

unnecessary. Elective rechallenge with amphotericin B was also impossible because the subject died.

Amphotericin B challenge is safe and well-tolerated and appears to be effective, as demonstrated in this case report. Avoidance of opiates, which perturb mast cells, and premedication with corticosteroids and antihistamines are recommended.

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Interleukin-5 production by T lymphocytes in atheroembolic disease with hypereosinophilia

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Atheroembolic disease is a consequence of widespread cholesterol microembolization, most often caused by catheterization of a severely atherosclerotic aorta. A transient hypereosinophilia has been reported in up to 80% of the patients; thus, eosinophilia is considered an important clue to the diagnosis of this disorder.¹

Interleukin (IL)-5 is a cytokine secreted by CD4⁺ T cells, mast cells, and eosinophils, which promotes the differentiation and activation of eosinophils.² Indeed, increased production of IL-5 has been demonstrated in several diseases associated with eosinophilia.² In this report we provide evidence that hypereosinophilia associated with

Abbreviations used

IFN- γ :	Interferon- γ
IL:	Interleukin
PBMCs:	Peripheral blood mononuclear cells

atheroembolic disease is related to IL-5 release by activated T cells.

CASE REPORT

A 63-year-old man was admitted to the hospital for treatment of unstable angina 1 week after an acute myocardial infarction. Laboratory findings included moderate renal failure (plasma creatinine, 150 μ mol/L) and normal leukocytosis (9.9×10^9 /L; eosinophils, 3.2%). Angiocardiology performed by femoral puncture (day 0 in Fig. 1) revealed trituncular disease. Ten days later, the patient had accelerated hypertension, mild fever, and leg pain. Livedo reticularis was noted over the abdomen and lower limbs. Renal failure developed (plasma creatinine, 433 μ mol/L on day 23) and blood eosinophilia progressively increased, reaching 3369×10^6 cells/L on day 19 (Fig. 1, A). Immunophenotyping of peripheral blood mononuclear cells (PBMCs) was normal. The cholesterol emboli syndrome was established by renal and skin biopsies. Except for

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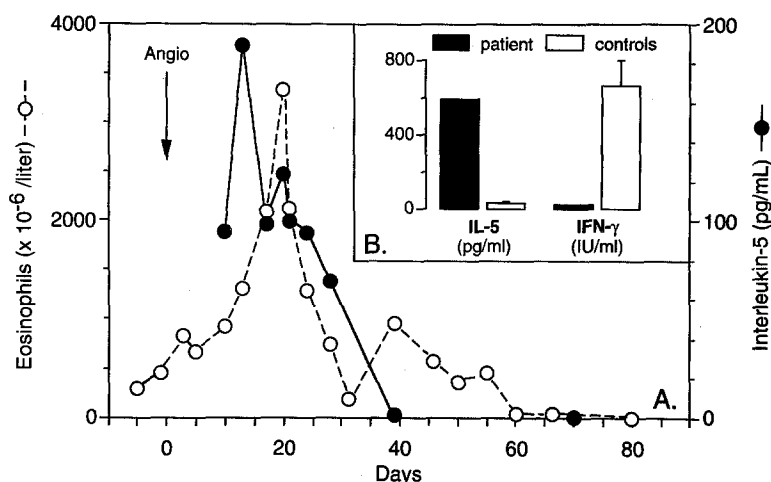


FIG. 1. A, Time course of eosinophil blood count and IL-5 serum levels. Angiocardigraphy (Angio) was performed 6 days after admission (day 0). The normal serum IL-5 level is less than 25 pg/ml. B, The in vitro secretion of IL-5 and IFN- γ in response to OKT3 by PBMCs obtained from the patient on day 19 (black columns) and from five normal control subjects (white columns). Bars represent the standard errors.

renal failure, all clinical and biologic abnormalities spontaneously regressed within 1 month.

METHODS

Isolation and culture of PBMCs

PBMCs of the patient and of five healthy volunteers were isolated from freshly drawn heparinized blood by density gradient centrifugation on Lymphoprep (Nycomed, Oslo, Norway) and then cultured at a density of 1.10^6 /ml either in medium alone (RPMI 1640 [Gibco, Grand Island, N.Y.] supplemented with 10% fetal calf serum) or with 10 ng/ml OKT3 (Ortho Biotech, Raritan, N.J.) as T-cell stimulating agent. After 48 hours of incubation at 37°C in a 5% CO₂ atmosphere, supernatants were collected and stored at -20°C until assayed for IL-5 and interferon- γ (IFN- γ).

Determination of IL-5 and IFN- γ levels

IL-5 levels in serum and culture supernatants were determined by an immunoenzymatic method developed in our laboratory, as previously described.³ IFN- γ levels were measured by ELISA with a commercially available kit (Chromogenic, Molndal, Sweden).

RESULTS

Time course of serum IL-5

Increased serum levels of IL-5 were found during the period of hypereosinophilia (Fig. 1, A). Blood eosinophil count was maximal on day 19 (3369×10^6 /L), 7 days after the IL-5 peak (190 pg/ml). Thereafter, IL-5 progressively decreased and reached undetectable levels on day 39.

In vitro production of IL-5 by PBMCs

In vitro production of IL-5 was assessed on day 19 when the eosinophilia was maximal and the serum IL-5 level was 125 pg/ml. In the absence of OKT3, PBMCs from the patient and from control subjects did not produce any detectable cytokine. In the presence of OKT3, which polyclonally activates T cells, the patient's PBMCs secreted much higher levels of IL-5 than PBMCs from control subjects; in contrast, their production of IFN- γ was clearly deficient (Fig. 1, B). IL-5 production by the patient's PBMCs returned to control levels on day 46, when both serum IL-5 and eosinophilia were normalized (data not shown).

DISCUSSION

This study shows that atheroembolic disease may be associated with the induction of IL-5 release by activated T cells. The decreased IFN- γ secretion associated with IL-5 hyperproduction suggests that these T cells belong to the type 2 helper T-cell subset, which preferentially produces IL-5 and IL-4.⁴ Indeed, the patient's PBMCs were also found to secrete high IL-4 levels in response to phorbol myristate acetate and A23187 calcium ionophore (data not shown). The immune disturbances were self-limited because both IL-5 production and hypereosinophilia spontaneously resolve within a few days. It should be noted that eosinophils

themselves might contribute to some of the measured IL-5. However, taking into account the in vitro data and the respective time courses of serum IL-5 and blood eosinophils, it is likely that most IL-5 originated from T cells. Interestingly, hypereosinophilia related to IL-5 secretion by helper T cells was previously demonstrated in post-traumatic eosinophilic pleural effusion.⁵ This indicates that different traumatic events can lead to T-cell activation, IL-5 release, and hypereosinophilia. Because activated T cells are known to infiltrate human atherosclerotic plaques, it is possible that in our patient they were mobilized and further stimulated by the catheterization procedure.

Whatever the precise mechanism underlying IL-5 secretion by T cells in atheroembolic disease, our observation strongly suggests that T-cell acti-

vation constitutes a major determinant in the hematologic and immunologic abnormalities encountered in this disorder.

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Severe anaphylactic reaction to topical administration of framycetin

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Framycetin is an antibiotic known to cause contact allergy and is mainly used in topical preparations.¹ Anaphylaxis caused by parenteral application of aminoglycoside antibiotics has also been described.² However, for the first time we report a case of severe anaphylactic reaction within minutes after topical administration of the aminoglycoside framycetin to the ground of a venous ulcer. The patient also had a systemic reaction within 10 minutes after prick testing, and specific serum IgG directed against framycetin could be detected.

CASE REPORT

A 77-year-old woman attended the office of a general practitioner to receive topical treatment for venous

ulcers on both lower limbs. The physician proceeded as always and placed a piece of Leukasekegel dressing on the ground of one ulcer. Leukasekegel (SmithKline Beecham, Munich, Germany) is used for topical fibrinolytic treatment of ulcers and consists of the enzyme trypsin, the aminoglycoside framycetin, the local anesthetic lidocaine, calcium arachidate, polyvinylpyrrolidone, and polyethylene glycol.

Within 1 minute after application, the patient experienced dizziness and collapsed with hypotension. (Respiratory rate was not measurable, and there was no peripheral pulse.) She had apnea with cardiac arrest after another 2 minutes. Cardiopulmonary resuscitation was successful with intubation and administration of epinephrine and dexamethasone. Five minutes later, arterial pressure was 80/60 mm Hg and normalized subsequently within another 10 minutes to 120/70 mm Hg. Three months later, the patient was referred to our clinic for allergological investigation.

Allergological investigation

All single compounds of Leukasekegel dressings were prick tested, and all except framycetin, produced negative results (Table I).

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