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Increased circulating levels of interleukin-5 in a case of steroid-resistant hypereosinophilic syndrome with ileal involvement

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GM-CSF Granulocyte-macrophage colony-stimulating factor

IL Interleukin

Idiopathic hypereosinophilic syndrome can present with a variety of clinical and laboratory manifestations, including gastrointestinal involvement.¹ Recently, interleukin (IL)-5 and other eosinophil hematopoietins capable of activating a number of eosinophil functions have been implicated in the pathogenesis of hypereosinophilic states.² Eosinophilic gastroenteritis, an uncommon disease characterized by abdominal pain, malabsorption, and eosinophilic infiltration of the gastrointestinal tract, can be difficult to distinguish from hypereosinophilic syndrome.³ Typically, eosinophilic gastroenteritis involves the proximal gastrointestinal tract and is responsive to steroids, whereas in hypereosinophilic syndrome, persistent eosinophilia and other systemic manifestations that are unresponsive to corticosteroids are often seen. Herein we report an unusual case of hypereosinophilic syndrome associated with increased serum levels of IL-5, hypercoagulability, malabsorption, and localized eosinophilic infiltration limited to the ileum.

Case Report

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A 41-year-old man was transferred for evaluation of weight loss, recurrent abdominal pain, and eosinophilia. He was in good health until 1982, when he underwent a Billroth II operation for control of upper gastrointestinal bleeding and a total colectomy with ileostomy for treatment of ulcerative colitis. He had multiple admissions for episodes of abdominal pain, hematochezia, and eosinophilia. A diagnosis of eosinophilic gastroenteritis was made, and he began receiving systemic corticosteroids and parental hyperalimentation but showed little improvement. His course was complicated by renal vein thrombosis, pulmonary embolism, and episodes of chest pain.

On transfer, medications included prednisone 40 mg daily, Fluorinef, Nitropaste, Compazine, Zantac, Pamelor, Buprenex, and sodium chloride. He appeared thin and wasted with a cushingoid facies. There was tachycardia without fever, peripheral adenopathy, or rash. Examination of chest and cardiovascular system was remarkable for a midsystolic flow murmur. The abdomen was nontender without organomegaly; a well-healed ileostomy was present. The white blood cell count was 23,800/mm³ with 14% bands, 51% neutrophils, 1% monocytes, 8% lymphocytes, and 26% eosinophils; the hematocrit was 31.2% with a mean corpuscular volume of 77 and red blood cell distribution width index of 19.

During his workup, an attempt to reduce the dose of corticosteroids below 30 mg of prednisone per day met with enhanced abdominal pain and increased eosinophilia to $\approx$ 25,000/mm³ (48% eosinophils with a white blood cell count of 48,500/mm³). Intravenously administered steroids at high doses led to some improvement and a decline in the eosinophil count to 1387/mm³ (17% eosinophils with a white blood cell count of 9800/mm³). Multiple stool examinations for ova and parasites were unremarkable except for *Blastocystis hominis* and Charcot-Leyden crystals. The hospitalization was complicated by *Pneumocystis carinii* pneumonia that responded to trimethoprim sulfamethoxazole; results of human immunodeficiency virus testing and levels of CD4 cells were normal. Workups for connective tissue disease, vasculitis, strongyloides, hepatitis, food allergy, hyperimmunoglobulinemia syndrome, and immunoglobulin deficiency were all unremarkable. Malabsorption was documented by low β -carotene, iron deficiency anemia, fecal fat levels (12 gm/day), and impaired D-xylose absorption. Upper gastrointestinal endoscopy with biopsies of the stomach and duodenum revealed only mild bile acid gastritis. Ileoscopy revealed grossly abnormal mucosa limited to a 10 to 25 cm region of the terminal ileum with edema and erythema; the mucosa appeared granulonodular. Biopsy specimens revealed massive eosinophilic infiltration of the

epithelium, submucosa, and lamina propria with ulceration and epithelial destruction.

Methods

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During the hospitalization when the patient had the dose of prednisone reduced to 30 mg/day and had a peripheral eosinophil count of $8732/\text{mm}^3$, serum was obtained for evaluation of levels of IL-5 and granulocyte-macrophage colony-stimulating factor (GM-CSF) with the eosinophil survival assay.⁴ Antibodies against GM-CSF (polyclonal sheep anti-human GM-CSF, 1:1500 dilution) or mouse monoclonal anti-IL-5 antibody MC17 (10 $\mu\text{g}/\text{ml}$, provided by Dr. Takatsu, Tokyo University) were used to neutralize cytokine activity.

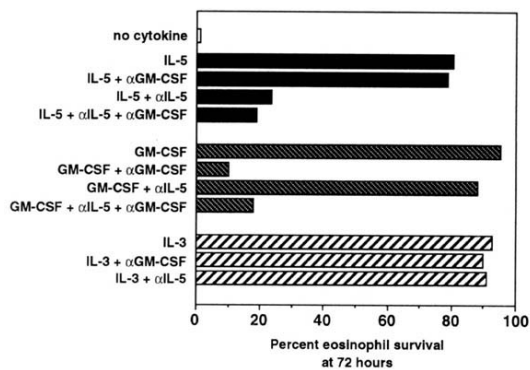
Discussion

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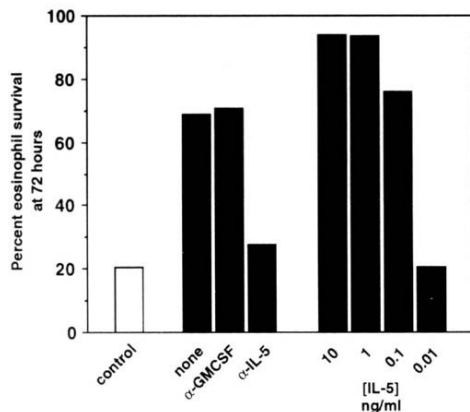
■ Fig. 1, A demonstrates the specificity of antibody neutralization for IL-5–, GM-CSF–, and IL-3–induced prolongation of eosinophil survival in vitro. As shown in ■ Fig. 1, B, a 1:10 dilution of the patient's serum contained detectable levels of eosinophil survival activity; control serum did not. Anti-IL-5 antibody completely neutralized this eosinophil survival activity, whereas anti-GM-CSF alone had no effect. By extrapolating to the activity of recombinant IL-5 in this assay, the patient's serum contained between 0.1 and 1 ng/ml of IL-5.

FIG. 1. A, Antibodies to IL-5, GM-CSF, and IL-3 specifically neutralize the ability of recombinant human cytokines to prolong eosinophil survival in vitro. Cytokines (1 ng/ml) were diluted in normal AB sera with or without the indicated combinations of neutralizing antibodies at the beginning of the 72-hour culture. **B**, The effect of AB serum from a normal subject (*open bar*), our patient (*middle bars*), or human recombinant IL-5 diluted in normal AB serum (*right bars*) on eosinophil survival in vitro. For patient serum, neutralizing antibodies were also used to determine the identity of the survival-promoting activity.

A.



B.



Click on Image to view full size

This case is reported because of the severity of this patient's disease and its atypical presentation, including unusual pathologic changes in the gastrointestinal tract localized to the distal part of the small intestine. Although localized eosinophilic disease of the ileum has been reported,⁵ relatively little extraintestinal involvement was seen. This finding and the intense peripheral blood eosinophilia, thromboembolic disease, and increased serum levels of IL-5 are more suggestive of hypereosinophilic syndrome than eosinophilic gastroenteritis.¹ Therefore this case is another example of the variety of presentation of hypereosinophilic syndrome and further substantiates the importance of IL-5 in this disorder. The development of *Pneumocystis carinii* pneumonia is puzzling but may be related to malabsorption and long-term steroid use. The exact reason for localized ileal recruitment of eosinophils remains unclear.

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References

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1. Spry CJF. The idiopathic hypereosinophilic syndrome. In: Makino S, Fukuda T, eds. Eosinophils: biological and clinical aspects. Boca Raton, Florida: CRC Press, 1992:403-19.
2. Sanderson CJ. Interleukin-5, eosinophils, and disease. Blood 1992;79:3101-9.

MEDLINE

3. Klein NC, Hargrove RL, Sleisenger MH. Eosinophilic gastroenteritis. *Medicine (Baltimore)* 1970;49:299-319.

MEDLINE

4. Wallen N, Kita H, Weiler D, Gleich GJ. Glucocorticoids inhibit cytokine-mediated eosinophil survival. *J Immunol* 1991;147:3490-5.

MEDLINE

5. Haberkern CM, Christie DL, Haas JE. Eosinophilic gastroenteritis presenting as ileocolitis. *Gastroenterology* 1978;74:896-9.

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ABSTRACT

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