The value of proximal small intestinal biopsy in the differential diagnosis of chronic diarrhoea

enteropathy due to coeliac disease or cows' milk protein intolerance. After the demonstration of a normal small intestinal mucosa on a normal diet the diagnoses associated with the presence of an enteropathy were excluded. Similarly although no cause was found to explain the symptoms in 9% of cases, the biopsy procedure allowed many gastrointestinal diseases to be excluded.

A diagnosis was established in 91% of cases. The commonest diagnosis was the postenteritis syndrome in 117 (31%). In 24 children a normal mucosa was demonstrated and 23 were continued on a normal diet with resolution of the diarrhoea—that is, the biopsy influenced management with a successful outcome in all but one case. Seventy patients had mild, 21 had moderate, and one had severe histological changes. These children were placed on cows' milk free diets with immediate clinical benefit and several months later a carefully controlled milk challenge was performed in hospital. Most cases were able to tolerate a milk containing diet by the age of 2 years. Thus, the presence or absence of histological changes has helped to indicate which patients with the postenteritis syndrome require treatment with a milk free diet.

In 46 cases pathogens were demonstrated. G lambia was identified in 20 (43%) and indicated treatment with metronidazole. Proximal small intestinal mucosal biopsy was a more effective method for the detection of G lambia than stool microscopy. One patient who did not improve after metronidazole treatment had further biopsies that established the additional diagnosis of coeliac disease. This underlines the value of the procedure in the differential diagnosis of chronic diarrhoea.

Enteropathogenic E coli, when identified adhering to the mucosa, were treated with appropriate antibiotics. The finding of cryptosporidium explained the presence of an enteropathy and indicated that therapeutic intervention would be ineffective. In all cases the diarrhoea resolved spontaneously.

Only 8% of the patients coming to biopsy had coeliac disease, even though it was considered as part of the differential diagnosis in the majority of cases. Thus a major role of the biopsy procedure is to exclude the presence of coeliac disease and thereby avoid the pitfalls of empirical treatment. As treatment of coeliac disease is for life it is crucial that the diagnosis is substantiated.

Other diagnoses associated with a severe enteropathy included autoimmune enteropathy, congenital microvillous atrophy, and the idiopathic intractable diarrhoea of infancy syndrome. A small intestinal biopsy is required for the diagnosis of microvillous atrophy and has allowed this discrete disorder to be recognised as part of the differential diagnosis of the intractable diarrhoea of infancy syndrome, along with autoimmune enteropathy. Indeed, proximal small intestinal biopsy has facilitated the evaluation of therapeutic trials in these diseases.

In conclusion, we have reviewed the use of proximal small intestinal mucosal biopsy in children presenting with chronic diarrhoea. The routine performance of this procedure has established different diagnoses within the umbrella of chronic diarrhoea and influences management. In experienced hands it is a simple and safe procedure and is an essential investigation in chronic diarrhoea.


Commentary

This paper comes from a department which has set standards for paediatric gastroenterologists so its conclusions must be treated with respect. Children with diarrhoea lasting more than 14 days, in whom an enteropathy was suspected, underwent small intestinal mucosal biopsy. The authors conclude that this investigative technique is essential in such children.

Apart from providing an interesting insight into the spectrum of chronic diarrhoeal disease as experienced in east London, what message does this paper hold for general practitioners and general paediatricians who, elsewhere in the country, treat the bulk of such patients?
Unfortunately we are not told the population base from which the study group originated, nor the routes of referral, nor do we learn how the children in whom an enteropathy was suspected were differentiated from those in whom it was not. Presumably the grounds were clinical and this decided whether or not to perform a small intestinal mucosal biopsy. It would have been instructive to know how accurate was clinical impression, particularly as we learn that the authors considered coeliac disease in 55% and confirmed this diagnosis in 8%.

We cannot, of course, what proportion of children who were not biopsied had an enteropathy. These children presumably lost their symptoms, which begs the question of how many of the biopsied children would have become asymptomatic without treatment.

Thus, the fact that 44% of children had an abnormal small intestinal mucosal biopsy specimen does not prove the procedure was necessary. One does not perform skin biopsies on children with eczema nor lung biopsy on those with lobar pneumonia even though they would be abnormal. The clinician treats the condition and anticipates improvement; if this does not occur then, of course, he might need to investigate further.

Of course, if the enteropathy is likely to be longstanding or permanent—as in coeliac disease—or if the clinical picture is confusing and disturbing, the need for small intestinal mucosal biopsy is not disputed. The timing is crucial: in our, admittedly favoured, part of the country general practitioner or self referral of a child with diarrhoea of two weeks’ duration is extremely unusual unless emergency admission had been sought because of anxiety about dehydration. Many general practitioners would have observed the effect of a cows’ milk free diet first. Are they to be deprived of that option in the way that they are, rightly, strongly discouraged from experimenting with a gluten free diet?

Biopsy evidence permitted patients with toddler's diarrhoea, postenteritic syndrome, and cryptosporidiosis to avoid a period of cows’ milk restriction but we question whether this justifies widespread adoption of the recommendations of the authors. Certainly, there were 14 cases of giardiasis not diagnosed by stool analysis (although three cases were missed on biopsy and duodenal aspiration). It would have been interesting to know whether any of those not biopsied had giardia infection and whether this diagnosis would have been entertained had their diarrhoea persisted and whether it would have been picked up by repeated stool sampling.

Jejunal biopsy is a very safe and not too distressing procedure in skilled hands, although complications such as haemorrhage and small bowel perforation have been described. Would it be as safe outside gastroenterological centres of excellence? Radiation protection regulations now demand, by statute, that individuals carrying out the procedure under fluoroscopic control must have attended a training course and acquired the necessary certification. The presence of a radiologist in the department does not confer exemption. In small hospitals, therefore, it is likely that consultants would be the only certificated investigators and cost effectiveness of the procedure would be in doubt.

This paper undoubtedly adds to the body of knowledge on chronic diarrhoeal disease in childhood. We consider, however, that the inference that toddler’s diarrhoea should not be diagnosed without biopsy will strain the credulity of general paediatricians. It remains incontrovertible that suspected coeliac disease must be confirmed histologically but the authors’ experience of proving this diagnosis in only one in seven of those suspected clinically demands better prebiopsy criteria. None of the many immunological and tolerance tests described have totally lived up to their original promise but we should look forward to the improvement of screening for coeliac disease both clinically and by such approaches as discriminant analysis of a cohort of tests.

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