

Small bowel enema in non-responsive coeliac disease

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Abstract

A small bowel enema was performed in patients with non-responsive coeliac disease, in coeliac patients on a normal diet (untreated) and those who had shown a good response to a gluten free diet, and in control subjects to determine whether there were any specific radiological features of the non-responsive state. A significant reduction in the average number of jejunal folds and an increase in the number of ileal folds (reversal of the jejunoileal fold pattern) was found in eight of nine non-responsive coeliac patients, one of seven untreated coeliac patients, and in none of the good responders or control subjects. This pattern identifies coeliac patients with a poor response to a gluten free diet who are likely to suffer major complications.

Barium follow through examination in adult coeliac disease often shows non-specific features of malabsorption, particularly dilatation of the bowel and coarsening of the valvulae conniventes with variability of fold thickness.¹ A unique appearance has been described in coeliac disease with a decrease in the number of folds in the jejunum and an increased number of folds in the ileum.^{2,3} This reversal of the normal jejunoileal fold pattern has been found only in patients with longstanding untreated coeliac disease, and in one study two of the five patients with this appearance developed complicating histiocytic lymphoma.² The small bowel enema (enteroclysis) technique is increasingly replacing the barium follow through examination in the study of small intestinal diseases.⁴ In untreated coeliac disease there is increased separation of the jejunal folds with a reduction in the number of folds per inch of proximal jejunum.⁵ There is also increased thickness of the ileal folds and in some patients an increase in the number of ileal folds. At its most extreme this results in reversal of the jejunoileal fold pattern with atrophy ('colonisation') of the jejunum and 'jejunalisation' of the ileum.³

Non-responsive coeliac disease is uncommon and difficult to diagnose and differentiate from non-compliance with a gluten free diet.⁶ The diagnosis depends on repeated jejunal biopsies, tests of malabsorption, and immunological tests

which are expensive, time consuming, and unpopular with patients. A more rapid or straightforward technique to identify these patients would be helpful. Initial observations suggested that the small bowel enema showed specific features in these patients, and we therefore used this technique to assess patients with non-responsive coeliac disease.

Methods

PATIENTS

A prospective search was made for reversal of the jejunoileal fold pattern in all patients who were having a small bowel enema to determine the prevalence and importance of this pattern. Detailed measurements were made in 50 control patients with irritable bowel syndrome or non-coeliac upper gastrointestinal disease; seven patients with untreated coeliac disease; eight treated coeliac patients with a good response to a gluten free diet; and nine patients with non-responsive coeliac disease.

The non-responsive patients had presented with malabsorption and jejunal villous atrophy and had been on a strict gluten free diet for more than three years. They were all reliable patients known to be strict with their diet, which was confirmed by home visits from a specialist dietitian.⁶ These patients, however, remained symptomatic and had evidence of persisting malabsorption with abnormalities such as folate deficiency, hypocalcaemia, and steatorrhoea. They did have coeliac disease in so far as their jejunal biopsies after a gluten free diet showed a mathematically significant improvement in villous height, a reduction in crypt depth, and a reduction in the number of intraepithelial lymphocytes. When compared with coeliac patients who had shown a good response to a gluten free diet, however, the degree of improvement in these parameters was appreciably less in the non-responsive group. Of these nine non-responsive coeliac patients, five had a coexisting hypersensitivity to soya protein,⁶ four had chronic inflammatory and fibrotic bronchopulmonary disease (coeliac lung disease) with impaired gas transfer,⁷ two had cutaneous vasculitis, and two had developed colonic carcinoma.

ENTEROCLYSIS TECHNIQUE

A Sellink enteroclysis tube with guide wire was passed to just beyond the ligament of Trietz and 300 ml of high viscosity barium sulphate suspension (90% w/v) was run in at a rate of 75 ml per minute. A 0.5% solution of methylcellulose in water was then infused. This distends the lumen, and as it propels the barium towards the colon it leaves behind a barium coating on the mucosa,⁴ resulting in double contrast views. Formal

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Accepted for publication 23 October 1989

TABLE I Mean number of folds in the proximal jejunum and distal ileum in patients and control subjects

	No of folds per inch of jejunum (mean (SD))	No of folds per inch of ileum (mean (SD))
Control subjects (n=50)	4.7 (0.63)	3.3 (0.64)
Coeliac disease:		
Untreated (n=7)	3.05 (0.99)	4.09 (0.59)
Good response to a gluten free diet (n=8)	4.54 (1.4)	4.14 (0.45)
Non-responsive (n=9)	3.89 (0.53)	5.59 (1.48)

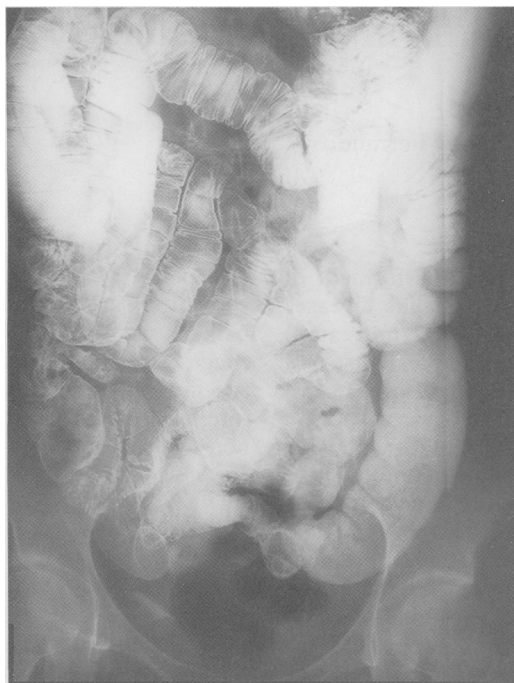


Figure 1: Normal small bowel enema with many circular mucosal folds in the proximal jejunum, and proportionately fewer folds with spiral configuration in the ileum.

measurements were made in the proximal jejunum and distal ileum. The number of folds in one inch of mucosal length was measured at three separate positions, and the mean number of folds per inch was obtained for each site.

STATISTICS

Student's *t* test was used to determine the significance of the difference between the mean number of mucosal folds in each group.⁸

Results

Figure 1 shows a normal small bowel enema and

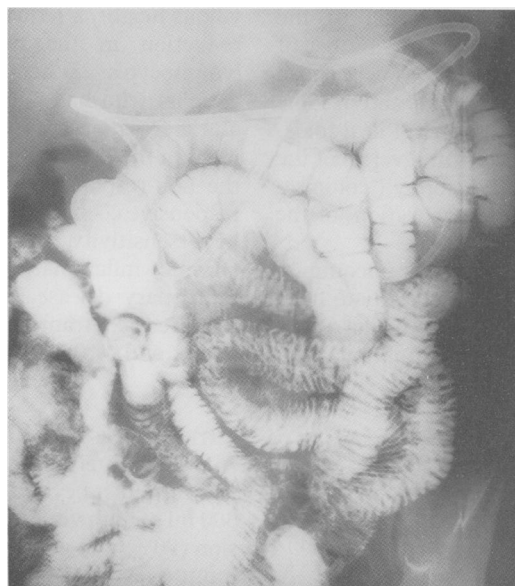


Figure 2: Small bowel enema in non-responsive coeliac disease showing reversal of the jejunoileal fold pattern, with a reduced number of folds in the upper jejunum and an increased number of folds in the ileum.

TABLE II Reversal of jejunoileal fold pattern: frequency

Coeliac disease:	
Untreated	1:7
Good response to a gluten free diet	0:8
Non-responsive	8:9
All other enteroclysis examinations	0:420

Figure 2 reversal of the jejunoileal fold pattern. The mean (SD) number of folds from three separate measurements in the proximal jejunum and distal ileum is shown in Table I. The control subjects had significantly more jejunal folds than the untreated and non-responsive coeliac patients ($p < 0.001$) and did not differ significantly from the treated coeliac patients ($p = 0.5$). The untreated coeliac patients had significantly fewer folds per inch of jejunum than the treated and non-responsive coeliac patients ($p < 0.05$). Conversely, there were significantly fewer folds per inch of ileum in the control subjects than in all the coeliac subgroups ($p = 0.001$). The non-responsive coeliac group had significantly more ileal folds than either the untreated or good responder groups ($p < 0.05$).

The number of patients in each group who were considered to have reversal of the jejunoileal fold pattern from direct observation of the x ray films is shown in Table II. This includes all the enteroclysis examinations performed in this hospital in the last five years. With the exception of one patient with untreated coeliac disease, this pattern was otherwise confined to non-responsive coeliac patients. The untreated newly diagnosed patient was a 17 year old woman with malabsorption, short stature, and primary amenorrhoea. Her response to a gluten free diet was initially poor, with persisting malabsorption and amenorrhoea for 18 months. After two years, however, her height and weight increased appreciably, periods started, and a jejunal biopsy (which originally showed subtotal villous atrophy) was nearly normal.

Discussion

Barium follow through examination shows non-specific features in coeliac disease.¹ Small bowel enema is more specific, showing increased separation of the circular folds in the proximal jejunum. (Increased jejunal fold separation is found in only 15% of follow through examinations in coeliac disease.^{5,9} Occasionally jejunal folds are absent, and this is found only in coeliac disease. Conversely, there is a noticeable increase in the number of folds in the ileum in untreated coeliac disease, though this is found in just over half of patients.^{3,5}

In the present study the findings in the untreated coeliac patients are similar to those described by Herlinger and Maglente.⁵ The radiological appearances in coeliac patients who show a good response to a gluten free diet revert towards normal with a decrease in jejunal fold separation, though there is no appreciable change in the number of ileal folds per inch. The striking abnormality, however, is in those patients with coeliac disease who have shown a poor response to gluten withdrawal and have persisting malabsorption. These patients have a decreased number of folds in the proximal

jejunum and an increased number of ileal folds. On examination of the x ray films, eight of these nine patients had obvious reversal of the jejunoileal fold pattern. This feature is strongly suggestive of non-responsive coeliac disease. In previously published studies the barium examinations have been done on untreated coeliac patients only, and there are few radiological data on coeliac patients who are refractory to gluten exclusion.

Approximately 10 to 15% of patients with adult coeliac disease have a poor response to a gluten free diet.⁶⁻¹² These poorly responsive patients have impairment of mucosal DNA synthesis,¹² and in some cases deficiency of Paneth cells¹⁰ and slowly reversible mucosal changes such as subepithelial collagen deposition.¹³ In some patients the poor response to a gluten free diet alone is due to coexistent food hypersensitivities to, for instance, soya protein,⁶ and in others it is due to associated zinc deficiency¹⁴ or underlying lymphoma.¹⁵ As further investigation and treatment is necessary in these patients it is important to be able to identify them and to distinguish them clinically from coeliac patients with a poor response due to non-compliance with a gluten free diet. As a reversed jejunoileal fold pattern is only rarely found in untreated or good responder coeliac patients, the small bowel enema offers a reliable means of identifying truly non-responsive patients.

Several mechanisms have been suggested to account for reversal of the jejunoileal fold pattern. There is a slowing of the basic electrical rhythm in coeliac disease and this could account for the distensibility and impaired peristalsis which result in increased separation of the circular folds in the jejunum.⁵ The 'jejunalisation' of the ileum is thought to represent adaptive compensatory hypertrophy of the ileum consequent to prolonged jejunal villous atrophy.² Certainly, enhanced absorption of glucose and amino acids has been shown in the ileum in coeliac disease.¹⁶ A similar response is seen after jejunal resection and after jejunoileal bypass surgery; and in all these conditions enteroglucagon concentrations are raised. The enteroglucagon concentration correlates with crypt cell production rate, and enteroglucagon is considered to be the 'growth hormone of the small intestine,' though this remains to be definitively proved.¹⁷ In this respect, however, a patient has been described with an enteroglucagon-secreting renal tumour in whom the small intestine, on follow through examination, was dilated with coarse, thickened mucosal folds.¹⁸ Microscopy of the intestine showed conspicuous hypertrophy of the villi. All these features returned to normal when the tumour was removed and the entero-

glucagon concentrations returned to normal, suggesting that this hormone affects intestinal adaptation. In coeliac patients the raised enteroglucagon concentrations found in response to jejunal villous atrophy presumably enhance absorption in the ileum.

Whatever the underlying mechanism, the finding of a reversed jejunoileal fold pattern in a coeliac patient on a gluten free diet strongly suggests that the patient is a non-responder. A small bowel enema should be performed in all coeliac patients who have persisting malabsorption or remain symptomatic despite gluten withdrawal. This will identify patients who may have additional food hypersensitivities and those likely to develop complications of coeliac disease and may be an early marker for histiocytic lymphoma in some patients,² allowing further investigations to be pursued.

We are grateful to Sister Lynch, SRN, for her help with the test and in the aftercare of patients, Miss Karen Chambers for typing the drafts, and Miss Tracey Green for typing the manuscript.

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