ORAL CAVITY AND SYSTEMIC DISEASES - INFLAMMATORY BOWEL DISEASES

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ABSTRACT
Inflammatory bowel diseases (IBD) refer to two chronic diseases which involve the large and small intestines: ulcerative colitis and Crohn’s disease.
The aim of this review is to focus on main oral signs related to IBD based on three important conditions:
1. Oral signs corresponding to the activity of the disease;
2. Oral manifestation which may precede the onset of intestinal lesions;
3. Oral findings which are related to a specific treatment.
Some particularities of the pathogenesis of IBD and the presentation of different oral lesions are discussed and general and specific practical dental recommendations for systemic and local therapy are presented.

Keywords: inflammatory bowel diseases, oral signs, dental recommendations

Oral manifestations in patients with IBD
Inflammatory bowel diseases form a group of inflammatory diseases of the colon and small intestine. The main forms of IBD are ulcerative colitis (UC) and Crohn’s disease (CD). Crohn’s disease can affect any part of the gastrointestinal tract, from mouth to anus (skip lesions), although a majority of the cases start in the terminal ileum and affect the whole bowel wall (“transmural lesions”). Ulcerative colitis, in contrast, usually is restricted to the mucosa of the colon and the rectum.

IBD is a chronic, uncontrolled inflammation of the intestinal mucosa with architectural distortion (e.g. transmural or superficial patchy granulomatous infiltration) and/or acute inflammatory cells infiltration (9, 17).

Crohn’s disease and ulcerative colitis are presented with extra-intestinal manifestations (such as arthritis, skin and oral manifestations and eye problems) in different proportions.

Ulcerative colitis was first described in 1859 by Samuel Wilk. The disease commonly begins during adolescence and early adulthood, mainly in people between 20-40 years. Antoni Lesniowski, a polish surgeon, first described Crohn’s disease in 1904, and later in 1932 an American gastroenterologist Dr. Burrell Crohn and his two colleagues, Dr. Leon Ginzburg and Dr. Gordon Oppenheimer, described fourteen cases, characterizing Crohn’s disease as “Terminal Ileitis: A new clinical entity”. Family predisposition has been proven in 20% of the patients.

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An epidemiological study on the prevalence of ulcerative colitis and Crohn’s disease conducted by 20 European centres demonstrated that the incidence of UC is two times higher than of CD – 10.4 (7.7-13.1) people per 100 000 at ages 15-64 vs. 5.6 (2.8-8.3) (15). Higher overall incidence was found in northern centres than in those from the south. This geographical phenomenon was confirmed for CD in France for the period 2000-2002 (13). Incidence rates for both diseases are higher in urban areas than in rural areas.

Inflammatory bowel disease is an idiopathic disease and appears to result from a dysregulated immune response to intestinal contents. In patients with Crohn’s disease or ulcerative colitis, the normal tightly controlled activity of the mucosal immune system becomes excessive resulting in profound tissue damage. Very often in patients autoimmune thyroid disease, diabetes mellitus and anemia perniciosa can be found (17).

The rectal bleeding and severe diarrhea are the main symptoms of ulcerative colitis. Usually Crohn’s disease affects young people and reveals intermittent episodes of abdominal distress, fever, and crampy abdominal pain accompanied by loose stools. Although bleeding is a prominent feature of ulcerative colitis, it is rare in cases of small-bowel Crohn’s disease (7). The laboratory test often reveals iron deficiency anemia, leukocytosis in active disease, low serum potassium and magnesium levels, hyposalbinemia.

The extraintestinal manifestations in IBD may be prominent: erythema nodosum on the thighs and legs; episcleritis, uveitis, corneal ulcers, and retinitis; ankles, knees, and wrists symptoms in up to 20% of the patients, liver involvement (7).
Once IBD is established, patients may suffer from episodic attacks during the chronic disease progression (1, 7, 8, 10, 11, 14) and in some patients can often be seen different nonspecific oral signs such as:

- recurrent aphthous ulcerations (Fig. 1);
- pyostomatitis vegetans (Fig. 2);
- cobblestone appearance of the oral mucosa;
- persistent lip swelling (Fig. 3);
- gingival swelling;
- orofacial granulomatosis;
- granulomatous inflammation of minor salivary ducts;
- chronic stomatitis;
- erythema migrans (Fig. 4);
- gingivitis and acute periodontitis (occurs more frequently and progresses more rapidly than in healthy patients);
- increased risk of dental caries;
- lichenoid mucosal reaction (Fig. 5);
- xerostomia;
- chronic bleeding;
- candidiasis (Fig. 6) and angular cheilitis;
- lymphadenomegaly.

Oral lesions that occur in ulcerative colitis are uncommon with an incidence of less than 8% (7). Oral finding in Crohn’s disease affect 6 to 20% (1, 7).

Oral manifestation may precede the radiographic lesions by as much as 1 year or more, especially in CD (37 to 60%) (4). As superficial lesions enlarge, they may be perpetuated by secondary bacterial invasion (6, 7, 16). Oral manifestations of IBD are related not only to the immune dysregulation, genetic and environmental factors, but also affect the development.

The new biological treatment of IBD with TNF-inhibitors such as adalimumab (Humira) could have a beneficial effect on severe oral lesions e.g. pyoderma gangrenosum.

Our aim is to present some particularities in the pathogenesis and clinical presentation of different oral manifestations in IBD.

Recurrent aphthous ulcers (Fig. 1) may appear in some people with IBD. Some theories include stress, bacterial infection, or trauma. Clearly, there is a link between severe aphthous stomatitis and a weakened immune system. In Crohn’s disease aphthous ulcers are specific manifestation of the disease. Some nutritional factors can be involved in the pathogenesis of the aphthous stomatitis (7):

- nutritional deficiencies of iron, folic acid and vit. B12 due to the poor absorption in the gut;
- adverse reaction of current treatment (5-aminosalicylates excreted in saliva).

In patients who are prone to develop aphthous ulcers, the appearance of a new crop of oral ulcers often heralds a flare-up of the bowel disease.

Pyostomatitis vegetans, cobblestone mucosal architecture, and minor salivary gland duct pathology represent granulomatous changes that constitute the hallmark of Crohn’s disease.

Pyoderma gangrenosum may occur in the form of deep ulcers that sometimes ulcerate through the tonsillar pillar (16).

Pyostomatitis vegetans is a purulent inflammation of the oral mucosa, characterized by the deep tissue vegetation or proliferative lesions, which can be ulcerative and supplicative. Predilection oral sites are gingiva, bucal, labial and palatinal mucosa. Oral findings are likened to the “grainy” mucosa. Male patients are prone to the disease and the prevalence is higher in the 30-60 years age range, with an average of 34 years (12).

The increased risk of dental caries and oral bacterial and fungal infection is multifactorial and related to dietary changes in patients, xerostomia and recent therapy. In a group of 32 patients with IBD, 31% had carious lesions, as those with just one caries were 12.5 %, and 19% had two or more (12).

Angular cheilitis and candidiasis, glossitis and pallor may be seen in patients with malabsorptions and anemia (7). Patients with Crohn’s disease may have diffuse swelling of the lip and face, orofacial granulomatosis, inflammatory hyperplasia of the oral mucosa with a cobblestone pattern (Fig. 2), indurative polypoid tag-like lesions in the vestibular and retromolar area and persistent deep linear ulceration with hyperplastic margins.
Granulomatosus lesions have also been observed in the salivary glands, where they may cause rupture of the ducts and localized mucocele formation (7).

Oro-facial granulomatosis is present characteristically with lip swelling (Fig. 3) but also affects gingivae, buccal mucosa, floor of mouth, and a number of other sites in the oral cavity. However in these cases sarcoidosis and Melkersson-Rosenthal syndrome should also be searched (12).

Fig. 3. Persistent lip swelling

Gingivitis and Acute Periodontitis
Previous reports have demonstrated that oral mucosa and periodontal lesions occur in patients suffering from inflammatory bowel disease CD and UC (5). Our study showed that 69% of the patients do have tooth agenesis, compared to 37% of the healthy controls. As patients in both groups have the same age a correlation between bowel disease and dentition status is probable (12). In confirmation of that fact is another study (3), which proves the overlap in clinical and pathological aspects in patients with IBD and parodontal disease (2).

Some of the oral findings could be a result of systemic medication (mainly glucocorticosteroids, sulfasalazine and immunosuppressants) and chronic use of topical corticosteroids (Table 1).

<table>
<thead>
<tr>
<th>Oral lesion</th>
<th>Drug</th>
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<tbody>
<tr>
<td>aphthous ulcerations</td>
<td>5-aminosalicylates</td>
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<tr>
<td>oral lichenoid drug reaction</td>
<td>anti-inflammatory drugs and sulfasalazine</td>
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<tr>
<td>macrocytic anemia</td>
<td>sulfasalazine</td>
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<tr>
<td>candidiasis</td>
<td>corticosteroids and bacteriostatic effect of sulfasalazine</td>
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<tr>
<td>hairy leucoplaikia</td>
<td>corticosteroids or other immunosuppressive agents</td>
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<tr>
<td>gingival hyperplasia</td>
<td>cyclosporine</td>
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Long-term treatment with some medication can induce systemic deteriorations such as:
1. Hypertension and hyperglycemia – due to the corticosteroids and ACTH;
2. Osteoporosis – due to the corticosteroids;
3. Adrenal suppression – due to the corticosteroids;
4. Changes in white or red blood cell counts- due to the azathioprine.

General dental treatment rules
Prior to the dental procedures, blood investigation is recommended in case of chronic bleeding, and in patients with recent extensive bowel surgery- including hemoglobin, hematocrit, red blood cell count, prothrombin time, INR (international normalized ratio), platelet count, blood glucose level, vit. B12 and folic acid. White blood cells > 15 000/cm suggest an abscess or perforation.

Practical dental recommendations
Treatment of the underlying disease in patients with IBD has favorable effect on the oral mucosa lesions. Moreover it has been demonstrated that the remission (absence of lesions in the oral cavity) could reflect treatment control and the response to therapy.

On oral lesions could be applied topically:
- Antiseptics (palliative rinses, e.g. palliative sodium bicarbonate mouth rinse (one to half teaspoon of baking soda in 8 ounces of water);
- Corticosteroids (e.g. fluocinonide 0.05% gel).
- Many patients require a systemic antibiotic therapy +/- Metronidazole and zinc suspensions.

Topical steroid therapy should be short term and closely monitored because of the side effect of mucosal atrophy and systemic absorption. Moderate-potency topical corticosteroid preparation such as 0.05% fluocinonide, desoximetasone and trimacinolone can be applied to the lesion 4 times daily, not to exceed two continuous weeks of treatment (10, 11).

Patients should be advised that prolonged use of topical steroids will result in mucosal atrophy, systemic glucocorticosteroid absorption and an increased incidence of oral candidiasis. Patients with higher risk of oral caries are recommended to use a local dental fluor gel mouth wash with chlorhexidine.

Stress component of dental treatment can lead to exacerbation of the disease which requires short oral procedures, and in some patients pre-sedation such as intake of St. John’s Wort extract (e.g. Remotiv) before dental manipulation is recommended (10, 11).

Maintaining good oral hygiene and frequent visits to the dentist are required (10, 11).
Specific recommendations

Aphtous stomatitis (Fig. 1)
Patients are advised to avoid foods containing benzoate, e.g. potato chips, chocolate, since the role of these foods in the early onset of oral lesions has been discussed. Therapy with vitamins and probiotics is recommended (10, 11).

Local therapy:
• Maintaining good oral hygiene (oral water containing chlorhexidine and triclosan, dilute hydrogen peroxide 3% solution of chamomile, etc.);
• Analgesic intake, pain-relief gels (Zilactin, Dentinox gel, Calgel) about 20 minutes before meals to reduce discomfort), and adhesive bases (Solcoseryl, Aloclaire, Oralbase);
• Anti-inflammatory medication (benzydamine hydrochloride, amlexanox);
• Topical corticosteroid therapy: 1 tabl. betamethasone sodium phosphate 0.5 mg to be dissolved in 15 ml water. The solution to be gargled with Arcol, three times daily; flucinonide (Lidex) or clobetasol propionate gel as a thin layer on the lesion, or dexamethasone (Decadron elixir (0.5 mg/5ml), preferred for lesions in the rear oral cavity sections;
• Antibiotic treatment – tetracyclines (250 mg caps. to be dissolved in 10 ml water) prepared as aqueous solution to gargle with Arcol, for 1 week.

Systemic therapy:
• Probiotics (Biogaia, Lactoflor, etc.);
• Bacterial oral vaccines (Dentavax, Imudon, etc.);
• Immunomodulators (Levamizol, Isoprinosine);
• Systemic corticosteroids in low doses: 10-20 mg/daily prednisone for 4-8 days, or in high doses: 40-80 mg/daily for 4-5 days;
• Pentoxifylline (Agapurin, Trental) 400 mg three times daily for at least 3-6 months, usually for 1 year;
• Colchicine 0.6 mg, 2 to 3 times a day for 2 weeks;
• Dapsone 100-200 mg/daily for 2 weeks or azathioprine (Imuran) 50 mg twice daily for 2 weeks;
• Thalidomide.

Cheilitis angularis and candidiasis (Fig. 6)
• Local therapy- antiseptics, antifungals (e.g. miconazole, effective against Candida and Staphylococcus-usually administered every 6 hours) and antibiotics.
• Treatment of underlying disease (diabetes, iron-deficiency anemia, anemia perniciosa) (10, 11).
Gingivitis and periodontitis require professional dental care (plaque and tartar) at least three times per year. After each procedure laser periodontal therapy is recommended and should be applied for at least four weeks.

In individual assessment Metronidazole treatment (250 mg tabl.) is prescribed (twice per year) for 7 or 10 days and daily mouth wash.

Patients are suggested to use two different toothpastes – one in the morning and one in the evening (priority of those with dental preventive effects on periodontal and children’s toothpastes).

In serious cases and non-responder patients, pre-examination of periodontal flora is needed and after results are taken into account an accurate antibiotic treatment should be prescribed (10, 11).

Gingival hyperplasia (Fig. 7)
Gingivectomy with carbon dioxide or laser is recommended for patients who have moderate-to-severe gingival enlargement that does not resolve when proper oral hygiene is maintained, or after a short course of antibiotics.

Orofacial granulomatosis
- Intralasional and systemic corticosteroids, sulfasalazine or clofazimine;
- Localized lesions without systemic connection can be treated by conservative surgical removal and plastic surgical reconstruction, especially in case of gingivitis hyperplastica and Cheilitis granulomatosa;
- Long-term patient monitoring in order to seek for early oral manifestations of suspected diseases with similar manifestations like CD and sarcoidosis;
- No therapy has proven to be universally effective in orofacial granulomatosis without systemic involvement

Xerostomia
- At least 2 liters of liquids intake a day (patient can hold ice chips in his or her mouth to provide moisture and possibly alleviate symptoms);
- Products promoting salivary gland secretions – cholinergic drugs such as pilocarpin, lemon juice, chewing gum;
- When conventional medical interventions do not provide satisfactory relief, it is recommended saliva substitutes and oral lubricants to be administrated. The volume of stimulated and unstimulated saliva could also be measured.

Conclusions
Oral lesions in patients with inflammatory bowel disease could be a major problem and dental care can ameliorate not only the oral health but could also improve the general patient condition by correcting the entrance to the gastrointestinal system.

REFERENCES