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Experience with a Gluten Free Diet in the Treatment of Linear IgA Disease

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A study was undertaken to determine whether the skin eruption of linear IgA disease (LAD) was gluten dependent. Six patients with LAD were treated with a gluten free diet (GFD) for an average period of 33 months (range 19–48). Although one patient with LAD had an enteropathy which was clearly gluten sensitive, there was no convincing evidence that the rash of any of the patients responded to a GFD. Four of the six patients showed no significant alteration in their drug requirements. The remaining 2 patients showed a fall in minimum drug requirement but there was no increase after gluten challenge indicating that they were entering spontaneous remission. This contrasts to the situation in dermatitis herpetiformis, where both the rash and the enteropathy are gluten dependent. These data add further to the evidence that LAD and dermatitis herpetiformis are separate entities. *Key words: Dermatitis herpetiformis; Coeliac disease; Gluten.* (Received August 15, 1986.)

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The purpose of this study was to investigate the efficacy of a gluten free diet (GFD) on the rash of patients with linear IgA disease (LAD). This would allow a judgement to be made on the relationship between LAD and dermatitis herpetiformis (DH) which has been shown to be gluten sensitive (1, 2).

PATIENTS AND METHODS

Six patients (3 men and 3 women) with LAD were studied. The average age was 51 years (range 28–71). All the patients studied presented with a sub-epidermal bullous dermatosis and in all cases the diagnosis of LAD was confirmed by demonstrating a homogeneous-linear deposit of IgA along the dermo-epidermal junction of uninvolved skin using direct immunofluorescence (3).

A jejunal biopsy was performed prior to starting a GFD where possible and examined for morphological and hitological evidence of a gluten sensitive enteropathy (GSE) (4). The minimum drug requirement for control of the rash was determined before starting the GFD.

The patients were seen by a dietician and given advice on how to maintain a strict GFD. The patients were then assessed at three monthly intervals. At each attendance the drug dosage required to control the rash was noted and the diet was assessed as to its strictness as previously described (5). An overall assessment of the strictness of the diet was made throughout the period of study.

The GFD was continued for an average of 33 months (range 19–48). In 3 of the 6 patients, a normal, gluten containing diet was resumed and in each patient the effect of a resumption of a normal diet on minimum drug requirements to control the rash was assessed.

RESULTS

The results of this study are summarised in Table I. Four of the 6 patients showed no appreciable reduction in their minimum drug requirement.

Table I. *Details of patients included in the study with response of the rash to a gluten free diet*

Grading of GFD-1 = absolutely strict with no lapses, 2 = very occasional gluten intake and usually unintentional. S-P = sulphapyridine, S-M = sulphamethoxypyridazine.

Patient	Sex	Age	Gut biopsy prior to GFD		Grade of GFD	Duration GFD (months)	Drugs before GFD (daily dose)	Drugs after GFD (daily dose)
			Morphology	IELC				
1	M	28	Normal	102	2	40	Dapsone 200 mg Prednisolone 10 mg S-P 0.5 g	Dapsone 200 mg S-M 1.5 g
2	M	38	Not done		2	30	Dapsone 50 mg*	Dapsone 50 mg*
3	F	64	Normal	128	1	19	Dapsone 50 mg	None
4	F	59	Normal	140	1	39	Dapsone 50 mg	Dapsone 50 mg/month
5	M	71	Normal	144	2	48	Dapsone 50 mg	S-M 0.25 g
6	F	46	Not done		1	24	S-M 0.5 g	S-M 0.25 g

* This patient had occasional relapses throughout the period of study when up to 200 mg of dapsone daily were required to control the rash.

Patient 1 had co-existing ulcerative colitis treated with prednisolone at the outset of the study. This became quiescent during the study and the drug was gradually withdrawn. His overall sulphone and sulphonamide requirement for control of the rash remained constant throughout the period of the GFD.

Patient 2 had started himself on a GFD 18 months prior to presentation at St. Mary's Hospital, in the belief that he had DH. The GFD was not entirely strict, however, and he was considered not to be on a GFD at the time of entry into the study. Over the next 30 months he was on a GFD but there was no appreciable fall in dapsone requirement—he then resumed a normal diet. A jejunal biopsy was taken prior to resumption of a normal diet which showed normal villi with an intra-epithelial lymphocyte count (IELC) of 328 lymphocytes/1 000 epithelial cells (normal upper limit 250). Six months after reintroduction of gluten there had been no increase in dapsone requirement to control his rash but he developed bloating of the abdomen with looseness of his stools. A repeat jejunal biopsy at that time showed sub-total villous atrophy (convoluted mucosa) with an IELC of 602. He was then recommenced on a GFD for the intestinal abnormality and there has been no reduction in dapsone requirement in the 2 years since then.

Patient 3 was able to slowly reduce her dapsone requirement over 19 months at which point she required no further drugs to control her rash. Six months after that she recommenced a normal diet but has had no recurrence of the rash after 24 months. A repeat skin biopsy at that time showed the homogeneous-linear deposit of IgA to still be present.

Patient 4 showed a marked fall in dapsone requirement from 50 mg/day to 50 mg/month after 39 months of a GFD. However, following resumption of a normal diet, there has been no increase in dapsone requirement for control of the rash.

Patient 5 showed no reduction in dapsone requirement in the first 12 months of a GFD. At that point he developed side effects from the dapsone and his medication had to be changed to sulphamethoxypyridazine 0.5 g daily. Over the following 36 months this was reduced to 0.5 g on alternate days.

Patient 6 showed a slight fall in the minimum dose of sulphamethoxypyridazine from 0.5 g/day to 0.25 g/day after 24 months of a GFD.

DISCUSSION

As the result of previous studies (3, 6) the classification of LAD amongst the bullous dermatoses remained uncertain. The finding of Leonard et al. (3) that 24% of patients with LAD had an abnormal jejunal mucosa, caused some reservation about regarding LAD as a separate entity from DH. At that time, however, there were no data on the efficacy of a GFD on the rash or the enteropathy of patients with LAD. Gluten sensitivity is inherent in the diagnosis of DH on the basis of the response of the rash to a strict GFD and relapse after challenge (2, 7, 8, 9, 10, 11). A more recent study (12) has shown the IgA deposits in DH to be qualitatively different from those of LAD. Failure of the rash of LAD to show the same response to a GFD as DH would give further evidence for regarding the two diseases as distinct pathological entities.

LAD is a rare disorder and this is the major reason for the difficulty in obtaining worthwhile data on the efficacy of a GFD in its management. The patient selection in this study was not ideal in that one patient was being treated for ulcerative colitis at the time of entry and a second patient had commenced a partial GFD prior to the study. A further difficulty arose when trying to assess patient compliance with the diet. In DH the dietary assessment can be supported in patients who are apparently resistant to the GFD by repeat jejunal biopsy. Failure of the small intestine to heal, in addition to an absence of a fall in the minimum drug requirement to control the rash of a patient with DH would indicate that the diet had not been strict. This was not possible in LAD where none of the 4 patients who had jejunal biopsies performed prior to commencement of the GFD had an abnormal mucosa. Therefore, the dietary assessment was the only measure of strictness of the diet that was available. From this, 3 patients had a diet that was considered to be absolutely strict, and the remaing 3 patients showed occasional lapses from the diet. On the basis of our previous studies in DH, 96% of the former group and 47% of the latter group would have been expected to have responded to the diet by complete withdrawal of drug therapy to control the rash after an average period of 25 months and 39 months respectively (5). The results of this study have shown the response of the rash of LAD to a GFD to be unimpressive and there seems to be little justification for recommending it to patients for treatment of their rash.

Two patients did show an appreciable fall in their drug requirement (No. 3 and No. 4). One of these (No. 3) appeared to enter spontaneous remission as the resumption of a normal, gluten containing, diet has not led to any recurrence of the rash after 24 months. In DH it took an average of 3 months for the rash to recur in 11 out of 12 patients challenged (2). The other patient (No. 4) also appears to be entering spontaneous remission as her drug requirements have not increased 12 months after resumption of a normal diet. Spontaneous remission in LAD has been previously described (3).

Patient 2 provided interesting data. Although he did not have a jejunal biopsy at the commencement of the study, one tekan prior to reintroduction of gluten was morphologically normal. The slightly raised IELC supported the impression that he had occasional lapses from his diet. A biopsy taken 6 months after reintroduction of gluten, at which stage he had symptoms suggestive of a GSE, showed sub-total villous atrophy with a markedly raised IELC. Throughout the period of study his drug requirements have fluctuated but they have not altered appreciably overall. These results indicate that he has a GSE but his rash is not gluten sensitive. This is of relevance when considering the findings of our previous study (3) in which 24% of patients had an abnormal jejunum, and that of de Franchis et al. (13) in which 3 out of 5 patients biopsied were abnormal. It thus appears that patients with LAD have a rash that is not gluten sensitive but that 24% of these patients have a co-existing enteropathy that may well be gluten sensitive on the basis of

the findings in this patient. Presumably, patients with LAD are genetically predisposed to develop a GSE, and this is supported by the report of Doherty et al. (14) who found an increased incidence of jejunal abnormality in individuals who were HLA-B8 positive. 56% of patients with LAD were reported to have HLA-B8 (3). A jejunal biopsy remains indicated in patients with LAD, therefore, as some may have an associated GSE that requires treatment with a GFD.

In conclusion, there is no evidence to suggest that the rash of LAD is caused by gluten and a GFD is not indicated for its treatment. The results of this study add further to the evidence that LAD and DH should be regarded as separate disease entities.

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REFERENCES

1. Fry L, Seah PP, Riches DJ, Hoffbrand AV. Clearance of skin lesions in dermatitis herpetiformis after gluten withdrawal. Lancet 1973; i: 288–291.
2. Leonard JN, Haffenden GP, Tucker WFG, Unsworth DJ, Swain AF, McMinn RMH, Holborow EJ, Fry L. Gluten challenge in dermatitis herpetiformis. N Engl J Med 1983; 308: 816–819.
3. Leonard JN, Haffenden GP, Ring NP, McMinn RMH, Sidgwick A, Mowbray JF, Unsworth DJ, Holborow EJ, Blenkinsopp WK, Swain AF, Fry L. Linear IgA disease in adults. Br J Dermatol 1982; 107: 301–316.
4. Fry L, Seah PP, Harper PG, Hoffbrand AV, McMinn RMH. The small intestine in dermatitis herpetiformis. J Clin Pathol 1974; 27: 817–824.
5. Fry L, Leonard JN, Swain AF, Tucker WFG, Haffenden G, Ring N, McMinn RMH. Long term follow-up of dermatitis herpetiformis with and without dietary gluten withdrawal. Br J Dermatol 1982; 107: 631–641.
6. Chorzelski TP, Jablonska S, Beutner EH. Adult form of linear IgA bullous dermatosis. In: Beutner EH, Chorzelski TP, Bean SF, eds., Immunopathology of the skin. New York: John Wiley & Sons, 1979: 316–319
7. Fry L, McMinn RMH, Cowan JD, Hoffbrand AV. Gluten free diet and reintroduction of gluten in dermatitis herpetiformis. Arch Dermatol 1969; 100: 129–135.
8. Heading RC, Paterson WD, McClelland DBI, Barnetson RStC, Murray MSM. Clinical response of dermatitis herpetiformis skin lesions to a gluten free diet. Br J Dermatol 1976; 94: 509–514.
9. Reunala T, Blomquist K, Tarpila S, Halme H, Kangas K. Gluten free diet in dermatitis herpetiformis. Br J Dermatol 1977; 97: 473–480.
10. Harrington CI, Read NW. Dermatitis herpetiformis; effect of a gluten free diet on skin IgA and jejunal structure and function. Br Med J 1977; i: 872–875.
11. Katz SI. Dermatitis herpetiformis—the skin and the gut. Ann Int Med 1980; 93: 857–874.
12. Leonard JN, Haffenden GP, Unsworth DJ, Ring NP, Holborow EJ, Fry L. Evidence that the IgA in patients with linear IgA disease is qualitatively different from that of patients with dermatitis herpetiformis. Br J Dermatol 1984; 110: 315–321.
13. de Franchis R, Primignani M, Cipolla M, Vecchi M, Agape D, Monti M, Berti E, Zuccato E, Mussini E. Small bowel involvement in dermatitis herpetiformis and linear IgA bullous dermatosis. J Clin Gastroenterol 1983; 5: 429–436.
14. Doherty M, Bary RE. Gluten induced mucosal changes in subjects without overt small bowel disease. Lancet 1981; i: 517–520.