Oral manifestations of gastrointestinal diseases in children. Part 2: Crohn's disease

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ABSTRACT

Alterations within the oral cavity can be the first sign of systemic diseases and may thus allow for an early diagnosis and treatment. In particular, being the oral cavity a part of the gastrointestinal system, oral alterations can be an expression of a gastrointestinal disease. Diffuse mucosal swelling, cobblestone mucosa, localised mucogingivitis, deep linear ulceration, fibrous tissue tags, polyps, nodules, pyostomatitis vegetans, and aphthous-like ulcers have been described in Crohn's disease.
A prompt recognition of systemic diseases through a careful examination of the oral cavity allows for proper investigations and timely treatment.

Keywords *Alterations of the oral cavity; Children; Crohn's disease; Gastrointestinal diseases.*

Crohn's disease

Crohn's disease (CrD) i) is a chronic relapsing inflammatory condition with a complex aetiology and an uncertain pathogenesis, which comprises, along with ulcerative colitis (UC), the two major subsets of inflammatory bowel disease [Baumgart, 2007; Hanauer, 1996].

As in CD any segment of the gastrointestinal tract may be affected, lesions within the oral cavity can represent an initial and primary manifestation of the disease [Daley, 2007; Hussey, 2011; Boirivant, 2012] or may occur concurrently, or follow the onset of GI involvement [Kalmar, 2000]; however oral lesions without gastrointestinal involvement are rarely reported in the literature [Zbar, 2012; Fatahzadeh, 2009; Chi, 2010; Daley, 2007]. Oral lesions in CD may be caused either by the low serum levels of micronutrients and macronutrients due to malabsorption [Jacobs, 1968] or to local immune reactions to oral antigens typical of CD [Lehner, 1972; Basu, 1976].

Alterations within the oral cavity have a widely variable prevalence rate of 0.5 to 80% [Boiravant, 2012; Pittock, 2001; Hyams, 2007; Greenstein,1976; Bernstein, 1978; Harthy, 2005; Scheper, 2002; Plauth, 1991] and often develop in adolescents and young adults [Plauth, 1991]. The highest reported rate of oral manifestations in children with CD is about 50% [Pittock, 2001]. Hussey et al. [2011] reported that over a mean follow-up of 55 months, 29% of the children in their study developed specific oral lesions thus highlighting the need for timely recognition and bioptic examinations in the paediatric population. Moreover, Harty et al. [2005] demonstrated a 100% presence of granulomatous inflammation in the biopsies performed in their study and highlighted the value of the easily accessible oral mucosa as a potential site for harvesting diagnostic material, especially in children (Fig. 1, 2).

As the incidence of inflammatory bowel disease is increasing [Armitage, 2001; Castro, 2008; Turonen, 2006; Tsironi, 2004], the number of young patients with oral manifestations of the disease might be increasing as well.

Oral CD may affect any part of the oral cavity, including the buccal mucosa, lips, tongue, hard and soft palate, salivary glands, gingiva and teeth. Alterations can either be typical and pathognomonic, occurring almost always in association with inflammatory bowel disease, or highly suspicious for inflammatory bowel disease, or nonspecific [Katsanos, 2015].

Pathognomonic oral alterations include orofacial CD, granulomatous cheilitis and pyostomatitis vegetans. Up to 5-15% of the patients with CD develop a typical acute oral manifestation of the disease, known as orofacial CD, which include recurring or persistent lip swelling, cobblestoning of the oral mucosa, stomatitis, mucogingivitis, deep linear or serpiginous ulcerations

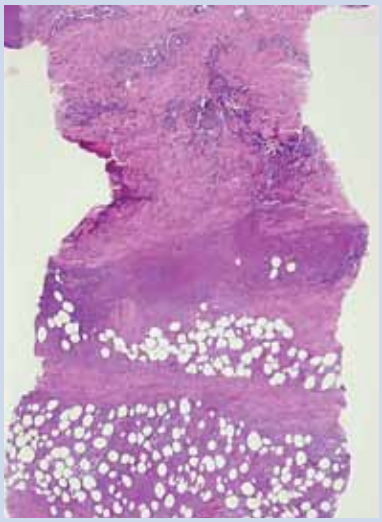


FIG. 1 Crohn's disease hystological view of granulomatous dermohypodermite.

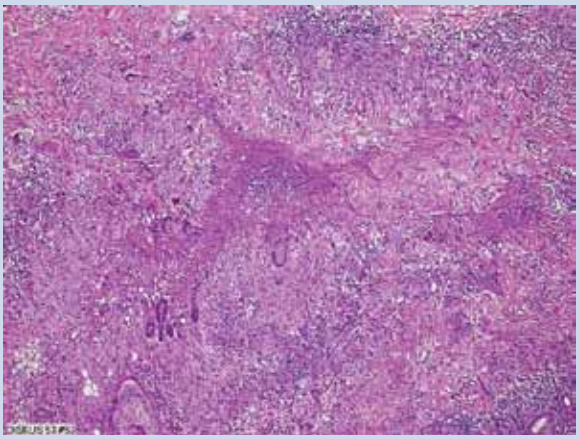


FIG. 2 Crohn's disease hystological view of granulomatous infiltration with Langhans giant cell.



FIG. 3 Granulomatosis cheilitis in Crohn's disease (patognomonic sign).

surrounded by epithelial hyperplasia, tissue tags or polyps, often related to Candida-associated angular cheilitis [Boirivant,2012; Fatahzadeh, 2009; Katsanos, 2015; Tilakaratne, 2008; Kolho, 2011; Wiesenfeld, 1985; Van der Waal, 2002]. This alteration macroscopically and histologically resembles the features found in the gastrointestinal tract [Stankler, 1972] and can be associated with pain on touch or on eating acidic or spicy foods, impairment of oral function, eating, speaking, and psychosocial stress [Plauth, 1991]. However orofacial CD is completely undistinguishable from orofacial granulomatosis, a clinical entity that can be found in several other different diseases including sarcoidosis, Miescher's cheilitis granulomatosa, Melkersson-Rosenthal syndrome, foreign body granuloma, rosacea, and various granulomatous infectious diseases [Wiesenfeld, 1985; Bogenrieder, 2003]. Up to 40-50% of young patients with orofacial granulomatosis might develop CD and CD may manifest several years after the first oral symptoms [Rowland, 2010].

Granulomatous cheilitis is a sub-acute uncommon granulomatous inflammation that involves just the lip area [Allen, 1990] (Fig. 3). A initial history of sudden swelling of the lips, mainly the lower lip, that resolves within hours or days, followed subsequently by permanent oedema and lumpy swelling is usally reported [Friedrich, 1990; Alawi, 2005]. However granulomatous cheilitis can be also an expression of other diseases such as allergy, sarcoidosis, Melkersson-Rosenthal syndrome, relapsing herpes simplex, relapsing erysipelas, cancers and genetic disorders [Katsanos, 2015] .

Finally, pyostomatitis vegetans is a rare expression that has been associated with inflammatory bowel disease. It is characterised by a thickened and erythematous oral mucosa covered with pustules and superficial erosions with a 'snail tracks' appearance. It is associated with inflammatory bowel disease in 75% of the cases [Ayangco, 2002; Lankarani, 2013; Delaporte, 1998]. Its histopathological features and inflammatory pattern are distinct and not dominated by granulomas but rather by eosinophilic microabscesses [Hussey, 2011]. However just few case reports can be found in the literature on paediatric CD and this oral alteration [Molnár, 2011; Pazheri, 2010]. Pyostomatitis vegetans can be also an expression of other pathologies such as autoimmune pemphigoid diseases and infections [Hansen, 1983].

Cobblestoning, mucogingivitis, gingival hypertrophy, lip swelling with vertical fissures, midline lip fissuring, deep linear ulcers of the buccal and labial mucosa and indurated tag-like lesions are oral lesions that can be highly suspicious for CD [Greenstein, 1976; Lisciandrano, 1996; Field, 1989; Colella, 1971; Lourenco, 2010].

Recurrent aphthous stomatitis (RAS), generally severe in presentation, dry mouth, presence of salivary duct fistula, recurrent buccal infection, persisting buccal space, aseptic abscesses, pustular ulcerations, erythema, swelling and cobblestoning of the gingiva, mandibular osteomyelitis and others have been described in CD and are defined as non-specific lesions [Correl, 1981; Delaporte, 1998; Gargiulo, 1989; Ciantar, 2007].

Opinions differ regarding the work-up of patients presenting with oral alterations suggestive of CD: Van der Waal et al. [2002] do not recommend routine

investigation of the gastrointestinal tract in patients with a negative history of gastrointestinal complaints, while Plauth et al. [1991] suggest thorough and repeated investigations for CD in cases of orofacial granulomatosis even in the absence of gastrointestinal symptoms. We would however recommend endoscopy in those patients with concomitant bowel symptoms or/and highly specific types of oral lesions [Katsanos, 2015].

The remaining children could be screened easily and periodically by measuring fecal calprotectin, a surrogate marker for mucosal inflammation (e.g. in Crohn's disease) [Roseth, 1999; Sipponen, 2008].

So far, no consensus on an effective paediatric oral CD treatment protocol has been developed [Benchimol, 2011]. Topical or systemic steroid therapy is the treatment most commonly employed [Hussey, 2011; Harikishan, 2012]. Tumor necrosis factor-alpha-antagonist agent infliximab has been administered with promising results in chronic granulomatous cheilitis and in a case of orafacial CD and lip swelling not responsive to any other treatment [Peitsch, 2007; Barry, 2005]. Moreover, few reports describe the utility of methotrexate for treatment of orofacial CD.

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