Disease outcome for children who present with oral manifestations of Crohn's disease

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Abstract

BACKGROUND: At the time of diagnosis of Crohn's disease there may be oral manifestations. The aim of this study was to describe the outcome for children with oral Crohn's disease (OCD) at diagnosis, and to determine if there was a difference in the Paediatric Crohn's Disease Activity Index (PCDAI) scores between those with and those without oral lesions at follow-up. **METHODS:** Thirty-one patients with OCD who had enrolled in two previous studies were invited to participate. Clinical and laboratory data were collected to calculate the PCDAI. Details of the management of Crohn's disease were also recorded. **RESULTS:** Twenty-four of 31 patients participated (77%), of whom 17 were boys (M:F = 2.4:1). Mean age at follow-up was 15.7 years (SD 1.98, range 11.9-19.7 years). Mean duration of follow-up was 55 months (SD 22, range 20-97 months). Oral manifestations were present at follow-up in 7 (29%) of 24 patients. There were no differences between patients with and without OCD at follow-up with regard to medical treatments received or intestinal disease location. There was no difference in median PCDAI scores between those who had and those who had not oral lesions at follow-up. **CONCLUSIONS:** OCD resolved in the majority of children treated for intestinal Crohn's disease. The occurrence of mouth lesions during follow-up of children who had oral manifestations at initial diagnosis was not a marker for Crohn's disease activity elsewhere in the intestinal tract.

Introduction

Crohn's disease is a chronic transmural granulomatous inflammatory disease that most frequently affects the distal ileum and colon but may occur in any part of the gastrointestinal tract including the mouth. The diagnostic histopathological feature of Crohn's disease is the presence of non-necrotising granulomas in biopsies from affected parts of the gastrointestinal tract. Abdominal pain and diarrhoea usually occur and complications of the disease include obstruction, fistulae and abscesses. The medical treatment of Crohn's disease includes the use of amino salicylic acid derivatives, steroids, immunosuppressants, biologics and elemental diets. Surgical treatment may be required to manage complications.

The oral cavity provides a useful source of easily accessible diagnostic material in the assessment of patients with suspected intestinal Crohn's disease. Muco-cutaneous findings may even herald the onset of inflammatory bowel disease [Scully et al., 1982; Galbraith et al., 2005]. The existing dental and medical literature documents a broad spectrum of oral Crohn's disease (OCD) manifestations in adults and children [Williams et al., 1991; Halme et al., 1993; Pittock et al., 2001; Harty et al., 2005]. We have shown previously that over 40% of children presenting with Crohn's disease harbour disease-specific manifestations in the mouth [Pittock et al., 2001; Harty et al., 2005]. While characteristic oral lesions may be diagnostically useful at initial evaluation there is limited information available on the outcome of oral lesions following treatment of intestinal disease. Our hypothesis was that oral lesions at follow up mirror luminal disease activity, as reflected by the Paediatric Crohn's Disease Activity Index (PCDAI) [Hyams et al., 2005]. The aim of this prospective study was to follow patients with OCD when Crohn's disease was originally diagnosed, to characterise oral and luminal disease, treatment and disease activity, and to compare those with and without oral lesions at follow-up.

Methods

Two previous studies of OCD were conducted between 1994 and 2001 at the gastroenterology department, Our Lady's Children's Hospital, Dublin [Pittock et al., 2001; Harty et al., 2005]. More than 75% of Irish children and adolescents with suspected inflammatory bowel disease undergo diagnostic evaluation at this centre annually. Thirty-one patients with OCD were enrolled during the 8 year study period. Their clinical, pathological, radiological and dental findings have been described previously [Pittock et al., 2001; Harty et al., 2005]. Patients were invited to participate in a follow-up re-evaluation study. Ethical approval for the study was obtained from the Ethics Committee Our Lady's Children's Hospital.

At a follow-up visit, each patient underwent a clinical examination by both a paediatric gastroenterologist (BB) and the paediatric dentist who had performed the initial oral examination (PF). Patients' symptoms and treatment since diagnosis were recorded. The type of medication used and the number and duration of each treatment course was recorded. Clinical examination included an assessment of extra-intestinal manifestations of Crohn's disease, perianal disease and growth. In addition blood samples for full blood count (FBC) and C-reactive protein (CRP) were taken to calculate the PCDAI. CRP (normal range 0-4 mg/l) is measured at our institution rather than ESR. In order to provide a PCDAI score, CRP was substituted for ESR with CRP values of ≤ 4, 5-50 and ≥51 given scores of 0, 2.5 and 5 respectively. PCDAI scores of <10, ≥10 < 30, and ≥30 represented inactive, mild-moderate

and severe disease, as previously described [Hyams et al., 2005]. Two children did not have a PCDAI index calculated because they did not have an ESR or CRP carried out at the time of follow-up. As all children had upper and lower endoscopies performed at diagnosis together with radiological investigations, disease phenotype was defined according to the Vienna classification (current at the time the study was undertaken) [Gasche et al., 2000]. One child was not classifiable according to the Vienna classification because despite typical disease symptoms, laboratory findings and subsequent course, there were no characteristic findings of Crohn's disease at endoscopy or on barium studies at presentation. The presence of granulomas in oral biopsies confirmed the diagnosis of Crohn's disease in this child. Dental examination included a systematic examination of regional lymph nodes, lips, labial mucosa and sulci, buccal mucosa and sulci, commisures, gingivae, tongue, floor of mouth, and hard and soft palate using standard dental lighting in a dental chair. Oral manifestations of Crohn's disease were noted including swelling and fissuring of the lips, angular cheilitis, cobblestoning of the buccal mucosa, deep linear ulceration in the buccal sulci, mucosal tags, mucogingivitis with erythematous swelling of marginal and attached gingiva, and pyostomatitis vegetans with multiple small gingival pustules.

Data were analyzed using Epi Info (CDC, Atlanta, GA). As the data in the two groups (OCD present, OCD absent) was not normally distributed comparison between groups was made using non-parametric tests. Differences in proportions were compared using the Fisher's exact test, with p=<0.05.

Results

Twenty-four of the 31 patients (77%) with OCD at initial diagnosis participated in this follow-up study, comprising 17 boys and 7 girls (M:F = 2.4:1). Of the 7 non-participants (5 girls), one patient had died and another was un-contactable. A further 5 patients declined to participate. The mean age of the children at diagnosis of Crohn's Disease was 11.9 years (SD 2.7 range 8.2 – 15.8) and at follow-up the mean age was 15.7 years (SD 1.98, range 11.9-19.7 years). The mean duration of follow-up was 55 months (SD 22, range 20-97 months).

Of the 24 patients with OCD at baseline only 7 (29%) had clinical manifestations of OCD at follow-up. There was little apparent relationship between the extent and severity of oral disease at diagnosis and resolution with time. For example, of 7 children with multiple OCD manifestations at diagnosis, 3 had OCD and 4 had normal oral mucosa at follow-up. Figure 1a, 1b demonstrate the clinical manifestations of OCD at presentation while Figure 1c, 1d show the resolution of OCD at follow-up in the same child. OCD findings included mucogingivitis (n=2), deep linear ulceration (n=3), angular cheilitis (n=3) and pyostomatitis vegetans (n=2). A number of patients had more than one finding.

Figure 1a-b. *Clinical manifestations of oral Crohn's disease (OCD) at time of diagnosis with swelling of lips and angular cheilitis in Figure 1a and an arrow identifying mucosal tag lesion in the same child in Figure 1b.*

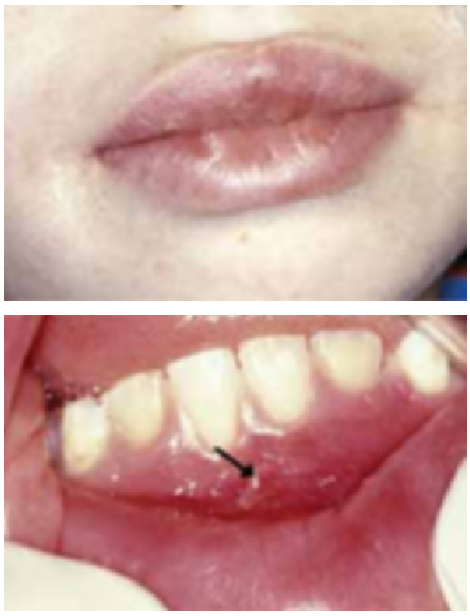
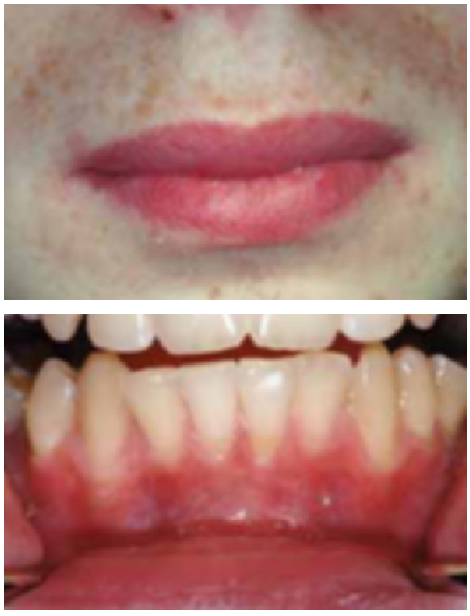


Figure 1c-d. *Resolution of oral Crohn's disease (OCD) at follow-up examination of the same child.*



PCDAI scores ranged from 0 – 67.5 with 5 children having a PCDAI score of 30 or more (severe disease). Median PCDAI scores did not differ between those children with and those without oral lesions at follow-up (Table 1). In addition there was no difference in the proportion of children with severe disease (PCDAI score ≥30) compared with those with inactive disease or mild to moderate disease (PCDAI < 30) (Odds Ratio 4.8 (95% CI 0.59 – 40.79 p = NS)). Weight and height z scores, Crohn's disease relapse, courses of prescribed

steroids, use of immuno-modulators, and number of surgical interventions were not different between patients with active oral disease and those with no oral lesions. Disease distribution based on the Vienna classification was the same in both groups. Upper gastrointestinal disease (excluding the mouth = Vienna L4) was present in 9 (37%) of the overall cohort (Table 2). While the numbers were small, perianal disease was more common in children with OCD (N=3) at follow-up compared with those without oral findings (N=2).

Table 1. *Paediatric Crohn's disease activity index in children with oral Crohn's disease (OCD) and without OCD at follow-up.*

PCDAI Score*	OCD Present n (%)	OCD Absent n (%)	p value
< 10	3 (42.8)	4 (26.6)	
≥10 < 30	1 (14.3)	9 (60.0)	
≥ 30	3 (42.8)	2 (13.3)	
Median PCDAI Score	25	10	NS

Paediatric Crohn's disease activity index (PCDAI) according to category of disease activity in children with manifestations of oral Crohn's disease (n = 7) at follow-up and those with no evidence of OCD at follow-up (n =15). ESR or CRP were note available for 2 children.

*Disease activity category < 10 inactive disease, ≥10 < 30 mild to moderate disease activity, ≥ 30 severe disease.

Table 2. *Classification of Crohn's disease in children with OCD and without OCD at follow-up.*

Disease Location		OCD Present n (%)	OCD Absent n (%)
L1	Terminal Ileum	0 (0)	0 (0)
L2	Colon	2 (28)	8 (44)
L3	Ileocolon	1 (14)	3 (17.6)
L4	Upper GI (excluding mouth)	4 (57)	5 (29.4)
Disease Behaviour			
1	Non-stricturing/non penetrating	5 (71.4)	14 (82)
2	Stricturing	1 (14)	2 (11.7)
3	Penetrating	1 (14)	1 (5.8)

Vienna classification at diagnosis in patients with (n = 7) and without (n =16) oral Crohn's disease (OCD) at follow-up. One child could not be classified according to the Vienna classifications because only oral biopsies provided diagnostic biopsy material.

Discussion

The prevalence and clinico-pathological findings of OCD are well documented, particularly in children [Plauth et al., 1991; Pittock et al., 2001; Harty et al., 2005]. The relationship of oral disease to the course and clinical management of Crohn's disease in children, however, has not been evaluated to our knowledge to date. We hypothesised that oral lesions at follow-up would reflect active disease elsewhere in the GI tract using the PCDAI as a measure of activity and demonstrated that over 70% of patients no longer had evidence of OCD on re-examination, after a mean follow-up period of 55 months. There was no difference in PCDAI scores between those with oral lesions and those without at follow-up. These data demonstrate that although the mouth can be a useful site for diagnostic material in children at initial presentation with suspected Crohn's disease [Pittock et al., 2001; Harty et al., 2005], the oral examination is much less useful in those with established disease as oral lesions do not predict active disease elsewhere in the GI tract. In addition oral findings were not associated with disease distribution (apart from perianal disease) or extra-intestinal manifestations of Crohn's disease at follow-up. More children with persistent OCD had perianal findings. Although the numbers were very small, this supports our previous observation [Harty et al., 2005] of an association between oral and perianal manifestations in Crohn's disease.

This is the first study, to our knowledge, to examine the outcome of oral lesions at follow-up present at initial diagnosis of Crohn's disease in children, but a number of limitations must be acknowledged. Follow-up studies in children who have progressed to adult services are often difficult, and in our study 5 patients who no longer attended our institution declined to participate because of time constraints due to work and college commitments. Without dental examination we cannot confirm the presence or absence of oral lesions in these 5 patients but based on the results of this study it is unlikely that all still had oral lesions. Our follow-up sample is small and the possibility of a type 2 error must be considered.

Conclusions

Oral manifestations present at diagnosis of Crohn's disease in children commonly disappear during follow-up, regardless of intestinal disease activity.

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