

Serum eosinophil cationic protein (ECP) in human immunodeficiency virus (HIV) infection

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HIV infection is immunologically characterized by progressive decrease of CD4⁺ lymphocytes and hypergammaglobulinemia.¹ Clinically, it spans from asymptomatic infection to full-blown AIDS, divided into definite stages by the Center for Disease Control classification.² A high incidence of atopic manifestations has been reported in HIV seropositive individuals^{3, 4} with increased serum levels of IgE.⁵ Recently, the rise of serum IgE has been related to the decrease of CD4⁺ cells.⁶ We selected 22 HIV seropositive subjects at different stages of disease, who presented allergic symptoms either for the first time or as a reexacerbation of previous atopic disease. In their sera, we measured the levels of total IgE, allergen-specific IgE, and ECP, a basic protein with cytotoxic properties released by EOSs, which is increased in sera and secretions of atopic patients.⁷⁻⁹

As control subjects, we chose 25 healthy nonatopic subjects, 20 patients with acute recurrent infection (both bacterial and viral), and 29 HIV seropositive cases without history or present symptoms of atopy. Care was taken to match the HIV groups for age, sex, and disease stages. Detailed data on the composition of the groups are reported in Table I.

Additional tests in HIV-positive subjects were white blood cell count, EOS count, both by standard methods, CD4⁺ lymphocyte count, with direct immunofluorescence with monoclonal anti-CD4 (OKT4, Ortho Diagnostic Systems, Raritan, N.J.) and read by flow cytometry (Cytoron, Ortho Diagnostic Systems), and serum levels of IgG, IgA, and IgM by nephelometry with a TDX analyzer (Abbott Diagnostics, Irving, Texas). Results of serum levels of IgE, mea-

Abbreviations used

ECP: Eosinophil cationic protein

EOS: Eosinophil

HIV: Human immunodeficiency virus

sured by Phadezym PRIST (Pharmacia, Uppsala, Sweden), demonstrated that levels were raised both in atopic and nonatopic HIV-positive patients (Table II). Hypergammaglobulinemia was also present in the HIV-positive groups, with significant ($p < 0.01$) increases of IgG and IgA in comparison to healthy control subjects.

Serum levels of ECP were assessed by radioimmunoassay (Pharmacia) with a sensitivity of 2 µg/L. We found that both atopic and nonatopic HIV-positive patients had significant increases of ECP. However, ECP serum levels were raised also in the control subjects with infectious disease (Table II), although this was with a wide scatter of values, as indicated by the high standard mean error. This latter finding was not unexpected, since a transient rise of ECP is known to occur in the first days of bacterial infections.¹⁰ ECP is also increased in atopic diseases, and therefore, its raised level in HIV-positive patients with allergic symptoms was in keeping with the existing knowledge. The finding of high levels of serum ECP also in nonatopic HIV-positive patients appeared to imply that EOSs were involved in the course of HIV infection or that persistent high turnover of EOSs takes place in all stages of HIV disease. Our series consisted of patients without other present or recent infections, without fever, and not taking drugs, with the exception of zidovudine (AZT) for most patients in stages IVC2 and IVC1. Since levels of ECP were not increased in these cases, compared to patients in stages IVA and III, release of ECP could not be considered an effect of zidovudine (AZT) treatment.

We found no relationship between ECP values and the following parameters: total IgE, IgG, IgA, IgM, EOS count, and CD4⁺ count.

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TABLE I. Clinical data on the groups studied

Subjects	Age (yr)	Sex (M/F)	CDC stages	Symptoms (No.)
Atopic HIV (N = 22)	17-57	17/5	II (2) III (7) IVA (1) IVC2 (3) IVC1* (9)	Conjunctivitis (3) Atopic dermatitis (4) Urticaria (6) Rhinitis (9)
Controls				
Healthy Nonatopic (N = 25)	16-42	15/10		
Nonatopic HIV (N = 29)	20-51	23/6	II (2) III (8) IVA (1) IVC2 (7) IVC1* (11)	
Infectious (N = 20)	25-60	12/8		Bacterial diseases (12) Urinary tract infection Pneumonia Salmonella Cholangitis Abscesses Viral diseases (8) Influenza Epstein-Barr virus Hepatitis B virus Hepatitis C virus Measles

CDC, Center for Disease Control.
*None of the IVC1 (AIDS) cases had Kaposi's sarcoma.

TABLE II. IgE and ECP serum values in HIV-positive cases and in control subjects

	IgE (IU/ml)	ECP (µg/L)
Healthy nonatopic subjects	22 ± 85	6.1 ± 5.6
Infectious disease controls	ND	15.6 ± 16.7*
Atopic HIV positive	95 ± 253†	15.6 ± 7.8†
Nonatopic HIV positive	63 ± 131*	15.8 ± 9.5†

ND, Not done.
Arithmetic mean ± SEM for ECP and geometric mean ± SEM for IgE values.
Highest levels of ECP in infectious control subjects were in bacterial infections; only three of 25 healthy subjects had ECP >10 µg/L.
No significant difference of ECP values was found in HIV at different stages.
**p* < 0.05 versus healthy control subjects.
†*p* < 0.01 versus healthy control subjects.

Since EOSs have been found to express CD4 on their surface and thus are able to bind gp120 of HIV,¹¹ the infection may involve these cells. Alternatively, the severe depletion of CD4⁺ lymphocytes in HIV disease may cause the dysregulated production of cytokines affecting EOS degranulation, such as granulocyte-monocyte colony-stimulating factor and in-

terleukin-5.¹² Low production of interferon-γ¹³ and increased levels of interleukin-6¹⁴ have been described in HIV infection.
The frequency of allergic symptoms, increased levels of IgE, and elevated serum ECP may represent additional evidence of the immunologic abnormalities caused by HIV.

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Spontaneous remission of common variable immunodeficiency of 20 years duration

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The manifestations of CVI are mainly pyogenic paranasal sinusitis and pneumonia, characteristic of Ab deficiency. Circulating B-lymphocytes are present, and T-lymphocyte abnormalities occur in about 50% of patients.^{1,2}

Few patients have benefitted from treatment with cimetidine.^{3,4} Spontaneous reversal of CVI has been reported in two HIV-infected patients.⁵ Short-lived immunoglobulin and Ab production occurred in two patients with CVI.⁶ We describe a patient with CVI

Abbreviations used

CVI: Common variable immunodeficiency
Ab: Antibody
HIV: Human immunodeficiency virus

for 20 years, who has maintained a low-normal IgG for 2 years, and has the ability to produce specific Ab.

CASE REPORT

A 25-year-old white woman was found to have hypo- γ -globulinemia in 1969 after recurrent upper respiratory tract infections and two hospitalizations for bronchopneumonia. She denied previous recurrent infections.

Results of a physical examination at that time were unrevealing except for obesity (height, 64 inches; weight, 195 pounds). Results of a complete blood count and chemistry were normal. Hypo- γ -globulinemia was present (Table I),

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