

Eosinophil involvement and serum IgE level in HIV-1-infected children

José Onorato, MD, Susanna Esposito, MD, Elena Scovena, MD, Beatrice Morandi, MD, Marco Morelli, MD, Monica Pizzi, MD, Giuliana Zisa, MD, Paola Marchisio, MD, and Nicola Principi, MD *Milan, Italy*

In HIV-1-infected adults, eosinophilia, increased eosinophil cationic protein (ECP), and elevated serum total IgE levels have been observed.¹ There is little data with respect to these factors in children. Our previous study showed a relationship between elevated serum total IgE level and HIV-1 disease progression in pediatric patients.² The objective of the present study was to define whether eosinophil involvement together with IgE elevation could be identified in HIV-1-infected children.

The study group consisted of 38 vertically HIV-1-infected subjects (median age, 6.5 years; range, 1 to 13 years; 15 boys), 15 of whom had acute respiratory infections (ARIs) at enrollment. The diagnosis of HIV-1 infection and the clinical and immunologic status of children met the criteria of the 1994 Centers for Disease Control (CDC) HIV classification for children.³ As regards clinical classification, 26 subjects were in classes N, A, or B (19 without ARIs and 7 with ARIs), whereas 12 were in class C (4 without ARIs and 8 with ARIs); as regards immunologic classification, 24 children were in classes 1 and 2 (18 without ARIs and 6 with ARIs), whereas 14 were in class 3 (5 without ARIs and 9 with ARIs). None of the class N patients was receiving antiretroviral therapy; patients in classes A and B were being treated with zidovudine, whereas patients in class C were taking zidovudine and didanosine.⁴ When needed, patients were receiving specific prophylaxis for opportunistic infections in agreement with published guidelines.⁴ According to the definition of Kline et al,⁵ among our HIV-1-infected children, 12 subjects had rapidly progressing disease (4 without ARIs and 8 with ARIs), whereas 26 patients had nonrapidly progressing disease (19 without ARIs and 7 with ARIs).

As control subjects, 70 HIV-1-negative children (median age, 5.5 years; range, 1 to 13 years; 28 boys), 26 of whom had ARIs at enrollment, were studied. To avoid the possible increase of eosinophil counts, serum ECP, and IgE concentrations caused by allergic activation, in both HIV-1-infected children and control subjects eligibility criteria included a negative personal and family history of atopy.

Abbreviations used

ARI: Acute respiratory infection
CDC: Centers for Disease Control
ECP: Eosinophil cationic protein

Each child was concomitantly evaluated for whole blood cell count by means of an automated hematology analyzer (Coulter Electronics, Inc, Miami Lakes, Fla), serum ECP concentrations by means of an RIA (Pharmacia ECP RIA, Pharmacia, Uppsala, Sweden), total serum IgE by immunocapture (Pharmacia CAP System IgE RIA, Pharmacia), allergy to common airborne and food allergens by means of skin prick tests, and individual and family history of atopy by means of a medical history. The diagnosis of ARI (both bacterial and viral) was based on clinical findings, radiologic data, and microbiologic isolation of pathogens, according to standardized conventional methods. A diagnosis of pneumonia was made in 8 HIV-1-infected children and 7 control subjects, rhinosinusitis in 3 HIV-1-infected children and 8 control subjects, acute tracheobronchitis in 2 HIV-1-infected children and 8 control subjects, and acute otitis media in 2 HIV-1-infected children and 3 control subjects. Informed consent was obtained from the parents or legal guardians of all the children. Comparison between groups were performed with the Mann-Whitney *U* test.

In both HIV-1-infected children and control subjects, none of the subjects had a positive family history of atopy, none had allergy since birth, and none had positive skin prick test responses.

Table I summarizes eosinophil counts, serum ECP concentrations, and serum IgE levels in the study population. Eosinophil counts and serum ECP concentrations showed no significant differences between HIV-1-infected children and control subjects either with or without ARIs, whereas IgE levels were significantly increased in HIV-1-infected children. Independent from HIV-1 status, ECP concentrations were significantly higher in patients and control subjects with ARIs in comparison to those without ARIs, whereas eosinophil counts and IgE levels showed no significant differences in the presence or absence of ARIs.

Table II describes the relationship between laboratory parameters and CDC setting in HIV-1-infected children. With respect to clinical setting, patients in clinical class C showed higher, even if not significantly increased, levels of serum ECP and significantly increased concentra-

From the Paediatric Department IV, University of Milan, L. Sacco Hospital, Milan.

Reprint requests: Nicola Principi, MD, Paediatric Department IV, University of Milan, L. Sacco Hospital, via G.B. Grassi 74, 20157 Milan, Italy.

J Allergy Clin Immunol 1999;104:245-7.

Copyright © 1999 by Mosby, Inc.

0091-6749/99 \$8.00 + 0 1/54/99013

TABLE I. Eosinophil counts, serum ECP concentrations, and serum IgE levels in the study population

Laboratory parameters	No ARI		ARI	
	HIV-1-infected subjects (n = 23)	Control subjects (n = 44)	HIV-1-infected subjects (n = 15)	Control subjects (n = 26)
Eosinophil counts (cells/ μ L)				
Median	130	160	190	180
Range	25-330	110-275	52-500	91-492
Serum ECP (μ g/L)				
Median	9*	12 [†]	20	20
Range	4-20	9-13	13-34	14-41
Serum IgE (KU/L)				
Median	58 [‡]	19	166 [§]	29
Range	2-181	11-28	17-2000	15-40

* $P < .0001$ versus HIV-1-infected children with ARIs.[†] $P = .0002$ versus control subjects with ARIs.[‡] $P = .03$ versus control subjects without ARIs.[§] $P = .02$ versus control subjects with ARIs.**TABLE II.** Laboratory parameters and CDC setting in HIV-1-infected children

Laboratory parameters	CDC setting					
	CDC clinical classes			CDC immunologic classes		
	N+A+B (n = 26)	C (n = 12)	P value	1+2 (n = 24)	3 (n = 14)	P value
Eosinophil counts (cells/ μ L)						
Median	158	141	.42	130	142	.55
Range	46-500	25-290		46-380	25-500	
Serum ECP (μ g/L)						
Median	14	20	.06	11	19	.02
Range	4-30	6-34		4-30	6-27	
Serum IgE (KU/L)						
Median	64	197	.02	29	296	.02
Range	2-1477	15-2000		2-1477	6-2000	

TABLE III. Laboratory parameters and HIV-1 disease progression

Laboratory parameters	HIV-1 disease progression		P value
	Rapid progression (n = 12)	Nonrapid progression (n = 26)	
Eosinophil counts (cells/ μ L)			
Median	166	137	.27
Range	25-500	46-360	
Serum ECP (μ g/L)			
Median	20	9	.0002
Range	14-34	4-30	
Serum IgE (KU/L)			
Median	316	43	.004
Range	26-2000	2-545	

tions of serum IgE than subjects in clinical classes N, A, and B. On the contrary, eosinophil counts were similar between children in clinical class C and those in clinical classes N, A, and B. With respect to the degree of immunodeficiency, patients in immunologic class 3 showed a significant increase of both serum ECP and IgE concentrations than subjects in immunologic classes 1

and 2. On the contrary, eosinophil counts were similar between children in immunologic class 3 and those in immunologic classes 1 and 2.

Table III shows the relationship between laboratory parameters and HIV-1 disease progression. Interestingly, serum ECP and IgE concentrations were significantly higher in subjects with rapidly progressing disease than in those with nonrapidly progressing disease, whereas no significant difference was observed in eosinophil counts between the 2 groups of children.

Our findings show that eosinophilia is not a feature of HIV-1-infected children, even in the presence of increased serum ECP and IgE concentrations. There are discordant data on eosinophil involvement in HIV-1-infected patients. In adults an increase of eosinophil counts in peripheral blood during HIV-1 infection has been shown.¹ In HIV-1-infected children, Bacot et al,⁶ in agreement with our results, failed to show a significant increase in eosinophil counts. As regards ECP, increased levels of this protein in both atopic and nonatopic HIV-1-infected adults either in the presence or absence of eosinophilia have been described.¹ To our knowledge, this is the first report on the measurement of serum ECP in HIV-1-infected children. In our study serum ECP concentrations seem to be increased in children with ARIs

independent of HIV-1 status and in HIV-1 infected children in clinical class C, in immunologic class 3, and with rapid progression of the disease. However, because of the high incidence of ARIs in our children with severe HIV-1 disease, we cannot finally establish whether the increase in serum ECP level is only a consequence of ARI or also represents a marker of HIV-1 disease progression. Further studies are necessary to clarify the significance of these data. Findings regarding IgE levels confirm our previous study in which elevated serum total IgE concentrations appeared as evidence of the immunologic abnormalities caused by HIV-1 infection in pediatric patients.²

In conclusion, HIV-1 infection does not seem to produce eosinophilia in children at baseline and with ARIs. On the contrary, eosinophil activation appears to be related to ARI and may also be associated with severe HIV-1 disease; moreover, serum IgE levels are increased in children with HIV-1 disease progression.

REFERENCES

1. Paganelli R, Scala E, Mezzaroma I, Pinter E, D'Offizi G, Fanales-Belasio E, et al. Immunologic aspects of hyperimmunoglobulinemia E-like syndrome in patients with AIDS. *J Allergy Clin Immunol* 1995;95:995-1003.
2. Viganò A, Principi N, Crupi L, Onorato J, Zuccotti GV, Salvaggio A. Elevation of IgE in HIV-infected children and its correlation with the progression of disease. *J Allergy Clin Immunol* 1995;95:627-32.
3. Centers for Disease Control. Classification system for human immunodeficiency virus (HIV) infection in children under 13 years of age. *MMWR Morb Mortal Weekly Rep* 1994;43:1-10.
4. Pizzo PA, Wilfert C. Antiretroviral therapy for infection due to human immunodeficiency virus in children. *Clin Infect Dis* 1994;19:177-96.
5. Kline MW, Paul ME, Bohannon B, Kozinetz CA, Shearer WT. Characteristics of children surviving to 5 years of age or older with vertically acquired HIV infection. *Pediatr AIDS HIV Infect: Fetus Adolesc* 1995;6:350-3.
6. Bacot BK, Paul ME, Navarro M, Abramson SL, Kline MW, Hanson IC, et al. Objective measures of allergic disease in children with human immunodeficiency virus infection. *J Allergy Clin Immunol* 1997;100:707-11.