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ORAL MANIFESTATION OF CROHN'S DISEASE

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ABSTRACT:

Introdution: Crohn's disease is a chronic inflammatory disease of the gastrointestinal tract, characterized by the cyclical onset and resolution of symptoms. It is a progressive disease that leads to intestinal damage and even disability. This disease can occur in any segment of the digestive system, from the mouth to the anus. The typical symptom is segmental inflammation in the small or large intestine, which is separated by healthy sections. The inflammation usually starts in the mucosa but, over time, spreads to the entire thickness of the intestinal wall, which can lead to intestinal damage, scarring, and the subsequent formation of fistulas and strictures. Inflammatory lesions most often occur in the last segment of the ileum, followed in order by the small and large intestines and the large intestine itself.

Aim of the study: The purpose of this paper is to provide a general overview of Crohn's disease, focusing on oral symptoms.

Materials and methods: An analysis of scientific articles available in Pubmed and Google Scholar databases was conducted. The study used publications from recent years that were most

pertinent to the topic under discussion. The search process consisted of using the following keywords: “crohn's disease”, “oral manifestations”, “oral healh”, “Crohn's disease symptoms”.

Results: In addition to the classic intestinal symptomatology, Crohn's disease can also manifest in the oral cavity. Symptoms that appear in the oral cavity may be early harbingers of Crohn's disease, occur concurrently with its onset, or manifest themselves several years after the onset of the condition. They most commonly involve the lips, buccal mucosa and gums. According to Malins and colleagues, these lesions can be divided into specific and non-specific ones.

Conclusions: Crohn’s disease diagnoses are increasing, and early awareness of symptoms is crucial for timely diagnosis and prevention of complications.

Key words: Crohn’s disease, oral health, oral manifestation.

Introduction:

Crohn’s disease is a persistent, idiopathic condition of inflammatory bowel disease marked by discontinuous lesions and full-thickness inflammation. It has the potential to involve any part of the gastrointestinal system, from the oral cavity to the rectum [1]. Crohn’s disease ranks as the second most prevalent type of inflammatory bowel disease, following ulcerative colitis [2]. A notable risk factor for the development of Crohn’s disease is a family history, particularly in first-degree relatives [3]. The disease does not preferentially affect any sex in adults. Typically, Crohn’s disease manifests between the ages of 20 and 40, with a secondary, smaller incidence peak observed between 50 and 60 years of age. The occurrence and prevalence of Crohn’s disease are higher in industrialized nations compared to developing ones and more common in urban settings than rural ones. The disease’s prevalence ranges from 3 to 20 cases per 100,000 individuals [4].

Crohn’s disease is a complex condition influenced by various factors, particularly abnormalities in immune and inflammatory responses. In predisposed individuals, an overactive immune reaction to bacteria within the gut lining leads to persistent inflammation that may affect the entire gastrointestinal tract [5]. The disease involves both innate and adaptive immunity. The former is implicated due to defects in the mucosal barrier, specifically in the Mut2 and FUT2 genes, while the latter is characterized by a TH1 lymphocyte response and TREG cells, driven by cytokines such as TNF-α, IL-12, IL-34, and IL-23. Additionally, the

remodeling of the extracellular matrix by metalloproteinases (MMP-1 and MMP-3) and the heightened expression of adhesion molecules like MAdCAM-1 and integrin α4β4 contribute to increased cell migration to inflamed areas. The interaction between the intestinal epithelium and the gut microbiota also plays a role in the disease's progression [6].

Endoscopic procedures, including colonoscopy, enteroscopy, and double-balloon endoscopy, are highly effective for examining the mucosa's superficial layers and identifying significant narrowing of the lumen, either visually or through the scope's inability to advance [7]. However, since these techniques only reveal endoluminal abnormalities, additional cross-sectional imaging modalities like ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are employed to diagnose strictures [8].

Given that Crohn's disease (CD) is a chronic condition, the therapeutic goal is to achieve short-term remission and sustain it over the long term [9]. For Crohn's disease affecting the ileal pouch, biologics are commonly used, and complications such as strictures and fistulas may be managed with endoscopic interventions or surgical procedures [10]. The medical management of Crohn's disease aims to dampen the hyperactive immune response within the intestines. The treatment strategy is twofold: induction and maintenance. Induction therapy involves administering a higher dosage of steroid-sparing agents in the initial phase to quickly bring about clinical remission. Maintenance therapy then utilizes a reduced dosage of these medications, which include immune modulators or biologics, to maintain remission and prevent relapses for the patient's lifetime [11]. Effective medications for inducing remission include steroids and TNF inhibitors. To maintain remission, treatments involve 5-aminosalicylic acid derivatives, immunomodulators (such as Azathioprine, 6-mercaptopurine, methotrexate), and TNF inhibitors (including infliximab, adalimumab, certolizumab, and golimumab) [12].

In the context of Crohn's disease (CD), dietary interventions, particularly exclusive enteral nutrition (EEN), have demonstrated efficacy in the preoperative phase by reducing the duration of surgical procedures and minimizing postoperative complications [3]. Surgery for Crohn's Disease (CD) is indicated for acute/chronic complications or when medical therapy fails. Emergency surgery is needed for toxic colitis, obstruction, perforation, abscess, and severe bleeding. Acute intestinal obstruction is the most common complication (35-59%), followed by perianal disease (17-43%). Other issues include colonic strictures (5-17%), abscesses (10-28%), perforation (1-6.5%), appendicitis (0.1-2%), and bleeding (1-6%). Oral symptoms also occur in 0.5-37% of CD cases [13].

Materials and methods:

The following review is based on articles from the PubMed and Google Scholar databases. This study used publications from recent years that were most closely related to the discussed topic. Key search terms included "Crohn's disease", "oral health", "oral manifestations", "oral symptoms".

Description of knowledge:

The oral region is acknowledged as a significant segment of the gastrointestinal system for diagnosing Crohn's Disease (CD). Consequently, dental practitioners are pivotal in detecting this condition early. This is particularly important for children, where an early diagnosis can profoundly influence their growth, sexual maturation, and psychological well-being [1]. Oral manifestations were initially reported in 1969 by Dudeney, with a prevalence ranging from 0.5% to 30% [2]. Research conducted by Laranjeira and colleagues on adults with Crohn's Disease (CD) indicates a progressive increase in oral mucosal lesions concurrent with the disease's advancement [15]. On average, patients exhibit minor oral symptoms approximately nine years post-diagnosis in childhood, with angular cheilitis being the most frequent occurrence [15].

Oral pathologies in CD patients are categorized into two types: disease-specific and nonspecific. The former are direct manifestations of the granulomatous inflammation characteristic of CD and are identifiable via histological examination. These include lip, cheek, and gingival edema, mucosal cobblestoning, profound linear ulcerations, and mucosal tags. Conversely, nonspecific lesions are reactive in nature and lack granulomatous tissue [(15)].

In active CD cases, there is an elevation in salivary cytokines such as IL-1β, IL-6, and TNF-α compared to inactive cases and healthy individuals. Notably, increased levels of IL-6 and TNF-α are associated with specific oral pathologies and may serve as biomarkers for active disease [17]. Additionally, vegetating pyostomatitis, a rare but distinctive indicator of CD, should be acknowledged. It presents as white or yellow pustules on an inflamed base within the oral cavity, resembling a snail's trail upon rupture [1]. These changes manifest in the upper and lower vestibule, tongue, gingiva, and both the soft and hard palate. Notably, these lesions lack granulomatous features microscopically [18].

The most prevalent oral signs of CD include mucosal cobblestoning, linear ulcers, granulomatous cheilitis (predominantly of the lower lip) and mucogingivitis [1]. Histological examination typically reveals granulomatous inflammation, with similarities between intestinal and oral lesions, characterized by mucosal fissuring, noncaseating granulomas, and Langhan-

type giant cells. Additionally, lymphedema in the upper dermis and lymphocytic infiltration are commonly observed [2]. The oral mucosa often exhibits hyperplasia, presenting a "cobblestone" appearance indicative of nodular, granulomatous inflammation. Other findings include indurated, polypoid lesions in the vestibule and retromolar area, as well as mucosal tags and deep ulcerations with hyperplastic borders, predominantly in the labial, buccal, and retromolar mucosa. The attached gingiva and alveolar mucosa may become swollen, granulated, and hyperplastic, sometimes accompanied by ulcerations [17]. Facial edema, including that of the lips and buccal mucosa, is another possible manifestation [18]. Lip enlargement is a common sign, with little distinction in occurrence between the upper and lower lips. Swollen lips often lead to painful vertical fissures, which can harbor various microorganisms, including S. aureus, potentially causing oral mucositis in individuals with inflammatory bowel disease [19].

In Crohn's Disease (CD), oral complications may manifest as either specific or nonspecific. Nonspecific include conditions such as gingivitis, periodontitis, higher rates of decayed, missing and filled teeth (DMFT). These changes are more common than specific ones and are observed with greater frequency in patients with CD (20). Individuals with CD are more susceptible to common oral conditions such as aphthous ulcers, angular cheilitis, lip fissures, and gingivitis [21]. Aphthous ulcers are reported in 5% to 60% of CD patients, particularly in pediatric cases and males [20]. These nonspecific lesions may arise from malnutrition, characterized by anemia and deficiencies in minerals and vitamins, which detrimentally impact oral health [17]. CD patients exhibit a higher incidence of dental decay and gum disease compared to the general population. This is attributed to a shift in oral microbiota, characterized by a reduction in protective species like Streptococcus mitis and a rise in periodontal pathogens such as Prevotella nigrescens and Prevotella intermedia, leading to increased vulnerability to periodontitis [21]. Active CD patients exhibit a higher incidence of nausea, vomiting, and dry mouth, which may correlate with an increased risk of dental erosions, caries, denture discomfort, and soft tissue abrasions and infections [22]. Approximately 30% of CD sufferers experience joint involvement, potentially affecting the temporomandibular joint, as evidenced by symptoms like clicking, crepitus, and trismus during examination [20].

Additionally, the pharmacological agents used in managing inflammatory bowel diseases can induce oral alterations due to their direct toxic impact on oral tissues and indirect immunosuppressive effects, heightening the risk of opportunistic infections and bone marrow suppression [17].

CD patients often suffer from malnutrition, which can disrupt the balance of the gut microbiome and lead to inflammation. The main causes of malnutrition include: limited food intake, problems with nutrient absorption, loss of protein and increased energy needs due to hypercatabolism [23]. Patients with Crohn's disease most commonly experience deficiencies in micronutrients such as iron, calcium, selenium, zinc, magnesium, water-soluble vitamins, especially B12 and folic acid, as well as fat-soluble vitamins like A, D, and K [24].

Anemia is a frequent issue associated with inflammatory bowel disease and can show up as oral pathology. Blood loss and diminished iron absorption (resulting from inflammation in the duodenum and upper jejunum) can result in a type of anemia that is microcytic and hypochromic [23]. Iron deficiency anemia is characterized by symptoms such as a pale oral mucosa, widespread atrophy of the oral mucosa, tingling sensations, tongue pain due to atrophic glossitis, and angular cheilitis [24]. A lack of B12 and folates can cause macrocytic anemia. B12 deficiency is most common in Crohn's disease due to impaired absorption in the terminal ileum, whereas folate deficiency can be due to decreased absorption, insufficient dietary intake, or as a side effect of medications like methotrexate and sulfasalazine [23]. A lack of vitamin B12 can lead to painful atrophy of the oral mucosa and tongue, recurring aphthous ulcers, angular cheilitis, oral candidiasis, widespread erythematous stomatitis, and a pale yellowish hue of the mucosa, particularly on the palate. Patients may also report changes in taste, a burning sensation in the mouth, and difficulty swallowing. If the anemia is due to a deficiency in folate, the oral symptoms are similar to those seen in vitamin B12 deficiency anemia, but without the neurological symptoms. In more severe cases, ulcerative stomatitis and pharyngitis may also be observed [24].

Inadequate absorption of calcium and vitamin K, often resulting from Inflammatory Bowel Disease (IBD), contributes to diminished bone mineral density. Furthermore, low levels of vitamin D are associated with a higher risk of gum diseases, including gingivitis and periodontitis, as well as increased dental caries and tooth loss [25]. Calcium is essential for the growth and hardening of teeth, and its insufficiency can impair the hardening process of dentin and enamel. It is expected that children with CD who lack adequate calcium and vitamin D will experience reduced hardening of both bones and teeth [26].

Patients with Inflammatory Bowel Disease (IBD) often exhibit shortages of vitamins A and C [27]. Oral symptoms of vitamin A shortage include angular cheilitis, thinning, and dryness of the oral tissues, with lips appearing to shrink inward. Deficiency in vitamin C typically presents as widespread gum swelling, unprovoked bleeding, sores, loose teeth, heightened risk of gum infections, and bone deterioration. Mucosal spontaneous bleeding is

also noted]. In children, the formation of bones and teeth is hindered due to the reliance of both dentin and osteoid on vitamin C for their development [17].

Zinc insufficiency is frequently observed in individuals with Crohn's Disease (29). This condition often presents itself in the oral region through symptoms such as erosive lesions, ulcerations, and cracks, accompanied by a crusted and desquamative dermatitis on the lips [17].

Topical treatments with antiseptic mouthwashes and local steroids are recommended. Using mouthwashes containing beclomethasone can alleviate symptoms. Swollen lips may benefit from the application of topical tacrolimus. Biological therapies with anti-TNF antibodies, have shown promise recently [2]; [28]. Alongside medication therapy, it's also advised to maintain a suitable diet, quit smoking, and take measures to prevent infectious diseases [31].

SUMMARY

Due to the increasing frequency of the diagnosis of Crohn's disease, dentists must remain vigilant and have up-to-date knowledge to effectively identify this disease. Recognizing the oral symptoms of people suffering from Crohn's disease and good cooperation between gastroenterologists and dentists can contribute to early detection of the disease. Early intervention can lead to better treatment outcomes and improved quality of life for patients.

DISCLOSURE

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