTOPATHOLOGY

The lesion was covered with stratified squamous parakeratinized epithelium.On histopathologic examination, which ranged from atrophic to hyper plastic areas. There were also areas of spongiosis and ulceration. The connective tissue was moderately fibro cellular and edematous, Chronic inflammatory cells primarily lymphocytes and macrophages, Hemorrhagic areas, blood vessels, and multiple non-caseating granulomas were found in a single location. They were also seen subepithelially. Each non-caseating granuloma was textured loosely and a focal mass of epithelioid cells surrounded by chronic inflammatory cells, as well as the occurrence of a foreign body type or langhans type of giant cells[2, 7.]

DIAGNOSTIC INVESTIGATIONS

Thrombocytosis elevated acute phase proteins (especially C-reactive protein), and anemia are common laboratory findings. C-reactive protein is a biomarker used to assess disease progression, but it has a weak correlation with endoscopic findings. Hypoalbuminemia and vitamin deficits are common in those with severe small intestinal illness. Antimicrobial antibodies are found in 60–70% of patients' serum, with anti-Saccharomyces cerevisiae antibody IgA being the most common[2, 10]. These antibodies sensitivity and specificity are insufficient for diagnostic purposes. Patients with high titers and high rates of positive markers, on the other hand, are more likely to develop aggressive phenotypes. Stool biomarkers, such as faecal calprotectin, are increasingly being used in inflammatory bowel disease as screening tests and to monitor disease activity. Calprotectin concentrations in the faeces correlate with neutrophil infiltrates in the gut and are a sensitive and specific surrogate biomarker of intestinal inflammation for the diagnosis of IBD. In patients with symptoms suggestive of irritable bowel syndrome, a faecal calprotectin content of less than 40 µg/g has been linked to a 1% likelihood of developing IBD. As a result, this marker could be helpful in primary care to screen individuals for colonoscopy[2,7]. Fecal calprotectin correlates strongly with endoscopic activity in individuals with established crohn's disease and is a helpful biomarker for monitoring disease activity, assessing response to medication, predicting clinical relapse, and surgical recurrence. The cutoff threshold for differentiating mucosal inflammation depends on the test and might range from 50 to 250µg/g [2]. A fecal calprotectin content of more than 100 µg/g has high sensitivity for predicting endoscopic recurrence in the postoperative condition. The gold standard diagnosis is endoscopy.Typical findings include segmental inflammation, apthoid, and longitudinal and serpiginous ulcerations. Finally, colonoscopy is useful for monitoring colorectal neoplasia and treating problems such as strictures. Ultrasonography, CT-enterography, and MR-enterography are examples of cross-sectional imaging studies that have become increasingly important in the management of Crohn's disease. At the time of diagnosis a CT or MR-enterography should be performed to determine the degree of the disease and the existence of complications such as strictures or fistulas, as well as to provide information regarding disease behavior. For proper assessment and delineation of fistulous pathways, pelvic MRI should be used to evaluate perianal fistulas or abscesses or both[1,2].

TREATMENT

Crohn's disease is treated using an induction and maintenance regimen. Corticosteroids, nutritional therapy, immunosuppressants (thiopurines [azathioprine and mercaptopurine] and methotrexate), biologicals (anti-TNF [infliximab, adalimumab, and certolizumab pegol], and anti-adhesion molecules) are the most often used medications in Crohn's disease (vedolizumab). 5-aminosalicylates are ineffective in preventing crohn's disease recurrence after surgery and have a low efficacy in the preoperative environment. Antibiotics should be restricted to Crohn's disease patients who have fistulas or abscesses, or both[2]. Assessing for and controlling intestinal disease is the first step in treating oral diseases. It's also crucial to construct a comprehensive differential diagnosis for oral manifestations, which includes pharmacological side effects, nutritional deficits, infections, and other granulomatous disorders with oral signs. If the oral findings are asymptomatic, no therapy is required, and the lesions will disappear over time in combination with the treatment of gastrointestinal disease. A combination of clinical, biochemical, radiographic, and endoscopic findings is used to make the diagnosis of CD[6, 8]. Symptomatic relief is provided by beclamethasone mouthwashes (0.5 mg diluted in water, up to 6 times a day). However, there is a significant risk of systemic steroid absorption and associated side effects, which makes this kind of treatment unsuitable for long-term use. Topical tocrolimus can aid with lip edema in rare cases. It has been reported that a steroid was injected intralesionally into swollen lips. This type of treatment, on the other hand, appears to provide just a short-term advantage and can be uncomfortable. Immunosuppressant can be considered early in the treatment of individuals suffering persistent discomfort, edema, and cosmetic deformity[6, 7].

CONCLUSION

Interactions of genetic, immunologic, microbiological, and environmental variables result in chronic intestinal inflammation. I believe Inflammatory bowel disease(IBD) is caused by a failure to adequately down regulate nonspecific inflammation caused by an environmental trigger, such as an acute, self-limited infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs).Infections are cleared very quickly in normal hosts.Downregulation of innate immunity by invasive enteric bacteria immunological responses and the healing of the mucosa that has been harmed without any sort of stimulation or reactions of T-cells. Genetically susceptible hosts, on the other hand, who are unable to clear an invading pathogen and/or generate tolerogenic immune responses to commensal pathogenic microbes- by mounting appropriate innate immunity, down regulating immune responses, or healing the mucosal barrier—activate pathogenic T-cell responses to commensal bacteria and develop chronic, relapsing intestinal inflammation. T-cell apoptosis resistance, a lack of sensitivity to down regulatory signals, and ongoing exposure to luminal antigens and adjuvant all contribute to the persistence of this inflammatory response. Diet, smoking, stress, a changed microenvironment, and NSAID exposure are all factors that can affect mucosal immune responses and enteric bacteria composition. Although I believe that self-limited, non-specific infections can trigger chronic inflammation and reactivate latent disease, it is possible that a persistent pathogen could cause disease in people who are unable to clear infections (e.g., those with certain CARD15 polymorphisms), or that the commensal bacteria of some patients could acquire virulence factors (e.g., toxins, adherence, and/or invasion properties) that cause chronic intestinal inflammation. It's a rare occurrence for dentists and other clinicians to diagnose the condition based on oral clinical signs. Oral mucocutaneous and granulomatous lesions should alert the clinician to look into the gastrointestinal tract. Early Crohn's disease diagnosis would result in better patient management and prognosis.

CONFLICT OF INTEREST

Conflict of interest declared none.

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