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Adult Coeliac Disease in Tropics

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Primary malabsorption syndromes occurring in the tropics were generally regarded as examples of tropical sprue, and sensitivity to gluten was not thought to be a significant aetiological factor. Even when steatorrhoea occurred among Europeans in those regions it was attributed to tropical sprue, and the possibility of coeliac disease or idiopathic steatorrhoea was usually not considered. Before the recognition of gluten-sensitivity in the causation of coeliac disease this illness was thought to be a separate entity from tropical sprue, chiefly because of its onset in early childhood and its chronic and often progressive course.

Recently, when working on the aetiology of malabsorption in North India, we found that, though most of the cases of primary malabsorption were examples of tropical sprue, there were a few cases of gluten-sensitive enteropathy among them. We came across patients who failed to show a favourable response when treated on the usual lines for tropical sprue. When they were further analysed and investigated the diagnosis of adult coeliac disease became obvious. The diagnostic evidence consisted of the clinical and biochemical features, the jejunal mucosal appearances, a favourable response to a gluten-free diet, and the occurrence of symptoms in certain patients in both their childhood and their adulthood.

Intestinal biopsy now affords an important criterion for the diagnosis of the disease. The presence of mucosal changes has been noted in a variety of diseases, but a severe lesion (flat mucosa) is usually a feature of coeliac disease if tropical sprue has been excluded (Fone *et al.*, 1960; Rubin *et al.*, 1960a; Girdwood *et al.*, 1961; Cooke *et al.*, 1963). Adult coeliac disease being the only recognized condition that responds to a gluten-free diet, the demonstration of the characteristic mucosal lesion and a favourable response to dietary therapy with relapse on reintroduction of gluten into the diet provide between them a fairly accurate basis for its diagnosis.

The present study aims to report seven cases of adult coeliac disease occurring in the tropics.

Material and Methods

This study was conducted at Irwin Hospital, New Delhi. Seven cases of suspected coeliac disease were investigated and followed from 3 to 30 months while they were on a gluten-free diet.

The patients were investigated by three-day quantitative determinations of stool fat (van de Kamer *et al.*, 1949), the D-xylose test as described by Santini *et al.* (1961), a barium-meal follow-through study with a non-flocculable barium suspension, and small-bowel biopsy performed by means of a Crosby capsule (Crosby and Kugler, 1957) before and at intervals after the gluten-free diet was begun. Three grades were recognized in the histological evaluation of the biopsy specimens. Grade I consisted of mild-to-moderate changes characterized by the irregularity of the surface epithelium, increased cellular infiltration of the lamina propria, and stunting of villous height. In grade 2 these changes were more advanced (partial villous atrophy), and grade 3 was characterized by subtotal villous atrophy, glandular hypertrophy, marked round-cell infiltration of the lamina propria, and epithelial cell degeneration.

Results

Details of the seven cases are given in the Table. In five cases the disease started in childhood and continued with remissions and exacerbations up to adulthood. In one patient (Case 7) there was a possible positive family history in that one of his elder sisters had died of chronic diarrhoea. All except two patients (Cases 2 and 4) were stunted in growth. They came to hospital either because of troublesome diarrhoea or because of stunted growth. All seven complained of weakness and loss of weight and were having diarrhoea of varying severity. Abdominal distension was noted by four, symptoms of anaemia by two, and stomatitis by four. A history of tetany was elicited in only one patient, and none had paraesthesiae, a bleeding tendency, bone pains, or oedema over the feet.

Response to a Gluten-free Diet

Clinical

To give a fair trial to this sort of therapy it is important to eliminate completely wheat, barley, oats, and their products from the diet. Strict adherence to the prescribed diet is necessary for judging the success of diet therapy. After six weeks

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of a gluten-free diet patients were re-evaluated. Clinical improvement within this period was striking in three of them (Cases 2, 5, and 7), with control of diarrhoea, increase in weight, and feeling of well-being. In Case 4 it was eight weeks before a clinical response occurred, and in two others the response was irregular, the reason being their inability to adhere to dietary instructions. In Case 6 the diarrhoea was not fully controlled even after one year of diet therapy, though the number of stools became fewer and their consistency improved. This patient, however, gained weight and felt much better.

Reintroduction of gluten after response to treatment was tried in every patient, and all showed signs of relapse in from 2 to 15 days. However, one of them (Case 3) was able to tolerate gluten much better than the rest.

Biochemical and Radiological

The return of fat-absorption to normal takes four to eight weeks in most patients (Benson *et al.*, 1964). However, a resistant steatorrhoea despite improvement in the clinical picture is well known (French *et al.*, 1957 ; Green *et al.*, 1959).

Faecal fat excretion was measured in the seven patients before the institution of a gluten-free diet and at varying intervals afterwards, all showing a marked decrease. In five it was found to be within normal limits after six weeks' therapy. In two others (Cases 6 and 7) the severity of the steatorrhoea decreased, but faecal fat excretion was still not within normal limits even after 12 and 6 months of diet therapy respectively, one of them (Case 6) being the patient in whom diarrhoea persisted. This patient was also given a six-weeks course of corticosteroids without much benefit. The present data support the view (Benson *et al.*, 1964) that a clinical remission can be obtained without restoration of fat-absorption to normal and that scrupulous adherence to a gluten-free diet is necessary if absorption is to be improved.

A D-xylose-excretion test by a 5-g. dose was also carried out before and after institution of diet therapy. Improvement in absorption was notable in these patients (see Table). The test is not specific for coeliac disease but is usually found to be abnormal in untreated cases (Shiner *et al.*, 1962). It has been a reliable screening test for the diagnosis of primary malabsorptive disorders, as the results are normal in cases of pancreatic malabsorption.

Radiographic examination of the small bowel, though not specific, is a helpful procedure for the evaluation of intestinal function.

Thickening of mucosal folds, flocculation and segmentation of barium in isolated intestinal loops, and dilatation are the abnormalities commonly encountered. Marked changes are helpful in the diagnosis. Radiographic studies were made of all seven patients as part of the initial evaluation. A non-flocculable barium suspension was used. As indicated in the Table, severe changes, with dilatation of loops, segmentation, and thickening of mucosal folds, were found in all cases except one. Of the five cases followed up four showed improvement in the radiographic picture, while in one it had returned to normal. The radiological abnormalities of coeliac disease are known to regress when clinical remission is obtained with a gluten-free diet, though this may not be the rule (Benson *et al.*, 1964).

Histological Abnormality in Proximal Jejunum

The mucosal lesion found by peroral biopsy of the upper small intestine is now regarded as an important feature in the diagnosis of coeliac disease in the absence of tropical sprue. It not only helps in establishing the diagnosis but is useful in evaluating the effect of diet therapy (Benson *et al.*, 1964). In this series biopsies were performed in six patients before institution of the gluten-free diet. Four of these showed grade 2 changes (Fig. 1), and in two the mucosa was flat and featureless, indicating grade 3 changes (Fig. 2). Serial biopsies were taken in four cases after they had been put on a gluten-free diet. For final evaluation only the first (pretreatment biopsy) and the latest biopsy taken when the patient had been on a gluten-free diet are considered. In Cases 4, 6, and 7 no significant change was found in repeat jejunal biopsies. In Case 1, where the biopsy was repeated after 30 months of gluten-free diet, improvement was observed, but it was not significant

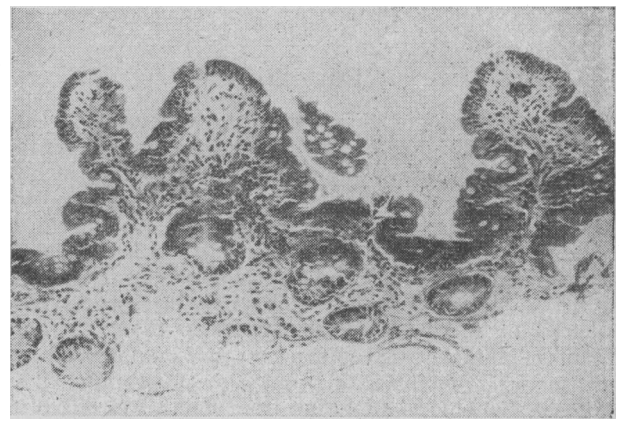

FIG. 1.—Pretreatment jejunal biopsy of Case 1 showing grade 2 changes consisting in broadening and blunting of villi. (Haematoxylin and eosin. ×100.)

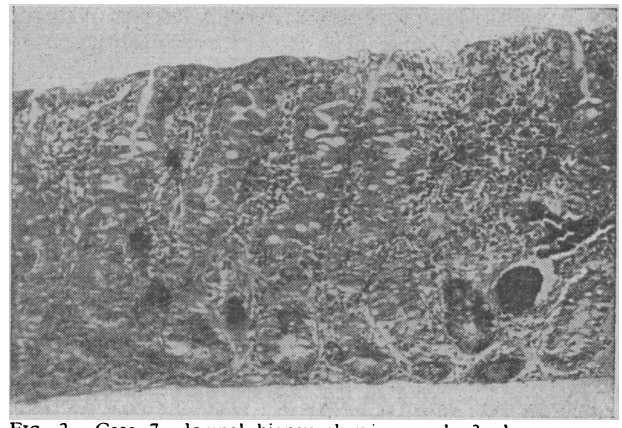

FIG. 2.—Case 7. Jejunal biopsy showing grade 3 changes consisting in complete fusion of villi, producing a flat, featureless surface. (Haematoxylin and eosin. ×100.)

Summary of Patient Data in Adult Coeliac Disease

Case No.	Age	Sex	Duration of Symptoms in Years	Before Treatment				Duration of Treatment in Months	Adherence to Gluten-free Diet	After Treatment			
				Fat in 24 hr.	D-Xylose 5 g. Dose	Barium Meal	Jejunal Biopsy Grade			Fat in 24 hr.	D-Xylose 5 g. Dose	Barium Meal	Jejunal Biopsy Grade
1	22	M	17	7·5	0·8	+ +	2	30	Lax	3·5	1·0	+	2*
2	35	F	10	10	—	+ +	—	30	,,	5·1	—	+	—
3	14	F	13	8	1·2	+ +	2	12	,,	6·0	—	—	—
4	39	F	2	13·2	0·22	+	2	10	Strict	5·0	1·5	Normal	2
5	15	M	5	8	1·2	+ +	3	3	,,	3·2	—	—	—
6	13	F	2	16·7	1·1	+ +	2	12	Lax	8·0	1·4	+	2
7	17	M	15	36·5	0·75	+ + +	3	6	Strict	10·0	0·75	+ +	3

* Grade not changed, but definite improvement shown (see Figs. 1 and 3.

enough to alter the grade of abnormality (see Figs. 1 and 3). These findings are understandable because changes in the mucosal abnormality are slow to take place and our group has not been studied long enough.

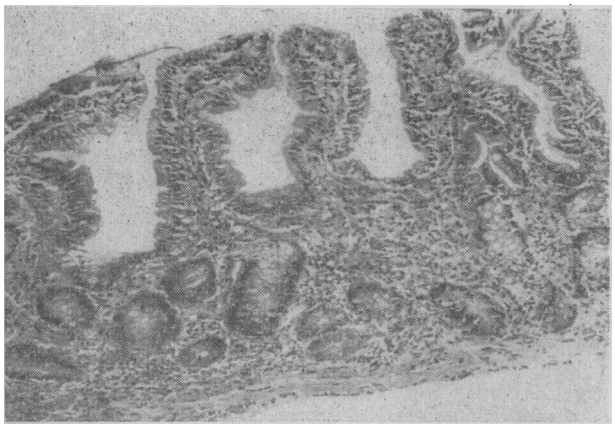

FIG. 3.—Post-treatment jejunal biopsy of Case 1 showing the improvement. (Haematoxylin and eosin. ×100.)

Discussion

The main purpose of the present communication is to report the occurrence of adult coeliac disease in a tropical region, as we have not come across any other study reporting such cases from the tropics. Maybe in some regions of the tropics it does not occur, or is rare, or is not brought to light because rice is the staple diet and wheat and its products are not consumed (e.g., South India and other countries of South-east Asia). There is an impression that the sprue syndrome is uncommon in tropical Africa (Gardner, 1958). It may be relevant to point out that gluten has been incriminated as one of the factors responsible for primary malabsorption syndrome in some of the reports appearing from South America (Cancio *et al.*, 1961).

The seven cases of adult coeliac disease reported here were collected in a period of three years. During this time our unit came across 87 cases of tropical sprue and 49 cases of secondary malabsorption syndrome. The cases of tropical sprue constitute the subject of a separate publication (Misra *et al.*, 1966).

In the present series the diagnosis was not accepted unless steatorrhoea, a definite histological abnormality of the small-intestinal mucosa, and improvement while on a gluten-free diet were all demonstrated. It is interesting to note that even in this small series there were five patients in whom the disease had started in childhood and had continued since with remissions and exacerbations. Marked stunting of growth in five of the series was noteworthy. Stunting of growth in patients with adult coeliac disease has been reported (Cooke *et al.*, 1953 ; Badenoch, 1960).

The only significant variation from the clinical picture as described in the West is the absence of bleeding tendencies, tetany, and a paraesthesiae. The response to a gluten-free diet was good in patients who followed the diet therapy strictly. In general, clinical remission was followed by biochemical and radiological improvement, but histological improvement was very minimal and in no patient was there reversal to normality. Initially the mucosal defect was thought to be irreversible (Shiner and Doniach, 1959 ; Rubin *et al.*, 1960b), but subsequent studies have shown that improvement occurs even in cases of adult coeliac disease, though it may be slow in coming (Rubin *et al.*, 1962 ; Shiner, 1963). Besides, failure of histological improvement may be due to the patient's inability to follow the gluten-free diet rigidly, and small doses of gluten may not affect the clinical remission but may be sufficient to injure the mucosa. The other explanation may be that in adult coeliac disease the mucosal injury reaches a stage where reversibility is no longer possible.

Hitherto, not much emphasis has been laid on the role of gluten-sensitivity in the causation of primary malabsorption syndromes in the tropics. These cases suggest that, though it can be incriminated in only a small fraction of the cases, it cannot be entirely ignored, particularly in those regions where wheat is the staple diet.

Summary

Seven cases of adult coeliac disease occurring in tropical regions are reported with clinical, biochemical, radiological, and histopathological data, suggesting that, even though gluten-sensitivity is a relatively uncommon cause of primary malabsorption syndromes in the tropics, it is not entirely absent. A follow-up study of these patients varying from 3 to 30 months is presented.

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