

## Successful intravenous immunoglobulin treatment for steroid-resistant eosinophilic enteritis in a patient with systemic lupus erythematosus

F. Ciccia<sup>1</sup>, A.R. Giardina<sup>1</sup>,  
N. Alessi<sup>2</sup>, V. Rodolico<sup>3</sup>, M. Galia<sup>4</sup>,  
A. Ferrante<sup>1</sup>, G. Triolo<sup>1</sup>

<sup>1</sup>Dipartimento Biomedico di Medicina Interna e Specialistiche, Sezione di Reumatologia, and <sup>2</sup>Sezione di Gastroenterologia, Università degli Studi di Palermo, Palermo, Italy;

<sup>3</sup>Dipartimento di Patologia Umana, Università degli Studi di Palermo, Palermo, Italy; <sup>4</sup>Dipartimento di Biopatologia e Biotecnologie Mediche e Forensi, Università degli Studi di Palermo, Palermo, Italy.

Francesco Ciccia, MD, PhD

Anna Rita Giardina, MD

Nicola Alessi, MD

Vito Rodolico, Associate Professor

Massimo Galia, MD

Angelo Ferrante, MD, PhD

Giovanni Triolo, MD, Professor

Please address correspondence to:

Prof. Giovanni Triolo,

Dipartimento Biomedico di

Medicina Interna e Specialistiche,

Piazza delle Cliniche 2,

90127 Palermo, Italy.

E-mail g.triolo@unipa.it

Received on February 3, 2011; accepted in revised form on July 8, 2011.

© Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2011.

### ABSTRACT

*Eosinophilic gastroenteritis is a rare condition of unknown etiology characterized by eosinophilic infiltration of the bowel. Corticosteroids are the mainstay of EG therapy. Although rare, steroid-resistant EG could be a life-threatening condition with tissue destructive evolution. Associations of eosinophilic gastroenteritis with systemic lupus erythematosus have rarely been reported. In this report we describe a case of successful IVIG treatment in a patient with systemic lupus erythematosus and steroid-refractory eosinophilic gastroenteritis.*

### Introduction

Eosinophilic gastroenteritis (EG) is a rare condition of unknown etiology characterised by eosinophilic infiltration of the bowel. Diagnostic criteria include demonstration of eosinophilic infiltration in the bowel wall, absence of extraintestinal disease, and exclusion of disorders mimicking a similar condition (1).

Corticosteroids are the mainstay of EG therapy. Although rare, steroid-resistant EG could be a life-threatening condition with tissue destructive evolution (2).

Associations of eosinophilic gastroenteritis with systemic lupus erythematosus (SLE) have rarely been reported (3-7) (summarised in Table I). In this report we describe a patient with SLE who developed a steroid-refractory EG. Since intravenous administration of high doses of IgG pooled from the plasma of healthy donors (immune globulin therapy, also known as 'IVIG') has consistently been shown to be a beneficial and safe therapeutic strategy for severe manifestations in patients with SLE (8-9), we choose to treat this patient with IVIG.

### Case report

A 37-year old woman, with a history of idiopathic thrombocytopenic purpura and photosensitivity was admitted in December 2009 for a sudden occurrence of abdominal pain, refractory nausea and vomiting. The patient denied taking any drugs or herbal medicines. She had no history of drug allergy, asthma, or allergic rhinitis.

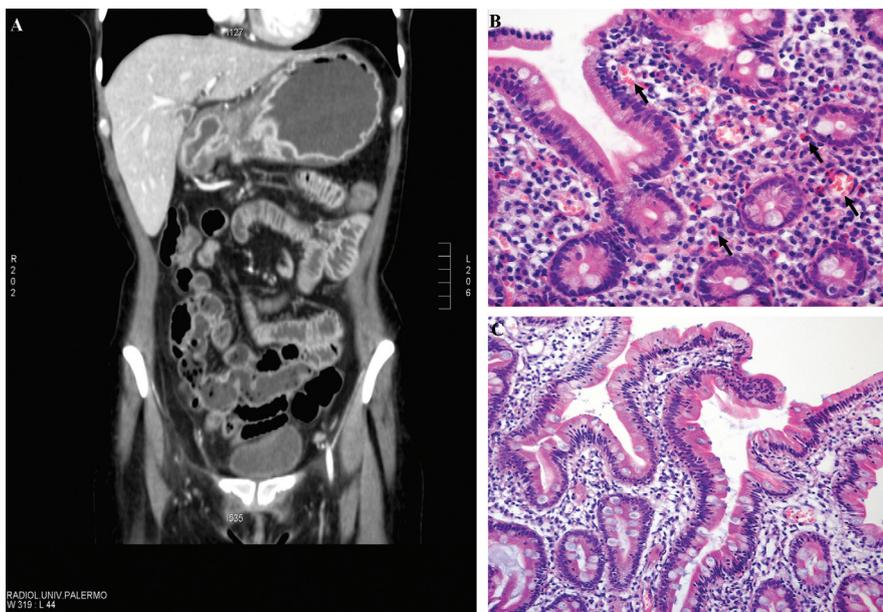
Laboratory studies revealed a high erythrocyte sedimentation rate (ESR) (88 mm/1sth) with normal C-reactive protein and an eosinophilic count of 1560 per microliter. A positive antinuclear antibody (ANA), a positive anti-double stranded (ds) DNA antibody and hypocomplementemia were also observed. CT scan showed nodular and irregular thickening of the folds in the proximal small bowel, and ascites (Fig. 1). The patient underwent a diagnostic esophagogastroduodenoscopy which revealed a normal-appearing esophagus, stomach and duodenum. Biopsies were obtained from the edges of the gastric mucosa and duodenum. Histological analysis of haematoxylin and eosin staining of paraffin-embedded sections revealed a prominent eosinophilic infiltration mainly involving the lamina propria of the duodenum (>25 eosinophils per high-power field). (Fig. 2A). Rapid urease test (Campylobacter-like organism test) and immunohistochemical stain were negative for Helicobacter organisms. The differential pathological diagnosis included Crohn's disease, allergic gastroenteritis, idiopathic eosinophilic gastroenteritis, drug reaction or parasitic infection. According to ACR criteria (10) the patient was diagnosed as having SLE with concomitant EG and intravenous methylprednisolone (1 g/day for three days) was started, followed by oral prednisone (50 mg/day) without any significant clinical improvement. An infusion protocol with IVIG was designed and informed consent was obtained from the patient. The patient was infused with IVIG (2 g/kg over a 5-day period). An improvement in symptoms was noticed within 48 hours after receiving the first infusion and remained stable throughout the observation period. Esophagogastroduodenoscopy was repeated one month after and duodenal biopsies were obtained. Histological analysis showed the disappearance of eosinophilic infiltrates (Fig. 2B). This is the first report, to our knowledge, of the treatment of EG in SLE with IVIG. Although the mechanisms of action of IVIG in autoimmune diseases are still not completely clear, a considerable body of evidences sug-

Competing interests: none declared.

Table I.

| Ref.                        | Age/sex | Clinical manifestations                                     | Hypereosinophilia n./ $\mu$ L | SLE criteria  | Treatment                    | Outcome                 |
|-----------------------------|---------|---|-------------------------------|---|------------------------------|-------------------------|
| Barbie DA (3)               | 37/F    | abdominal pain, nausea, vomiting, and diarrhoea             | yes                           | Malar rash, arthritis, lymphopenia, ANA   | mPDN 50–100 mgX3/daily       | Improvement of symptoms |
| Sunkureddi PR (4)           | 47/F    | abdominal pain, nausea, vomiting, and diarrhoea             | yes                           | Serositis, thrombocytopenia, ANA, anti-dsDNA  | PDN 40 mg/daily hdx          | Resolution              |
| Aslanidis S (5)             | 24/F    | abdominal pain, nausea and vomiting                         | no                            | NR  | PDN 1 mg/kg/daily cefotaxime | Resolution              |
| Jaimes-Hernandez J (6)      | 36/F    | abdominal pain, nausea, vomiting and melena                 | yes                           | Pleural effusion, haemolytic anaemia, thrombocytopenia, ANA, anticardiolipin antibodies | mPDN pulse                   |                         |
| Yamazaki-Nakashimada MA (7) | 10/M    | abdominal pain, constipation, bilious and fecaloid vomiting | no                            | Lymphopenia, seizures, serositis, cylindruria, ANA, anti-b2GPI                          | mPDN pulse, oral Cyc         | Improvement of symptoms |
|                             | 15/F    | abdominal pain, vomiting and diarrhoea                      | NR                            | Serositis, proteinuria, cylindruria; ANA, anti-Sm                                       | mPDN pulse                   | Resolution              |

Cyc: cyclophosphamide; hdx: hydroxychloroquine; IVIG: intravenous immunoglobulin; mPDN: metil-prednisolone; NR: not reported; PDN: prednisone



**Fig. 1.** Axial computed tomographic (CT) enterography scan shows circumferential wall thickening of proximal small bowel (arrow) (A). Representative photomicrographs showing 3- $\mu$ m-thick paraffin embedded sections of proximal ileal biopsy specimens obtained from the patient before (B) and after (C) IVIG therapy. Abundant eosinophilic infiltrates (lamina propria eosinophils >15 per high power field) was observed in ileal specimens before IVIG therapy (B). IVIG treatment dramatically reduced eosinophilic infiltrates (C). (H&E staining; 40x magnification).

gest their potential role in autoimmune diseases. IVIG might act enhancing the catabolism of IgG, blocking Fc $\gamma$  receptor-mediated mechanisms, and inhibiting Fas receptor-induced apoptosis. In addition, IVIG seem to contain anti-DNA idiotypic antibodies, which might influence the idiopathic network (8)

Despite the absence of randomised controlled studies of the use of IVIG in SLE, IVIG therapy has been shown to be effective in the management of patients with various manifestations of SLE, especially those with thrombocytopenia (11), psychosis (12), and pleural effusions (13). On the basis of these findings, considering the refractoriness

to steroid treatment and the risks and benefits of a 5-day, high-dose IVIG treatment, we chose to treat this patient with IVIG therapy. Treatment with IVIG led to a complete remission of all disease manifestations with disappearance of eosinophilic infiltrates in our patient and there was no recurrence for up to sixteen weeks after the last infusion. This effect appears to be remarkable as standard treatment had failed in our patient. Considering that IVIG treatment in our patients with SLE-associated EG was safe and effective, we conclude that this regimen may be used as an addition to conventional therapy.

**References**

1. TALLEY N, SHORTER R, PHILLIPS S, ZINSMEISTER A: Eosinophilic gastroenteritis: a clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. *Gut* 1990; 31: 54-8.
2. TYTGAT GN, GRIJM R, DEKKER W, DEN HARTOG NA: Fatal eosinophilic enteritis. *Gastroenterology* 1976; 71: 479-83.
3. BARBIE DA, MANGI AA, LAUWERS GY: Eosinophilic gastroenteritis associated with systemic lupus erythematosus. *J Clin Gastroenterol* 2004; 38: 883-6.
4. SUNKUREDDI PR, BAETHGE BA: Eosinophilic gastroenteritis associated with systemic lupus erythematosus. *J Clin Gastroenterol* 2005; 39: 838-9.
5. ASLANIDIS S, PYRPASOPOULOU A, SOUFLERIS K *et al.*: Eosinophilic enteritis with ascites in a patient with overlap syndrome. *Case Report Med* 2009; 734206. Epub 2009 May 24.
6. JAIMES-HERNANDEZ J, ARANDA-PEIRERA

- P, MELENDEZ-MERCADO CI: Eosinophilic enteritis in association with systemic lupus erythematosus. *Lupus* 2009; 18: 452-6.
7. YAMAZAKI-NAKASHIMADA MA, RODRIGUEZ-JURADO R, ORTEGA-SALGADO A *et al.*: Intestinal pseudoobstruction associated with eosinophilic enteritis as the initial presentation of systemic lupus erythematosus in children. *J Pediatr Gastroenterol Nutr* 2009; 48: 482-6.
8. TRIOLO G, FERRANTE A, ACCARDO-PALUMBO A *et al.*: IVIG in APS pregnancy. *Lupus* 2004; 13: 731-5.
9. ZANDMAN-GODDARD G, BLANK M, SHOENFELD Y: Intravenous immunoglobulins in systemic lupus erythematosus: from the bench to the bedside. *Lupus* 2009; 18: 884-8.
10. TAN EM, COHEN AS, FRIES JF *et al.*: The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271-7.
11. AKASHI K, NAGASAWA K, MAYUMI T *et al.*: Successful treatment of refractory systemic lupus erythematosus with intravenous immunoglobulins. *J Rheumatol* 1990; 17: 375-9.
12. TOMER Y, SHOENFELD Y: Successful treatment of psychosis secondary to SLE with high dose intravenous immunoglobulin. *Clin Exp Rheumatol* 1992; 10: 391-3.
13. BEN-CHETRIT E, PUTTERMAN C, NAPARSTEK Y: Lupus refractory pleural effusion: transient response to intravenous immunoglobulins. *J Rheumatol* 1991; 18: 1635-7.