Figure 3 Awake EEG record showing generalised spike and wave discharges.

or without CNS manifestations, the possibility of abdominal epilepsy should be considered after exclusion of more common aetiologies for the presenting complaints. The investigation in these patients should proceed with an EEG. Treatment typically begins with anticonvulsant drugs; oxcarbazepine is an effective anticonvulsant in this syndrome.

Sangit Ranjan Dutta, Indrajit Hazarika, Bhabani Prasad Chakravarty

Department of Medicine, Gauhati Medical College and Hospital, Bhangagarh, Guwahati, Assam, India

Correspondence to: Dr S Dutta, Department of Medicine, Gauhati Medical College and Hospital, Bhangagarh, Guwahati 781032, Assam, India; indrajit25@yahoo.com

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The pattern of cytokine expression determines the degree of mucosal damage

It is widely accepted that both qualitative and quantitative differences in cytokine expression determine the extent of mucosal damage in different intestinal pathologies.¹ However, few comparative analyses of these conditions have been published to date.

We analysed mRNA expression of several cytokines and effector molecules in intestinal biopsies by real time polymerase chain reaction (summary of study groups and results are shown in table 1). These included samples from healthy controls (duodenal biopsies from patients suspected of having an intestinal pathology, later ruled out), non-specific small bowel inflammation (mild histological changes in the biopsy consisting of a non-specific lamina propria infiltrate but no villous

atrophy), active coeliac disease (on a gluten containing diet) and ulcerative colitis from affected tissue areas. These pathologies show mild, moderate and severe degrees of mucosal damage, respectively, and the cytokine pattern varies significantly, from lack of cytokine upregulation in mild inflammations to the highest levels and widest array of proinflammatory cytokines in ulcerative colitis, together with a parallel increase in levels of effector molecules involved in mucosal damage (inducible nitric oxide synthase (iNOS), matrix metalloproteinase-3 (MMP-3) and granzyme B).

In tissue samples from patients with non-specific small bowel inflammations, levels of cytokines or effector molecules did not increase in any case, despite the findings of microscopic mild alterations in these tissue samples. We hypothesise that the immune activation which triggers the mucosal damage might have occurred during one or several past inflammatory episodes, although these were no longer measurable at the molecular level.

In active coeliac disease, effector molecules showed raised levels above healthy controls and, moreover, iNOS mRNA levels correlated with the degree of mucosal damage (Marsh score) ($p = 0.001$). Of the cytokines analysed, only interferon γ (IFN γ) was clearly increased

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Figure 4 EEG record showing left temporal dysrhythmia in the form of slowing.

in active coeliac disease. These data may indicate the presence of a longstanding inflammation at the time of sample collection, characterised by maintained high IFN γ levels together with other cytokines previously reported, such as interleukin (IL)-18,² and these might be responsible for the moderate

induction of effector molecules in coeliac disease. Additionally, patients with coeliac disease might undergo stronger mucosal immune activation during the short term response following each episode of gluten challenge, characterised by higher levels of proinflammatory cytokines.³

Tissue samples from patients with ulcerative colitis showed increased levels of proinflammatory cytokines (IFN γ , IL-1 β , IL-6 and IL-12) and effector molecules (iNOS, MMP-3 and granzyme B) above healthy controls, and these were also higher than those found in coeliac disease. Moreover, significant

Table 1 mRNA expression in the different study groups

	Healthy controls duodenum (n = 19)	Inflammatory controls duodenum (n = 15)	Active coeliac disease (n = 36)	Ulcerative colitis $\ddagger$ § (n = 26)
IFN γ	0.548 [3.479]	0.904 [2.572]	1.895 [12.229]**	3.092 [7.591]*††
TGF β	4.275 [15.464]	5.460 [12.696]	2.845 [6.055]*	3.524 [8.794]
TNF α	0.628 [2.085]	2.700 [4.208]	0.754 [4.559]	0.989 [1.844]
IL-1 β	3.302 [7.133]	1.036 [2.646]	2.031 [11.048]	34.255 [1684.999]**††
IL-4	0.000 [0.476]	0.000 [0.000]	0.000 [0.549]	5.261 [13.988] **††
IL-6	8.134 [72.997]	2.984 [23.648]	6.202 [17.220]	303.136 [3223.885]**††
IL-12(p40)	0.000 [0.602]	0.000 [0.000]	0.000 [0.007]	2.069 [30.536]*††
iNOS	2.236 [17.828]	3.814 [6.619]	10.781 [68.578]**	28.857 [106.052]**†
MMP-3	0.000 [1.234]	0.000 [0.000]	2.438 [27.497]*	30.586 [271.060]*††
TIMP-1	12.692 [26.881]	13.856 [47.133]	10.395 [20.357]	133.928 [772.964]**††
Granzyme B	28.704 [81.825]	13.720 [25.880]	65.589 [195.397]*	142.376 [365.682]**†

IFN γ , interferon γ ; IL, interleukin; iNOS, inducible nitric oxide synthase; MMP-3, matrix metalloproteinase-3; TGF β , transforming growth factor β ; TIMP-1, tissue inhibitor of matrix metalloproteinase-1; TNF α , tumour necrosis factor α .

Results were normalised to β -actin as the housekeeping gene, and are expressed as arbitrary units (median [interquartile range]).

Mann-Whitney U test: compared with healthy controls (* $p < 0.05$, ** $p < 0.001$) and active coeliac disease († $p < 0.05$, †† $p < 0.05$).

‡For simplicity, results from ulcerative colitis patients were compared with duodenal healthy controls; mRNA levels did not significantly differ from those found in colonic healthy controls (data not shown).

§Of 26 patients with ulcerative colitis, 11 had no treatment, 15 received either 5-ASA or salazopyrine (two cases additionally had a low dose of corticotherapy) and none received immunosuppressants.

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Figure 5 EEG record showing right frontal focal discharges.

correlations between mRNA levels of upregulated cytokines and effector molecules were found (data not shown). These data suggest that high levels of proinflammatory cytokines in ulcerative colitis directly trigger effector molecules, leading to a severe degree of mucosal damage.

A J León, E Gómez, J A Garrote

Department of Paediatrics and Immunology and Institute of Biology and Molecular Genetics (IBGM), Universidad de Valladolid, Valladolid, Spain

J A Garrote

Research Unit, Hospital Clínico Universitario, Valladolid, Spain

E Arranz

Department of Paediatrics and Immunology and Institute of Biology and Molecular Genetics (IBGM), Universidad de Valladolid, Valladolid, Spain

Correspondence to: Dr E Arranz, Department of Paediatrics and Immunology, and Institute of Biology and Molecular Genetics, University of Valladolid, C/ Ramón y Cajal 7, 47005-Valladolid, Spain; earranz@med.uva.es

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Weight loss induced by orlistat reverses fatty infiltration and improves hepatic fibrosis in obese patients with non-alcoholic steatohepatitis

Non-alcoholic steatohepatitis (NASH) may cause progressive hepatic fibrosis and cirrhosis.^{1,2} To date, treatment has been restricted to diet and weight loss, but without compelling results. Orlistat (Xenical) is a natural lipase inhibitor, which reduces the absorption of dietary fat by 30%³ and improves insulin resistance and lipid profile.^{4,5} Whether or not orlistat reverses hepatic fibrosis and inflammation in obese patients with NASH has not been assessed.

A total of 14 obese patients with NASH underwent liver biopsy before and after 6 months treatment with orlistat (120 mg thrice daily). Patients were also provided a

moderate calorie-restricted diet with a median daily intake of 25 kcal/kg body weight/day. Parameters of oxidative stress, insulin resistance, lipids and liver histology were measured. All patients signed informed consent. Of 22 recruited patients, 14 (10 women and 4 men, mean (SD) age of 42 (3) years, and body mass index of 31.5 kg.m²) completed the study. In all, four patients had mixed hyperlipidaemia, five had diabetes mellitus type 2 and five had obesity alone.

Orlistat reduced fatty infiltration in 10 patients (70%, $p < 0.01$), 3 of whom had normal liver fat content after treatment. Orlistat improved inflammatory activity by 2 grades in 28% and by 1 grade in 50% of patients and effected no change in 22% of patients. A total of 5 (35%) patients returned to normal inflammatory activity. Orlistat improved hepatic fibrosis by 2 grades in 3 (21%) patients and by 1 grade in 7 (50%) patients. There was no change in 4 (28%) patients. The mean (SD) weight decreased from 94.1 (15.5; median 93.5) kg pretreatment to 89 (15.1; median 87.0) kg post treatment (-5.3% change). One patient did not lose weight. Of the patients who lost weight, the percentage of body weight lost ranged from (-2.3% to -16.3%, median -5%, mean (SD) 5.4 (4.3)%). Seven patients lost at least 6% of their body weight. The weight loss correlated only with the extension of fat ($r = 0.5$), but not with the changes in fibrosis or in inflammation. A significant improvement in serum levels of alanine aminotransferase, aspartate aminotransferase and lipids occurred