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Eosinophilic gastroenteritis

I wish to respond to the article "Primary eosinophilic disorders of the gastrointestinal tract" by Yan and Shaffer.¹

In this article Yan *et al*¹ wrote extensively on the physiology of the recruitment and activation of eosinophils in the gastrointestinal tract.

We wish to present a case that serves to bring to light an alternative route of recruitment and activation of eosinophils.

A 47-year-old man underwent laparoscopic high anterior resection for recurrent bouts of acute diverticulitis. This diagnosis was based preoperatively on CT and colonoscopic findings, and confirmed postoperatively on pathological examination of the resected specimen.

He had no personal or family history of atopy, inflammatory bowel disease or connective tissue disease.

He re-presented to the Accident and Emergency Department 3 weeks later with severe crampy abdominal pain and vomiting, and small bowel obstruction was diagnosed by small bowel follow-through. At laparotomy there was an inflammatory small bowel mass in the right iliac fossa related to a pinhole perforation of the ileum. The colonic anastomosis was intact. The affected small bowel was resected and a small bowel anastomosis formed. The patient suffered severe persistent pain in the postoperative period; however, vital signs remained normal and there was no clinical evidence of peritonism.

Haematological and biochemical investigations including white cell count and differential were normal. CT abdomen and pelvis and gastrograffin enema revealed no cause for the ongoing symptoms.

Histological examination of the resected specimen of small bowel revealed eosinophilic infiltrate of the lamina propria and evidence of perforation, leading to a diagnosis of perforated eosinophilic gastroenteritis.

The gastroenterology service was consulted and the patient commenced on oral steroid treatment. The pain settled completely over 48 h and he was discharged home on a reducing dose of steroids.

A review of the literature and >200 case reports of eosinophilic gastroenteritis revealed that this is the first report of eosinophilic gastroenteritis developing as a postoperative complication. It is also one of only 16 reports of perforated eosinophilic gastroenteritis.

This case highlighted to us the possibility of an alternative pathway of eosinophilic recruitment and activation in certain susceptible individuals.

The traditional model of eosinophil activation as a result of an antigenic response of the gastrointestinal epithelium, releasing eotaxin and interleukin-5 (IL-5) to upregulate, attract and activate eosinophils in the local area, may also co-exist with a propensity for a similar reaction from the gastro-

intestinal epithelium in response to local trauma, in place of the conventional inflammatory response.

The patient in this case underwent surgery 3 weeks prior to developing the symptoms he presented with. We postulate that this patient was susceptible to, and exhibited an abnormal inflammatory response to the postoperative intra-abdominal inflammation associated with his abdominal surgery.

Thus, in the place of a traditional inflammatory response, this patient developed a predominantly eosinophilic response of sufficient intensity to cause perforation of his small bowel, and causing him to re-present to hospital.

Evidence to substantiate further that he underwent a widespread gastrointestinal eosinophilic reaction is that even after resection of the affected segment, his pain did not subside. It was only once he had been treated with systemic steroids that his pain responded, and it did so dramatically, his pain being much reduced just 12 h after commencing steroid treatment and not present at all after 48 h.

Thus, in conclusion, we present this case to highlight the possibility of alternative pathways of eosinophilic activation in patients susceptible to such a process and hope to advance our understanding of this complicated disease process.

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Hyponatraemia during terlipressin therapy

We have read with interest the study by Lo *et al*¹ in a recent issue of *Gut*. Apart from the findings that short-term therapy with terlipressin in combination with ligation seems to improve outcome in bleeding oesophageal varices (BOVs) compared to longer treatment with terlipressin, a shorter treatment period with terlipressin most likely reduces the risk of severe side effects. Recently,

a study observed that during a 5-day terlipressin treatment with 1 mg/4 h, the serum sodium decreased from 138±5 to 130±9 and in the 10-day treatment group, serum sodium decreased from 135±7 to 121±8.² Twenty randomised trials, which compare terlipressin in BOV with no intervention or another treatment modality, have been carried out and published between 1982 and 1996. The majority of these studies only report on severe side effects. Hyponatraemia is reported in two trials: Escorsell *et al*⁵ observed four cases of hyponatraemia in 105 patients treated with terlipressin compared with no cases in the sclerotherapy group, and Feu *et al*⁶ observed five cases of hyponatraemia among 80 patients in the terlipressin group compared with three among 81 treated with somatostatin. Two case reports^{7, 8} on hyponatraemia during terlipressin treatment, included one patient who developed a tonic-clonic seizure after a decrease in serum sodium from 132 to 115 mmol/l. Among 62 patients with BOVs who were treated in our department with high-dose short-term terlipressin 2 mg/4 h at mean 1.7 days (range 1–6 days) serum sodium decreased from 136±6 to 130±7. A confounding factor could be blood transfusions. However, in these patients there were no differences in the number of given blood transfusions between the group with serum sodium <130 mmol/l and those with sodium levels >130 mmol/l (3.8 vs 3.5, p=0.83).

Terlipressin is a vasopressin receptor agonist with predominant effect on the vasopressin-1 receptors, which is responsible for the haemodynamic effects. But, terlipressin also has affinity to vasopressin-2 receptors, which are located in the collecting ducts of the kidneys and induce water retention through insertion of the water canal aquaporin-2.³ Terlipressin improves renal function and induces natriuresis but decreases excretion of solute-free water, which can explain the development of hyponatraemia.^{3, 4}

We would like to stress that the described changes in serum sodium may be clinically significant and suggest that development of hyponatraemia should be included in the surveillance of side effects during terlipressin therapy. It would be most interesting to know the changes in serum sodium during the study by Lo *et al*.

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Insulin resistance, viral load and response to peginterferon and ribavirin in patients with chronic hepatitis C virus infection

We read the article by Moucari *et al* in *Gut* recently¹ with great interest. The authors concluded that insulin resistance (IR) is correlated independently with serum hepatitis C virus (HCV)-RNA and frequently encountered in patients with HCV genotype 4 (HCV-4) infection. Also IR is a major predictor of response to peginterferon and ribavirin in 108 HCV-4 patients receiving a 48-week course of peginterferon plus ribavirin.

In our previous study we enrolled 330 Taiwanese patients with chronic hepatitis C (CHC) (150 HCV genotype 1 (HCV-1) and 180 genotype non 1 (HCV-non 1) to evaluate the association between homeostasis model assessment of IR (HOMA-IR) and response to therapy.² We checked the association between HOMA-IR and serum HCV-RNA level. The mean serum HCV RNA levels were similar between high HOMA-IR (>2.5) and low IR (≤ 2.5) in all 330 patients (5.25 ± 1.14 vs 5.19 ± 1.00 log IU/ml, $p = 0.117$) and in 150 HCV-1 patients (5.56 ± 0.94 vs 5.36 ± 0.99 log

IU/ml, $p = 0.417$). The mean serum HCV RNA level was lower between high HOMA-IR (>2.5) and low IR (≤ 2.5) in 180 HCV-non 1 patients with borderline statistical significance (4.97 ± 1.23 vs 5.05 ± 0.99 log IU/ml, $p = 0.056$). When using HOMA-IR 2 as a cut-off of high and low HOMA-IR as Moucari *et al*, we found the mean serum HCV RNA levels were similar between high HOMA-IR (>2) and low IR (≤ 2) in all 330 patients (5.26 ± 1.12 vs 5.18 ± 1.00 log IU/ml, $p = 0.260$) and in 150 HCV-1 patients (5.54 ± 0.94 vs 5.36 ± 1.00 log IU/ml, $p = 0.464$). The mean serum HCV RNA level was lower between high HOMA-IR (>2) and low IR (≤ 2) in 180 HCV-non 1 with borderline statistical significance (5.04 ± 1.20 vs 5.02 ± 0.98 log IU/ml, $p = 0.067$). Since Moucari *et al* elucidated that the IR was correlated independently with serum HCV-RNA in HCV-4 patients, whether there is association between HOMA-IR and different HCV genotypes needs further studies.

Moucari *et al* reported that IR is a major predictor of response to peginterferon and ribavirin in HCV-4 patients, which indeed meets with applause. We have found that HOMA-IR was associated with SVR to peginterferon plus ribavirin in HCV-1 patients, but not in HCV-non 1 patients. Romero-Gomez *et al*³ and Conjeevaram *et al*⁴ have also reported the high HOMA-IR impairs the response to combination therapy in HCV-1 patients in different countries and all the studies strengthen the important role of IR on the response to anti-HCV combination therapy in HCV-1 and -4 patients. By the way, the HCV viral load was an independent factor, in addition to HOMA-IR, associated with SVR in HCV-1²–4 patients. In HCV-4 patients Kamal *et al* reported that the viral load was highly correlated with and the best predictive marker for peginterferon plus ribavirin responsiveness.⁵ It is noteworthy that Moucari *et al* reported the HOMA-IR rather than the HCV RNA level is a predictor of viral response in HCV-4 patients which minimised the role of pretreatment HCV RNA level on the viral response when taking the HOMA-IR into consideration in HCV-4 patients.¹ We just wonder whether the association between the HOMA-IR and HCV RNA level still exists in these 108 HCV-4 patients? On the other hand, the impact of HOMA-IR on SVR rate was especially discovered among patients with HCV-1 infection and high serum HCV RNA level (defined as 'difficult-to-treat' patients) in our previous study. It seems interesting that whether this finding can also be depicted among the HCV-4 patients in the study of Moucari *et al*.

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Coeliac disease: emerging in China?

We read with interest the leading article by Hunt and van Heel on recent advances in coeliac disease (CD) genetics.¹ They suggested that further investigation of the coeliac-associated single nucleotide polymorphisms (SNPs) in other populations was needed. Our recent work may help to push this research work in the Chinese population. Here we report on a serological screening for CD in China. CD has been historically considered to be absent in the Far East (China, Japan, Korea, Malaysia, etc.).² However, since the major known risk factors for CD are common in China, we used serological tests for immunoglobulin G (IgG) anti-glutadin antibodies (AGAs) and IgA anti-tissue transglutaminase antibodies (tTGs) to screen for CD in high risk patients,³ 4 comprising 73 cases of diarrhoea-predominant irritable bowel syndrome (IBS-D) and five cases of insulin-dependent diabetes mellitus (IDDM), 30 women and 48 men, mean age 50 ± 15 years old. Patients with IBS fulfilled symptom-based diagnostic ROME II criteria and in addition had loose stools with undigested food, frequent stools after eating