

diarrhoea and immune dysregulation syndrome. It was first described as a distinct entity in 1982 by Walker-Smith et al. in a boy aged 9 years, although McCarthy et al. had already described the clinical picture in a boy with IgA deficiency in 1978. It manifests with chronic and intractable diarrhoea in infants following an uncomplicated gestation and neonatal period. Cases with onset in adolescence and adulthood have also been described.¹ It is generally believed to predominantly affect males, but Singhi et al. found a similar prevalence in both sexes in a large case series that was published recently.² The differential diagnosis must include diarrhoea of infectious or allergic aetiology and other, less frequent diseases such as microvillus inclusion disease or intestinal epithelial dysplasia.

The pathogenesis of AIE is unknown. It has been hypothesised that it involves changes in T cell activation, but larger studies are required to elucidate the exact underlying mechanisms.³

The presence of anti-enterocyte antibodies is not a specific finding, as they are also detected in other conditions such as inflammatory bowel disease, HIV infection and allergic enteropathy.⁴ Furthermore, the antibody titre is not correlated to the degree of mucosal damage. An association with other autoimmune disorders of the endocrine system, lung, liver, blood or other systems is frequently found in these patients, as was the case in our series.

Immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX) syndrome, caused by a mutation in the FOXP3 gene, and autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) syndrome, caused by mutations in the AIRE gene, frequently cause AIE.

Autoimmune enteropathy usually involves the small intestine, although gastric and colonic involvement are not rare. In our series, we found gastric atrophy in most patients, and colonic involvement in 3. The histological examination revealed villous atrophy with crypt hyperplasia and a marked T cell infiltrate in the intestinal mucosa. Crypt apoptosis is characteristic of AIE.⁵

The management of AIE in children is based on providing the necessary nutritional support to ensure adequate growth. These patients also require immunosuppressive therapy, with corticosteroids being the first-line treatment, although steroid resistance is frequent. In cases where steroid therapy fails, alternative immunosuppressive agents

are used, such as cyclosporine, tacrolimus, sirolimus or mycophenolate, with variable results. In addition, some authors have proposed the use of biologic agents after observing good outcomes in clinical practice.⁶

To conclude, AIE is a rare cause of severe mixed-type diarrhoea with protein-losing enteropathy. It can involve the entire gastrointestinal tract and is frequently associated with other autoimmune diseases. Further research is required to elucidate the underlying mechanisms of the disease and improve its management.

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2341-2879/

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Hematemesis as debut of eosinophilic gastroenteritis in infants[☆]

Hematemesis como debut de gastroenteritis eosinofílica en lactantes



Dear Editor:

Eosinophilic gastroenteritis (EGE) is a rare type of gastroenteritis characterised by eosinophilic inflammation in different segments of the GI tract in the absence of known causes for eosinophilia (parasitic infestation, drug toxicity, malignancy, inflammatory bowel disease or hyper-eosinophilic syndrome, among others).¹

The clinical manifestations of EGE are nonspecific and vary based on the location and the depth of eosinophilic infiltration in the layers of the gastrointestinal tract, and may include chronic abdominal pain, vomiting, upper or lower gastrointestinal bleeding, diarrhoea and/or ascites.² Its aetiology and pathophysiology is not understood, although

[☆] Please cite this article as: Soriano-Ramos M, Salcedo Lobato E, Rodríguez Gil Y, Medina Benítez E, Urruzuno Tellería P. Hematemesis como debut de gastroenteritis eosinofílica en lactantes. *An Pediatr (Barc).* 2018;88:351–353.

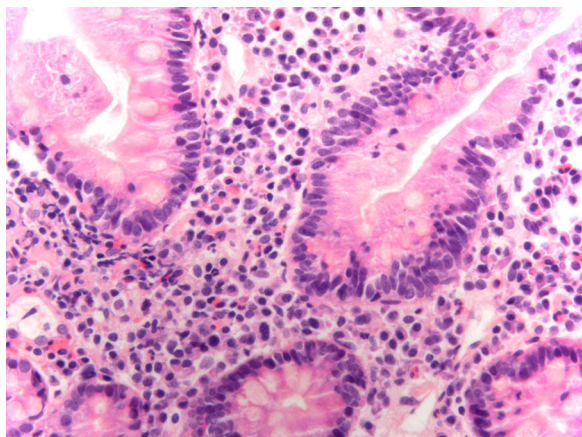


Figure 1 Microscopic image of duodenal mucosa. Significant mixed inflammatory cell infiltrate with eosinophils. HE stain. 400 \times magnification.

they seem to be involve hypersensitivity mechanisms, and the antigen involved most frequently in infants is cow's milk protein (CMP).^{3,4} The diagnosis is confirmed by histological examination, and at present there is no established threshold for the definition of eosinophilia in the gastrointestinal tract.^{2,4,5}

Eosinophilic gastroenteritis is rare in infants and its presentation can vary widely, so diagnosis requires a high level of suspicion. In patients that present with upper gastrointestinal bleeding, the disease may range from mild forms that are well tolerated to severe forms leading to anaemia or haemodynamic instability that may require transfusions. We present the cases of two infants with eosinophilic gastroenteritis and gastritis managed in our hospital.

Case 1: infant aged 4 months, previously healthy, who in the context of acute gastroenteritis had three episodes of vomiting with presence of coagulated blood in the vomit. He had not received ibuprofen and had been fed infant formula since age 1 month. At the time of evaluation, he was in good general health with normal vital signs. He had several eczematous lesions in the trunk and retroauricular area. The complete blood count revealed a haemoglobin concentration of 11.2 g/dL, a white blood cell count of 18 800 cells/mm³ (18.9% neutrophils, 56.4% lymphocytes, 22.8% monocytes, 1.8% eosinophils, 0.1% basophils) and a platelet count of 283 000/mm³. The abdominal ultrasound findings were normal. Fresh blood was found on gastric suction, and oesophagogastroduodenoscopy revealed erosions in the antral mucosa and diffuse fibrin-coated lesions in the gastric body and a pale duodenal mucosa. Histological examination (Fig. 1) revealed a significant although heterogeneous eosinophilic component in the duodenal mucosa (>20 eosinophils/high power field [HPF] with focal involvement) and a mixed inflammatory cellular infiltrate in the gastric mucosa that included abundant eosinophils (25–30 eosinophils/HPF). The infant was managed by switching to elemental formula, to which he showed a favourable response. Allergen-specific IgE testing detected low titres of antibodies against CMP (casein, 0.44 kIU/L; β -lactoglobulin, 0.24 kIU/L, α -lactalbumin, 0.12 kIU/L). Followup: from age 12 months, CMP was progressively reintroduced in the diet without negative repercussions.

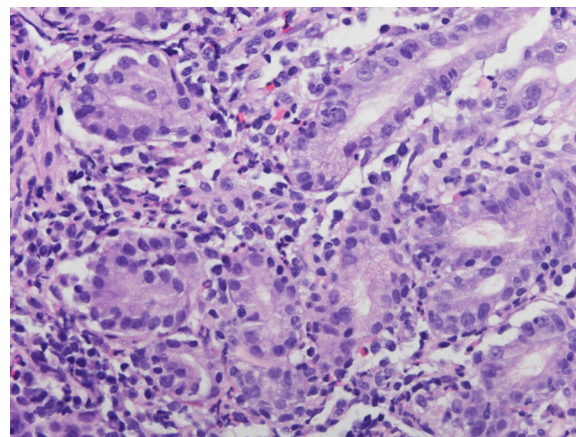


Figure 2 High-magnification microscopic view of gastric mucosa revealing erosive gastritis with a significant eosinophil component in the inflammatory infiltrate (>30 cells/HPF). HE stain. 400 \times magnification.

Case 2: infant aged 2 months, previously healthy, who had three episodes of vomiting with fresh blood and a darker-than-normal bowel movement the day before evaluation. She presented with urticarial-like lesions in the lower extremities that had developed 24 h earlier, which she had also exhibited transiently at age 1 month. The patient had been formula-fed from birth. She was in good general health at the time of physical examination, whose salient findings were a marked paleness of the skin and mucosae and a red and swollen exanthema in the lower extremities that was spreading to the upper limbs. Auscultation of heart sounds revealed tachycardia, with 165 beats per minute, and a mild systolic murmur. The findings of the complete blood count were: haemoglobin concentration of 6.5 g/dL, white blood cell count of 16 700 cells/mm³ (24.2% neutrophils, 61.3% lymphocytes, 13.5% monocytes, 0.7% eosinophils, 0.3% basophils) and 338 000 platelets/mm³, with normal features in the peripheral blood smear. The results of the blood chemistry and coagulation panel were normal, and haematuria was not detected in the urine test strip. The patient underwent gastric lavage and suction, and blood was not found in the recovered contents. Since the loss of blood had caused haemodynamic instability, the patient received a transfusion of packed red blood cells, which led to improvement of symptoms and laboratory parameters. Oesophagogastroduodenoscopy revealed diffuse erythema and multiple fibrinous lesions in the gastric mucosa and a normal duodenal mucosa. Biopsy examination revealed superficial gastritis and a mixed inflammatory cell infiltrate with a predominance of eosinophils, with up to 30 eosinophils/HPF (Fig. 2). The patient was switched to an exclusive diet of elemental formula, with resolution of symptoms. Allergen-specific IgE testing detected antibodies against CMP (casein, 1.24 kIU/L; β -lactoglobulin, 2.82 kIU/L; α -lactalbumin, 0.14 kIU/L; cow's milk, 3.69 kIU/L). Followup: the patient is still keeping a CMP-free diet, which is well tolerated.

The two patients whose cases we present here had onset during infancy with upper gastrointestinal bleeding and a different degree of haemodynamic impact, and received final diagnoses of eosinophilic gastroenteritis and

eosinophilic gastritis, respectively. Recently, Choi et al.⁴ published a study assessing the clinical, endoscopic and histologic features and the response to treatment of 13 children with a histological diagnosis of EGE. They found that the most prevalent symptom at onset in the infant group (8 patients) was haematemesis (7 patients, 87.5%), followed by melena (2 patients, 25%). In contrast, recurrent abdominal pain was the predominant symptom in the group of children aged more than 1 year (60%). Furthermore, CMP was the allergen most frequently suspected to be involved based on the clinical manifestations, suspected in 76.9% of patients, and all infants in this study responded favourably to switching from cow's milk to extensively hydrolysed/elemental formula. These findings are consistent with the outcomes of the two patients managed in our hospital, although it is important to keep in mind that absence of peripheral eosinophilia or negative results of specific IgE assays are not sufficient to exclude a diagnosis of EGE.^{1,2}

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2341-2879/

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Paracetamol: Useful treatment of choice for persistent arterial duct in very low weight premature newborns[☆]



Paracetamol: tratamiento útil de elección para el ductus arterioso persistente en prematuros de muy bajo peso

Dear Editor:

The presence of a haemodynamically significant patent ductus arteriosus (hsPDA) in preterm newborns (PTNBs) is associated with prolonged need of mechanical ventilation, bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), metabolic acidosis, intraventricular haemorrhage (IVH), pulmonary haemorrhage and periventricular leukomalacia.¹ For this reason, pharmacological closure of the ductus is common practice, usually through administration of non-selective cyclooxygenase (COX) inhibitors, indomethacin or ibuprofen. Since these drugs may cause adverse events, other agents, such as paracetamol, are being investigated that may be safer while still effective. In this article, we describe our experience with paracetamol in these patients.

In our unit, active measures for closure of PAD are implemented in PTNBs that develop symptoms or with sonographic signs of moderate to severe haemodynamic compromise in whom spontaneous closure is unlikely. The first line of treatment is ibuprofen, which is delivered intravenously. In the last 4 years, we have used paracetamol by the oral or intravenous route in 15 PTNBs with satisfactory results. In all these newborns, paracetamol was administered because treatment with ibuprofen had failed or the patient had contraindications for it. Parents gave consent to the use of paracetamol after being informed that it was an off-label use of the drug. [Table 1](#) summarises the basic characteristics of the patients. The mean gestational age at birth was 26⁺⁴ weeks (median, 26⁺⁶ weeks; range 24⁺⁶–29⁺¹ weeks) and the mean birth weight was 928 g (median, 980 g; range, 480–1480 g). The most frequent indication for treatment with paracetamol (7/15 patients) was a recent history of IVH, which had been severe in 6/15 patients. Three patients developed NEC and 2 died. [Table 2](#) summarises the findings of the sonographic assessment of PDA and the main treatment-related variables. Half of the patients had been previously treated with ibuprofen. Paracetamol was given at a dose of 15 mg per kilogram of body weight every 6 h. We considered that closure of the PDA was successful if complete closure was achieved, or if the hsPDA improved to a minor PDA with no haemodynamic effects and requiring no further treatment. In our case series, successful closure was achieved in 10/15 patients, with the remaining 5 requiring surgical closure. None of the patients had side effects that could be attributed to paracetamol in the short term.

Since Hammerman et al.² discovered by chance that paracetamol can achieve closure of PDA in PTNBs, several studies have been published that propose its use as

[☆] Please cite this article as: Gálvez Criado R, Rodríguez Blanco S, Oulego Erroz I, Jiménez González A, Alonso Quintela P. Paracetamol: tratamiento útil de elección para el ductus arterioso persistente en prematuros de muy bajo peso. *An Pediatr (Barc).* 2018;88:353–355.