

Sodium cromoglycate in the treatment of eosinophilic gastroenteritis

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Two patients suffering from eosinophilic gastroenteritis (EG) were treated with sodium cromoglycate (SCG). Before treatment they showed enteric and cutaneous symptoms, such as abdominal pain, nausea, vomiting, diarrhoea and recurrent urticaria and angioedema. The histological findings were a notable amount of eosinophilic infiltration in the lamina propria and gastric glands, a villous shortening and thickening and weak eosinophilic inflammation in the duodenum. The patients were treated with 300 mg SCG, 4 times daily, for 4/5 months. During treatment, the clinical symptoms disappeared and at the end of treatment a reduced inflammation with an almost complete decrease of eosinophilic infiltration was observed. The results provide evidence of SCG efficacy in the treatment of EG and suggest its employment as an alternative to the steroids commonly used in EG.

Key words: sodium cromoglycate; eosinophilic gastroenteritis.

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Eosinophilic gastroenteritis (EG) is an uncommon inflammatory process, histopathologically marked by gastrointestinal eosinophilic infiltration. Its clinical picture is characterized by abdominal pain, vomiting and/or diarrhoea with protein-losing enteropathy and, usually, recurrent urticaria and angioedema. Peripheral eosinophilia, with iron deficiency anaemia and stools positivity for occult blood have frequently been identified. Allergic or pseudoallergic food reactions are not always noticeable in EG, which is, however, often associated with other allergic diseases, such as asthma and rhinitis. Accordingly, elimination diets or food challenge are often unsuccessful and corticosteroids are traditionally the treatment of choice. However, in view of the proved effectiveness of sodium cromoglycate (SCG) in the treatment of other inflammatory bowel diseases, its possible employment has recently been suggested also for the treatment of EG. Even though inconstant

results have been described, this report concerns two patients with EG who responded to oral SCG.

Patient 1

History. R. T., 33 year-old woman, who for 2 years had had fits of abdominal pain, nausea, vomiting and recurrent urticaria, alternating with short periods of remission. Symptoms frequently exacerbated after dinner, but no relationship was evidenced with specific foods. There was slight weight loss and clinical control was obtained only by means of steroids, whereas antihistamines and metoclopramide proved ineffective.

Investigation. Iron deficiency anaemia was observed (red blood: 3,600,000/mm³, Hb: 11 g%, iron concentration: 16µg/dl), while eosinophil

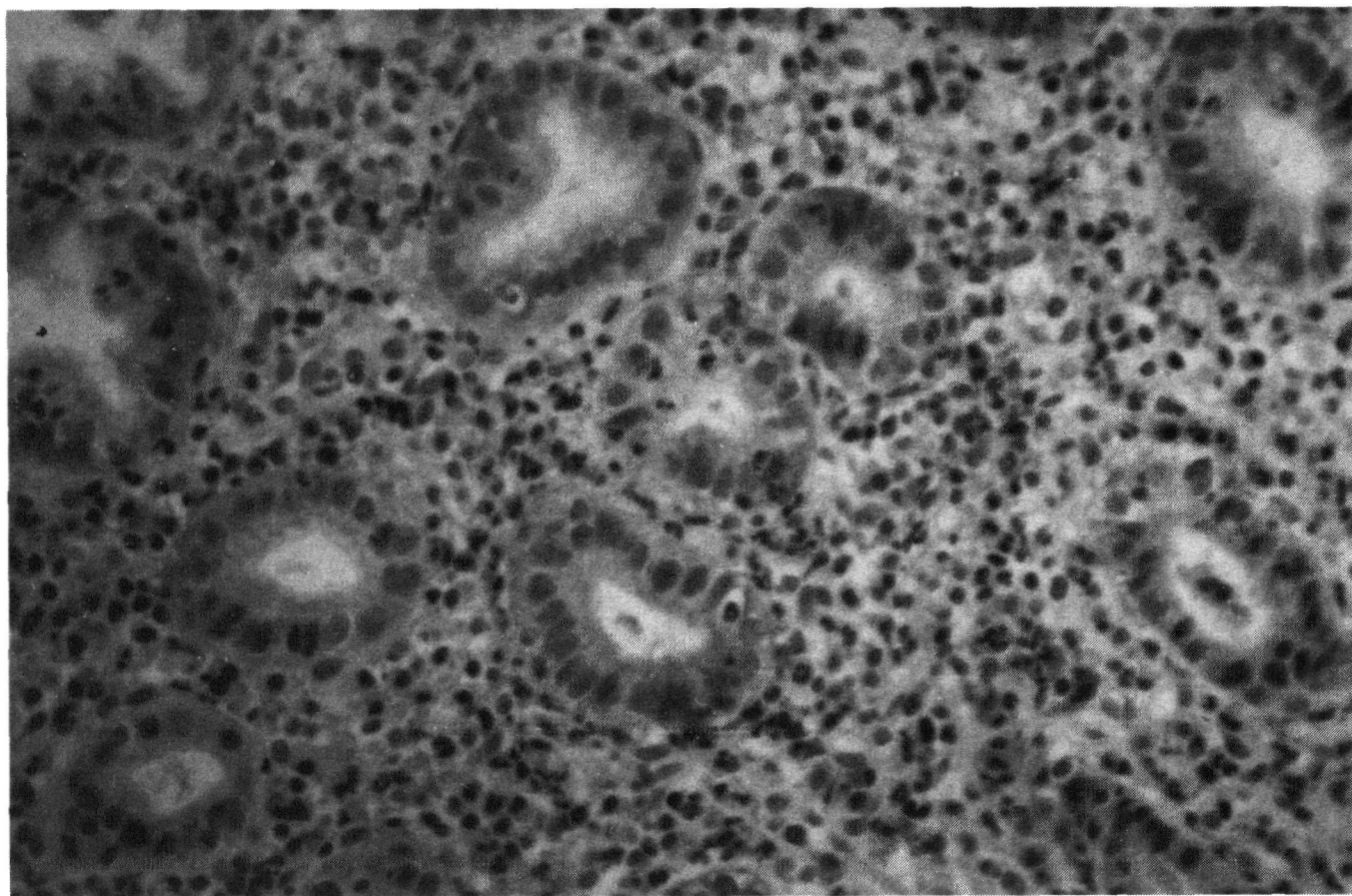


Fig. 1. Patient 1: Gastric biopsy before SCG, showing abundant eosinophilic infiltration, in both the lamina propria and glandular lumen. Capillary and lymphatic vessels are extended and oedema is focally present in the lamina propria. (H & E $\times$ 250).

blood count, liver and renal function, electrolyte balance, protein, lipid and glucose metabolism, IgG, IgA, IgM, IgE, C3 and C4 levels, erythrocyte sedimentation rate and circulating immunocomplexes were normal. Moreover, rheumatoid factors, LE cells and anti-nuclear, anti-mitochondrial, anti-smooth muscle and anti-DNA antibodies were absent and worm research was negative. The skin prick test to foods and enzyme-like immunosorbent assay (ELISA) for specific IgE to food allergens were negative. No clinical improvement was observed during 4 weeks of exclusion diet. An upper gastrointestinal endoscopy showed irregularity of the antral mucosa, with a pseudo-polyp-like appearance and duodenal cap full of biliary juice, with hyperemia of the underlying mucosa. Antral and duodenal biopsies showed a remarkable infiltration of lymphocytes, plasma cells, neutrophils and, above all, eosinophils in the gastric mucosa. The eosinophils were present both in the lamina propria and in the

glands (Fig.1). In contrast, at duodenal level the inflammation was less evident.

Subsequent course. The patient was treated with an initial dose of 100 mg SCG, 4 times daily, subsequently increased to 300 mg, 4 times daily.

After 2 weeks of therapy, there was a significant improvement in the clinical condition, while after 4 months the stomach and duodenum appeared normal at endoscopy and biopsies revealed a large decrease of gastric and duodenal inflammation and almost complete disappearance of eosinophilic infiltration (Fig.2).

Patient 2

History. B.C., 42 year-old woman, who had had headache, nausea, vomiting, diarrhoea, labial and palpebral angioedema and recurrent urticaria for 1 year. Like the previous patient, she

had short periods of remission and reported frequent exacerbation of the symptoms after dinner, with no association with specific foods. Antihistamines were ineffective, whereas steroids administered during the attack of angioedema were usually successful.

Investigation. The laboratory findings showed only iron deficiency anaemia (red blood: 3,000,000 mm, Hb: 10 g%, Iron: 20 µg/dl). The immunological pattern, liver and renal function, sedimentation rate, and electrolyte balance were normal; worm research was negative. The skin prick test for 20 principal foods and the ELISA for specific IgE to milk, egg, fish and wheat were negative. An exclusion diet did not produce any improvement in the clinical picture. The upper gastrointestinal endoscopy showed a reddish appearance of the folds in the gastric fundus and body with a normal antral mucosa and a superficial oedema in the duodenal bulb. The biopsies obtained from antral and duodenal mucosa showed an eosino-

philic infiltration in the lamina propria and gastric glands (Fig.3), while a villous shortening and thickening were the prevalent damage in the duodenum.

Subsequent course. Also in this patient oral SCG was used at the initial dose of 100 mg, 4 times daily, subsequently increased to 300 mg, 4 times daily.

The improvement was very evident and the symptoms were no longer observed after 3 weeks. The endoscopy and biopsies were repeated after 5 months, showing the disappearance of endoscopic and histological (Fig.4) signs; only a slight villous shortening persisted in the duodenum.

DISCUSSION

Oral SCG has been used for many years in gastrointestinal food allergy with excellent results (5, 8, 17), while inconstant results have been obtained in inflammatory bowel diseases,

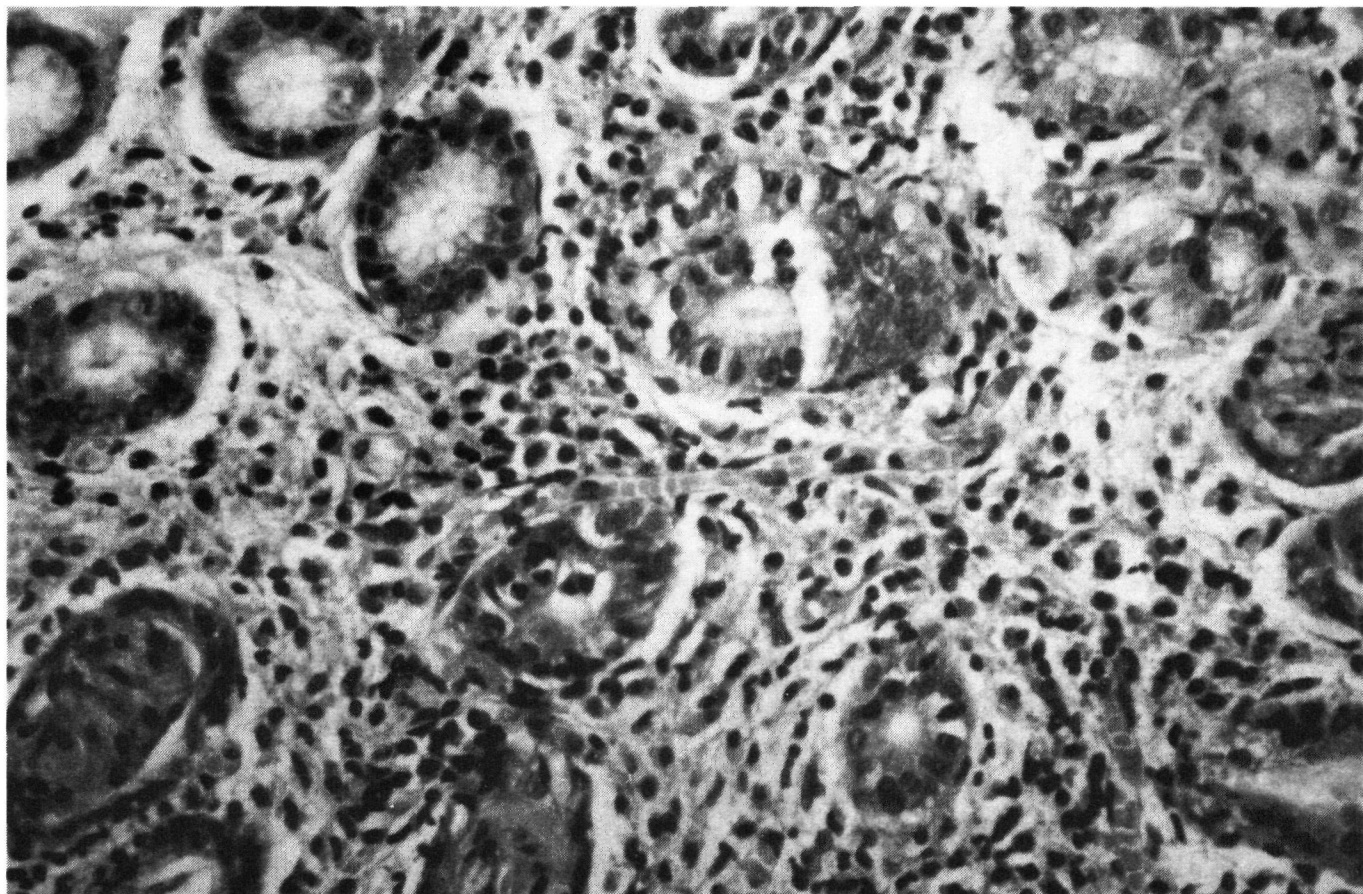


Fig. 2. Patient 1: Gastric biopsy after SCG, showing a greatly lessened eosinophilic infiltration. Oedema still persists in the lamina propria. (H & E $\times$ 250).

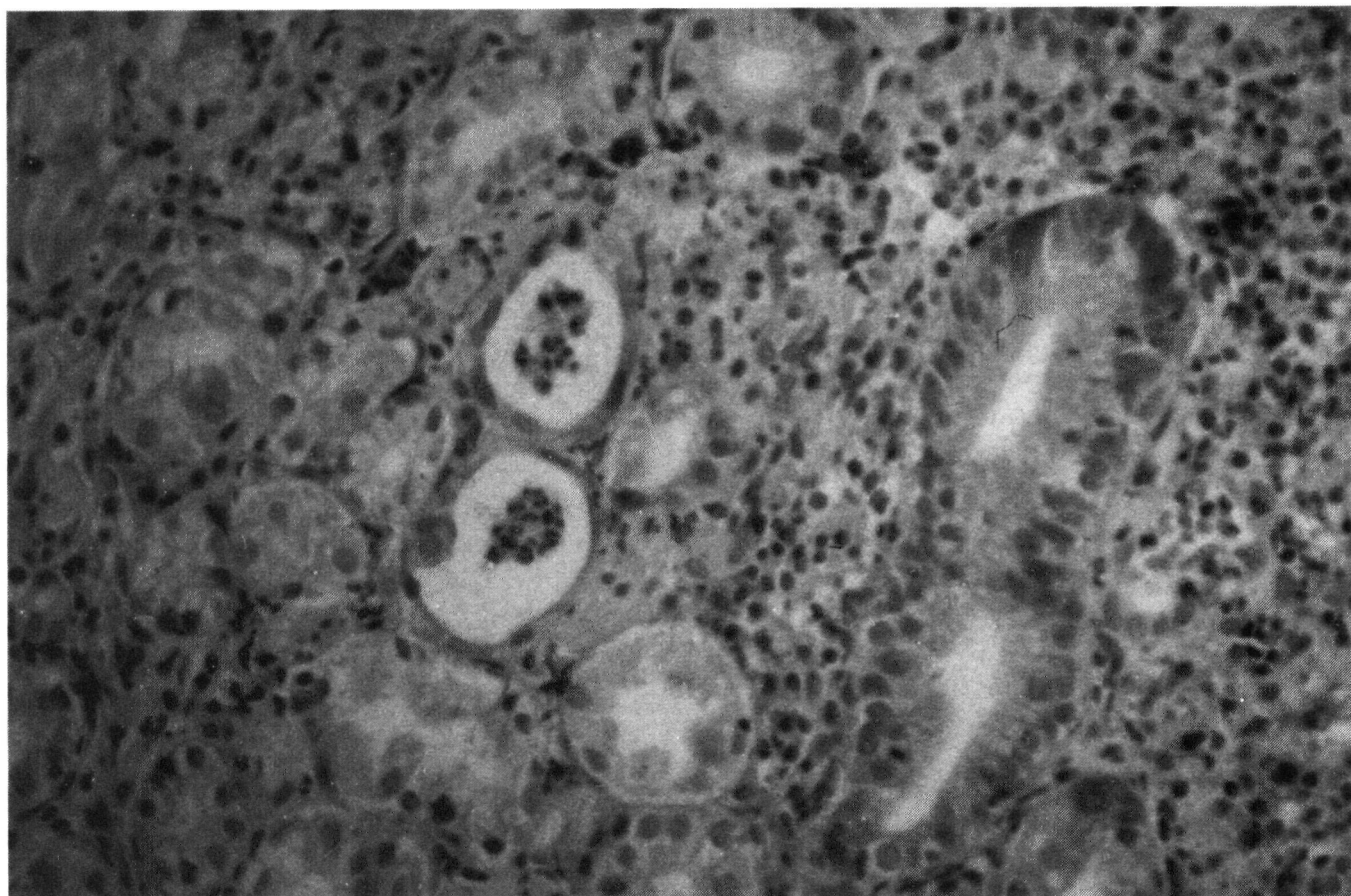


Fig. 3. Patient 2: Gastric biopsy before SCG, showing intense inflammatory reaction, with prevalence of eosinophilic infiltration, which concerns the glandular epithelium, also affected by regressive phenomena. (H & E $\times$ 250).

such as ulcerative colitis (10, 24) and Crohn's disease (4) and also in chronic urticaria and food intolerance (2, 19). More recently, the use of oral SCG has proved successful in varioliform gastritis (1), probably because Type 1 hypersensitivity plays some part in the pathogenesis of this disease. There are some reports showing a clinical efficacy of SCG also in EG (11, 14), while other authors report absolute therapeutic failure (7, 9). The rationale for the employment of oral SCG in the treatment of EG has been founded on the histology of this disease: eosinophilic infiltration of the gastrointestinal tract and an increase in mucosal mast cells (13). These findings are clearly similar to those of food allergy, and some authors, at present, believe that EG may be due to severe food allergy or be regarded as its extreme consequence (18). Consequently, eosinophilic infiltration could result, also in EG, from the effect of eosinophilic chemiotactic factors, activated during mast cell degranulation. However, the

frequent insensitivity of patients to elimination diets or food challenge seems to confirm a different pathogenesis with respect to food allergy, thus suggesting that mast cell degranulation may be IgE-independent in EG, or that eosinophilic infiltration may be independent of mast cell degranulation. However, SCG has been proved effective in inhibiting mast cell degranulation even in diseases which obviously do not depend on an allergic reaction, as exercise-induced asthma. It is worth noting that some authors have demonstrated the effectiveness of SCG in inhibiting the mast cell degranulation in human jejunal mucosa (25), whereas others showed only a partial inhibition of histamine release from isolated human intestinal lamina propria mast cells (3) but not from rat intestinal mucosal mast cells (22). Apart from its role in stabilizing mast cell membrane and preventing the release of mediators and chemiotactic factors, the SCG effectiveness in EG could be largely due to a direct antiflogistic effect on

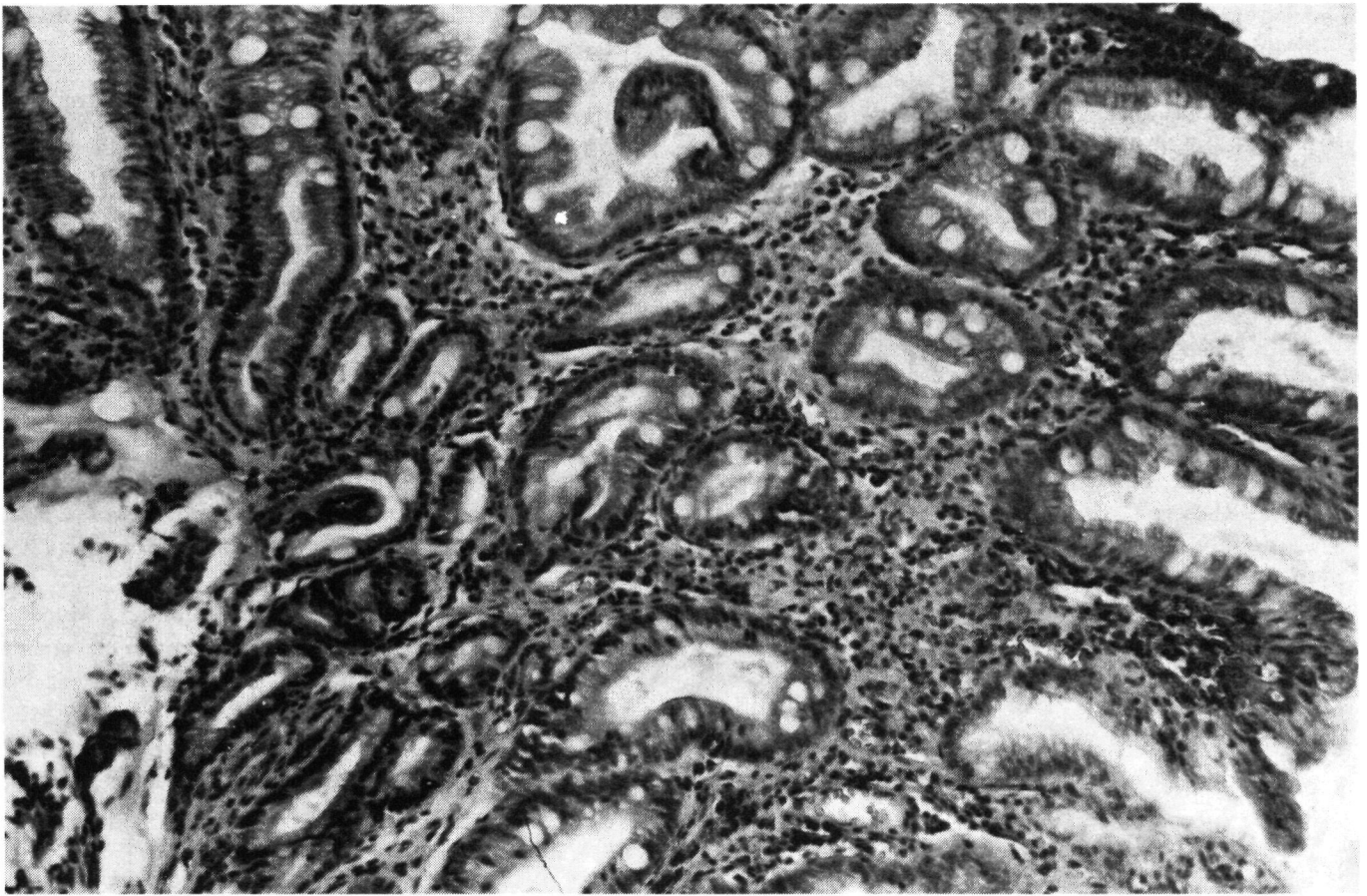


Fig. 4. Patient 2: Gastric biopsy after SCG, showing a reduced flogosis. Disappearance of eosinophils from the glandular lumen is remarkable. (H & E $\times$ 100).

eosinophils (20, 23). Moreover, gastrointestinal inflammatory diseases could favour an absorption of macromolecules, inducing generalized symptoms; these could be inhibited by SCG, which reduces the absorption of macromolecules (21).

Finally, some clinical remarks should be emphasized in our patients. They were affected by EG with mucosal involvement, but did not present peripheral hypereosinophilia, malabsorption and/or protein-losing enteropathy, which are rather common in this form (6, 26). However, it has been recognized that blood eosinophilia may fluctuate enormously, often resulting in the normal range in EG (15, 16, 26, 27). This phenomenon has been related to migration of eosinophils from the blood to the intestinal mucosa, as it occurs after food challenge in some allergics (6). However, malabsorption and/or protein-losing enteropathy are usually associated with more remarkable inflammation in the small bowel mucosa (6, 12), but this was not the case

in our patients, who showed only a slight eosinophilic infiltration in the jejunal mucosa.

It is worth noting that patients with EG may occasionally experience periods of remission without treatment (26). Accordingly, the patients presented in this report underwent short phases of spontaneous remission, but SCG therapy was followed by a prolonged control of the clinical picture and a dramatic fall in the mucosal eosinophilia. This evidence seems to confirm SCG effectiveness in the treatment of EG, thus suggesting its employment as an alternative to corticosteroids. Otherwise, EG requires prolonged steroid therapy, frequently eliciting harmful side effects, which do not occur with SCG treatment.

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