

Original article

## Oral manifestations of patients with inflammatory bowel disease

Flora Zervou<sup>1</sup>, A. Gikas<sup>2</sup>, E. Merikas<sup>2</sup>, G. Peros<sup>3</sup>,  
Maria Sklavaina<sup>2</sup>, J. Loukopoulos<sup>2</sup>, J.K. Triantafillidis<sup>2</sup>

### SUMMARY

**Background:** Crohn's disease (CD) is considered to be a disease involving the whole gastrointestinal tract, while ulcerative colitis (UC) is a disease exclusively located in the large bowel. The aim of this study was to examine whether patients with either CD or UC are at increased risk for developing oral manifestations. **Patients-Methods:** A wide spectrum of oral lesions was carefully sought by the same oral dentist in a consecutive series of 30 patients with inflammatory bowel disease (IBD) (15 with CD and 15 with UC). Forty-seven healthy individuals (matched for age and sex), attendants of our dental clinic served as controls. **Results:** 93% of UC and 87% of the CD group had at least one lesion compared to 55% of the control group ( $P < 0.005$ ). Significantly more patients with CD had mandibula lymphadenopathy ( $P < 0.0001$ ), ulcers ( $P = 0.011$ ), angular cheilitis ( $P < 0.0001$ ), hair tongue ( $P = 0.011$ ), periodontitis ( $P = 0.011$ ), gingival bleeding ( $P < 0.0001$ ), gingivitis ( $P = 0.002$ ), cobblestone appearance of the mucosa ( $P = 0.002$ ), polypoid tags ( $P = 0.002$ ), buccal trauma ( $P < 0.0001$ ) and lip swelling ( $P = 0.002$ ) as compared to healthy controls. Ulcerative colitis patients had in a significantly higher proportion of involvement of salivary glands ( $P < 0.0001$ ), as well as lymphadenopathy ( $P = 0.002$ ), buccal trauma ( $P < 0.0001$ ) and angular cheilitis ( $P < 0.0001$ ), compared to healthy controls. Significantly more patients with CD or UC had concurrently 3 or more oral manifestations as compared to normal controls ( $P < 0.0001$ ). On mul-

tivariate analysis, age and IBD were the only factors significantly related to the existence of oral lesions (OR 1.07, 95% CI: 1.02 – 1.13,  $P = 0.009$ ). No correlation between activity and duration of disease, sex and smoking habit, with the presence of oral manifestations, was noticed. No significant differences between patients and controls in the incidence of other lesions, including leukoplakia, and aphthous-like ulcers were found. No cases of pyostomatitis vegetans in either patients with IBD or controls were found. **Conclusion:** Although the number of patients included in the study is small we can conclude that oral manifestations in patients with IBD (especially in those with CD), is a frequent and underestimated event that needs further clinical validation.

**Key words:** Inflammatory bowel disease, Crohn's disease, Ulcerative colitis, Oral manifestations

### INTRODUCTION

Oral manifestations is a well-documented clinical feature in patients with inflammatory bowel disease (IBD) especially in those suffering from Crohn's disease (CD). The spectrum of these lesions described so far in the medical and dental literature is quite wide and includes oral ulceration<sup>1</sup>, labial, buccal and gingival swelling, buccal abscesses,<sup>2,3</sup> mucosal inflammatory hyperplasia, mucosal tags and fissuring,<sup>4</sup> gingivitis, granulomatous inflammation of minor salivary glands, granulomatous cheilitis,<sup>5</sup> candidiasis, angular cheilitis, lichen planus, pyostomatitis vegetans,<sup>6,7</sup> lymphadenopathy, perioral erythema, orofacial granulomatosis, midline lip fissuring, cobblestone appearance of the mucosa,<sup>8</sup> and dental caries.<sup>9</sup>

The prevalence of oral lesions in newly diagnosed patients has been estimated at 48% in some reports.<sup>10</sup> Mucosal tags constituted the most frequent lesion. It is of interest that, like other extraintestinal manifestations, oral lesions may precede the onset of the underlying intes-

<sup>1</sup>Department of Oral Medicine, <sup>2</sup>Gastroenterology, Saint Panteleimon General State Hospital, Nicaea, Greece, and <sup>3,4</sup>Surgical Department, University of Athens, Athens, Greece

#### Author for correspondence:

John K. Triantafillidis MD, 8, Kerasountos Street, 12461, Haidari, Athens, Greece, Tel (+)210-5819481, Fax: (+)210-5810970, e-mail: jkt@panafonet.gr

tinal inflammatory disorder.<sup>11</sup> However, it is difficult to determine exactly which oral manifestation is definitely related to IBD. It is logical to hypothesize that some of these lesions are in fact consequence of the disease or secondary reaction to medical treatment. So, pyostomatitis vegetans, cobblestone appearance of the mucosa and minor salivary duct pathology represent macroscopic lesions compatible with CD.<sup>12</sup>

There are only scattered systematic descriptions in the literature concerning the incidence of oral lesions in IBD patients and none originated from South Europe or Mediterranean basin countries. Therefore, the aim of this study was to evaluate the incidence of almost all kind of lesions and manifestations described so far in the literature in a series of patients with CD and ulcerative colitis (UC), hospitalized in a gastroenterology IBD referral center.

## PATIENTS AND METHODS

A total number of 30 consecutive inpatients with a definite diagnosis of CD or UC (15 with CD and 15 with UC, aged 40+/-16 years) were enrolled into the study. Disease activity was assessed by the CDAI for CD patients and the Truelove and Witts criteria for UC patients respectively. Twenty patients had active disease at the time of examination but none in either group of patients had severe disease. The mean duration of disease was 7+/-5yr (range: 2 months to 19 years). All patients with UC were on maintenance treatment with mesalazine. Forty-five percent of patients with CD were on mesalazine and 15% on azathioprine as maintenance treatment.

The control group consisted of 47 people aged 43+/-12 years, visitors of the outpatient dental clinic. Control individuals were well matched for sex and age. In fact, there were no statistically significant differences between patients and controls as far as the parameters age and sex were concerned.

Oral examination was performed by the first of us

(F.Z.), who is director of the oral clinic of the dental department of our hospital. Careful oral examination included the following parameters: *i) Gingivae*: gingivitis, periodontitis, and gingival bleeding *ii) Other lesions*: cobblestoning, polypoid tag, swelling (labial, buccal or gingival), angular cheilitis, ulcers (aphthous or deep surrounded by hyperplastic margins), pyostomatitis vegetans, fissuring (lip: midline, elsewhere and other), vitiligo, erythema migrans, perioral erythema, mandibular lymphadenopathy (expressed as palpable mandibular nodes that normally are not palpable), involvement of salivary glands (manifested clinically mainly as xerostomia), and mucosal bleeding, *iii) tongue lesions*: Hairy, fissured and geographic tongue.

Equipment for oral examination included mouth mirrors and a suitable high voltage lamp. A standardized procedure was carried out in each patient following the WHO recommendations.<sup>13,14</sup>

In addition to the above mentioned data, details of smoking habit were also recorded.

Statistical analysis of the results was carried out by using Pearson's chi square test, t-test and multivariate analysis.

## RESULTS

Eighty-seven percent of patients with CD and 93% of patients with UC had at least one oral lesion as compared with 55% of controls ( $P < 0.005$ ). Significantly more patients with CD and UC had concurrently 3 or more lesions as compared with controls ( $P < 0.0001$ ) (Table 1).

Table 2 shows the gingival lesions found in patients with IBD and healthy controls. As the table indicates, significant differences between patients with CD and controls were found in the incidence of gingivitis, periodontitis and gingival bleeding ( $P = 0.002$ ,  $0.011$  and  $< 0.0001$  respectively). Concerning the same parameters, no significant differences between patients with UC and controls were noticed.

**Table 1.** Number of lesions concurrently found in patients and controls.

Number of lesions	Controls	Crohn's disease	P-value	Ulcerative colitis	P-value
None	45%	13%		7%	
One	38%	7%		40%	
Two	15%	13%		20%	
Three or more	2%	67%	<0.0001	33%	0.001

Comparisons: Controls vs Crohn's disease & Controls vs Ulcerative colitis

**Table 2.** Gingival lesions in patients and controls

Parameter	Controls	Crohn's disease	P-value	Ulcerative colitis	P-value
Periodontitis	0/47 (0%)	2/15 (13%)	0.011	0/15 (0%)	NS
Gingivitis	0/47 (0%)	3/15 (20%)	0.002	1/15 (7%)	0.07
Gingival bleeding	0/47 (0%)	4/15 (27%)	<0.0001	0/15 (0%)	NS

NS= No significant differences. Comparisons: Crohn's disease vs Controls & Ulcerative colitis vs Controls

Table 3 shows the incidence of lesions found in lips, bucca and tongue. As the table indicates, significant differences between patients with CD and controls were found in the incidence of a variety of lesions including mandibular lymphadenopathy ( $P<0.0001$ ), ulcers ( $P=0.011$ ), angular cheilitis ( $P<0.0001$ ), hairy tongue ( $P=0.011$ ), periodontitis ( $P=0.011$ ), gingival bleeding ( $P<0.0001$ ), gingivitis ( $P=0.002$ ), cobblestone appearance of the mucosa ( $P=0.002$ ), polypoid tags ( $P=0.002$ ), buccal trauma ( $P<0.0001$ ) and lip swelling ( $P=0.002$ ). Patients with ulcerative colitis patients exhibited a significantly higher incidence of salivary glands involvement ( $P<0.0001$ ), lymphadenopathy ( $P=0.002$ ), buccal trauma ( $P<0.0001$ ), and angular cheilitis ( $P<0.0001$ ) compared to healthy controls. No significant differences between patients and controls in the incidence of other lesions such as leukoplakia, perioral erythema, buccal space abscess, perioral erythema and erythema migrans, fissured and geographic tongue and aphthous-like ulcers,

were found. No cases of pyostomatitis vegetans in patients with IBD and controls were noticed.

Table 4 shows the results of multivariate analysis. As the table indicates, age and IBD were the only factors significantly related with the presence of oral lesions (OR 1.07, 95% CI: 1.02 – 1.13,  $P=0.009$ ).

No correlation between activity and duration of disease, sex and smoking habit with the presence of oral lesions was noticed.

Figures 1 to 6 show some paradigms of lesions found in the oral cavity of patients with IBD.

## DISCUSSION

Our series consisted of patients with either UC or CD, who were hospitalized or followed-up in our department, a referral center for IBD, and followed-up for a long period of time (>5 years). The majority of them were

**Table 3.** Other oral lesions in patients and controls

Lesion	Controls	Crohn's disease	P-value	Ulcerative colitis	P-value
Cobblestoning	0/47(0%)	3/15(20%)	0.002	0/15(0%)	NS
Polypoid tags	0/47(0%)	3/15(20%)	0.002	0/15(0%)	NS
Lip swelling	0/47(0%)	3/15(20%)	0.002	1/15(7%)	0.07
Buccal swelling	0/47(0%)	1/15(7%)	0.07	0/15(0%)	NS
Ulcers	0/47(0%)	2/15(13%)	0.011	1/15(7%)	0.07
Aphthous ulcers	0/47(0%)	0/15(0%)	NS	1/15(7%)	0.07
Fissures: Lip	15/47(32%)	2/15(13%)	NS	2/15(0%)	NS
Medline	16/47(34%)	2/15(13%)	NS	0/15(0%)	0.009
Elsewhere	0/47(0%)	3/15(20%)	0.002	0/15(0%)	NS
Leukoplakia	0/47(0%)	1/15(7%)	0.07	0/15(0%)	NS
Erythema migrans	0/47(0%)	1/15(7%)	0.07	0/15(0%)	NS
Angular cheilitis	0/47(0%)	5/15(33%)	0.000	4/15(27%)	<0.0001
Hairy tongue	0/47(0%)	2/15(13%)	0.011	1/15(7%)	0.07
Buccal trauma	0/47(0%)	6/15(40%)	0.000	3/15(20%)	<0.0001
Lymphadenopathy	0/47(0%)	7/15(47%)	0.000	3/15(20%)	0.002
Salivary gland involvement	0/47(0%)	0/15(0%)	NS	4/15(20%)	<0.0001

NS= No significant differences. Comparisons: Crohn's disease vs Controls & Ulcerative colitis vs Controls

**Table 4.** Multivariate analysis of the results.

Parameter	OR	95% CI	P-value
<b>Age</b>	1.07	1.02-1.13	0.009
<b>Sex</b>			
Female	1.00		
Male	1.07	0.30 - 3.90	NS
<b>IBD</b>			
Controls	1.00		
Crohn's disease	16.6	1.51 - 33.4	0.022
Ulcerative colitis	12.8	1.20 - 25.6	0.034
<b>Smoking</b>			
Non-smokers	1.00		
Smokers	0.99	0.11 - 1.63	NS
Ex-smokers	0.61	0.06 - 6.29	NS
<b>Duration</b>	0.99	0.06 -3.29	NS
<b>Activity</b>			
Inactive disease	1.00		
Active disease	0.59	0.13 - 2.71	NS

**Figure 1.** Fissuring of the lips and angular cheilitis in a female patient with UC.**Figure 3.** Erythema, ulcers and Fordyce's granules in a male patient with CD.**Figure 2.** Leukoplakia of the buccal mucosa on the angle of the mouth in a female patient with UC.

under treatment with mesalazine or azathioprine. Almost one third of patients were in remission. The group of controls consisted of normal people who visited our dental department regularly in the frame of a preventive policy for dental hygiene that has been carried-out in our hospital for more than 4 years.

Our study has some limitations. So, despite the large number of controls included in the study, the small number of IBD patients in both arms was an important limitation making the statistical analysis of the results biased in some way. We must also emphasize the fact that only



**Figure 4.** Hairy tongue and median rhomboid glossitis in a male patient with CD.



**Figure 5.** Fissured tongue and atrophic glossitis in a male patient with CD.



**Figure 6.** Fissured tongue with hyperplastic and atrophic areas in a male patient with UC.

one examiner evaluated the oral lesions. However, as was previously stressed, this was an expert in oral medicine with great experience in a variety of oral manifestations that otherwise might not be easily identified.

The results of this study revealed that: i) patients with IBD had a significantly higher proportion of oral manifestations compared to healthy controls, ii) patients with CD had a significantly higher proportion of multiple

oral manifestations compared to UC patients and normal controls, iii) a wide spectrum of oral manifestations was found in the group of patients with IBD, including lymphadenopathy and salivary gland involvement.

From the spectrum of manifestations found in our series of patients it is worth mentioning that, in accordance with other reports,<sup>15</sup> the incidence of oral lesions in our patients did not differ significantly between patients with active or inactive disease, although the number of patients included in the study is relatively small. This finding was also confirmed in the multivariate analysis. However, we can not exclude the possibility of the existence of differences in histological level, as Halme et al found histological oral inflammation to be more common in patients with active than inactive disease.<sup>16</sup> Similarly, smoking habit and duration of IBD did not have any influence on the incidence of oral lesions found in patients with IBD. In fact, on multivariate analysis, only the presence of IBD and age of patients remained significant. The increase in the incidence of oral manifestations as the age goes up is an event not previously described in the literature. We have no obvious explanation for that, although it may related to nutritional and/or immunological alterations appearing at advanced age.

In our series of patients, the incidence of gingivitis and gingival bleeding was significantly higher in the group of patients with CD, compared to healthy controls. It

previously has been suggested that patients with active CD tended to have higher scores of gingivitis than patients with inactive disease.<sup>17</sup> However, in the multivariate analysis, we found that activity of the disease did not influence the incidence of gingivitis. No significant differences in the incidence of gingivitis, gingival bleeding or periodontitis between patients with UC and normal individuals were found.

In agreement with a previous report,<sup>15</sup> we found no difference in the incidence of aphthous ulcers, between patients and controls. Nevertheless, a significant proportion of patients with CD had a higher incidence of other type of ulcers compared to healthy controls. The discrepancy between our results and the common belief concerning the "high" incidence of aphthous-like ulcers in IBD could be attributed to different interpretation of the lesions made by the examiner. In our study, oral examination was performed by an expert in oral medicine, who was able to distinguish between real aphthous ulcers and oral lesions giving the impression of "aphthous" ulcers.

Cobblestone appearance of the mucosa was noticed in 20% of our patients with CD and in none of the patients with UC or healthy controls. Cobblestone appearance of the buccal mucosa is a characteristic oral lesion that can be found exclusively in patients with CD.

A very high incidence of angular cheilitis was observed in our patients with IBD. Compared with other reports (15), the incidence of angular cheilitis found in our patients was quite high (33% vs 13%), thus representing the most common oral lesion found in patients with IBD.

Traumatic lesions (buccal trauma) were observed in both groups of patients with IBD (especially in those with CD) compared to normal controls (40% vs 20% vs 0% respectively). Moreover, lymphadenopathy was observed in almost half of the patients with CD and 20% of patients with UC compared to 0% of normal controls. This finding, not previously reported, obviously needs further validation. The finding concerning salivary gland involvement is curious and largely unexplained. Salivary gland involvement was a feature exclusively noticed in patients with UC.

Pyostomatitis vegetans is a rare oral disorder often associated with gastrointestinal and other disorders.<sup>6</sup> It is characterized by erythematous, thickened oral mucosa with multiple pustules and superficial erosions. According to some descriptions, it can be related to the activity of the underlying Crohn's disease.<sup>7</sup> However, none of our series of patients with IBD or normal controls had clinical

signs of pyostomatitis vegetans.

The etiology of oral lesions is unknown although various factors including levels of vitamins and trace elements, other nutritional components, and certainly the underlying IBD (at least for a proportion of oral lesions) could be involved in their etiopathogenesis. Mycobacterium paratuberculosis has not been found to be implicated in the pathogenesis of orofacial granulomatosis or oral Crohn's disease.<sup>17</sup>

Concerning medical treatment of oral lesions in IBD patients, it seems certain that topical application of corticosteroids, in conjunction with systemic treatment of the bowel disease, could be of benefit, at least in some cases.<sup>18,19</sup> It has been suggested that Laser therapy can be applied in gingival Crohn's disease, with optimal esthetic results.<sup>20</sup> However, so far, these results have not been confirmed by other reports.

**In conclusion**, the findings of our study suggest that oral manifestations in patients with IBD, and especially in those suffering from CD, is a frequent and underestimated event that needs further clinical validation. We suggest that future research could be focused on the incidence of these lesions in newly diagnosed patients and on patients of various ages. Oral manifestations must be correlated with histology, nutritional status and other biochemical parameters (including trace elements and serum levels of vitamins), in order to make valuable suggestions concerning the primary or secondary nature of these lesions.

## REFERENCES

1. Croft CB, Wilkinson AR. Ulceration of the mouth, pharynx and larynx in Crohn's disease of the intestine. *Br J Surg* 1972; 59:249-252.
2. Gaqoh OK, Qureshi RM, Hendrickse MT. Recurrent buccal space abscesses: a complication of Crohn's disease. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; 88:33-36.
3. Malins TJ, Wilson A, Ward-Booth RP. Recurrent buccal space abscesses: a complication of Crohn's disease. *Oral Surg Oral Med Oral Pathol* 1991;72:19-21.
4. Basu MK, Asquith P, Thompson RA, Cooke WT. Oral manifestations of Crohn's disease. *Gut* 1975; 16:249-254.
5. Kano Y, Shiohara T, Yagita A, Nagashima M. Granulomatous Cheilitis and Crohn's disease. *Br J Dermatol* 1990; 123:409-412.
6. Hegarty AM, Barrett AW, Scully C. Pyostomatitis vegetans. *Clin Exp Dermatol* 2004; 29:1-7.
7. Ayangco L, Rogers RS 3<sup>rd</sup>, Sheridan PJ. Pyostomatitis vegetans as an early sign of reactivation of Crohn's disease: a case report. *J Periodontol* 2002; 73:1512-1516.

8. Issa MA. Crohn's disease of the mouth. *Br Dental J* 1971; 130:247-248.
9. Rooney TP. Dental carries prevalence in patients with Crohn's disease. *Oral Surg* 1984; 57:623-624.
10. Pittock S, Drum B, Fleming P, et al. The oral cavity in Crohn's disease. *J Pediatr* 2001; 138:767-771.
11. Dupuy A, Cosnes J, Revuz J, Delchier JC, Gendre JP, Cosnes A. Oral Crohn's disease: clinical characteristics and long-term follow-up of 9 cases. *Arch Dermatol* 1999; 135:439-442.
12. Stavropoulos F, Katz J, Guelmann M, Bimstein E. Oral ulcerations as a sign of pediatric patient: a case report. *Pediatr Dent* 2004; 26:355-358.
13. Krame I, Pindborg J, Bezroukov V, et al. Guide to epidemiology and diagnosis of oral mucosal disease and conditions. *Commun Dent Oral Epidemiol* 1980; 8:1-26
14. World Health Organization. Oral health surveys. Basic methods, 3<sup>rd</sup> ed. Geneva: World Health Organization, 1987.
15. Lisciandrano D, Ranzi T, Carrassi A, et al. Prevalence of oral lesions in inflammatory bowel disease. *Am J Gastroenterol* 1996; 91:7-10.
16. Meurman JH, Halme L, Laine P, von Smitten K, Lindqvist C. Gingival and dental status, salivary acidogenic bacteria, and yeast counts of patients with active or inactive Crohn's disease. *Oral Surg Oral Med Oral Pathol* 1994; 77:465-468.
17. Riggio MP, Gibson J, Lennon A, Wray D, MacDonald DG. Search for *Mycobacterium paratuberculosis* DNA in orofacial granulomatosis and oral Crohn's disease tissue by polymerase chain reaction. *Gut* 1997; 41:646-650.
18. Plauth M, Jenss H, Meyle J. Oral manifestations of Crohn's disease. An analysis of 79 cases. *J Clin Gastroenterol* 1991; 13:29-37.
19. Field EA, Tyldesley WR. Oral Crohn's disease revisited – a 10-year review. *Br J Oral Maxillofacial Surg* 1989; 27:114-123.
20. Giller JP, Vinciguerra M, Heller A, Kunken FR, Kahn E. Treatment of gingival Crohn's disease with laser therapy. *N Y State Dent J* 1997; 63:32-35.