

Short communication

Incidence of peripheral blood eosinophilia and the threshold eosinophile count for indicating hypereosinophilia-associated diseases

Background: A definite threshold of the peripheral blood eosinophile count that indicates the presence of hypereosinophilia-associated diseases has not yet been determined.

Methods: The threshold eosinophile count at which cases of hypereosinophilia-associated diseases ($n = 25$) can be differentiated from those of bronchial asthma ($n = 101$) was determined. Then, the incidences of eosinophile counts greater than $1.0 \times 10^9/l$ or the threshold level, were studied by analysis of 43 805 samples sent to the laboratory, and the diseases associated with the increased counts were determined.

Results: The eosinophile count in cases of hypereosinophilia-associated diseases and in those of bronchial asthma were $10.967 \pm 1.680 \times 10^9/l$ and $0.574 \pm 0.045 \times 10^9/l$, respectively ($P < 0.001$); the threshold was $2.052 \times 10^9/l$. The percentages of samples with an eosinophile count of more than $1.0 \times 10^9/l$ and $2.052 \times 10^9/l$ were 0.6% and 0.1%, respectively; the latter comprised of 41 samples from 24 patients including eight with hypereosinophilia-associated diseases. The patients with hypereosinophilia-associated diseases had a significantly higher count, and a higher incidence of counts of more than $2.052 \times 10^9/l$, than others, including patients with malignancies and symptoms conventionally referred as “atopic diseases”.

Conclusion: Hypereosinophilia-associated diseases are associated with a very high eosinophile count of more than $2.052 \times 10^9/l$, which was observed rarely.

**S. Kobayashi¹, S. Inokuma¹,
K. Setoguchi¹, H. Kono¹, K. Abe²**

¹Department of Allergy and Immunological Diseases; ²Department of Laboratory, Tokyo Metropolitan Komagome Hospital, Japan

Key words: asthma; eosinophile; hypereosinophilic syndrome; IgE; malignancy.

Dr Shigeko Inokuma
Tokyo Metropolitan Komagome Hospital
3-18-22 Honkomagome Bunkyo-ku
Tokyo 113-0826
Japan

Accepted for publication 16 April 2002

Peripheral blood eosinophilia has been commonly associated with allergic disorders, parasite infections, malignancies, various diseases with eosinophile infiltration of a specific organ including eosinophilic enteritis and eosinophilic pneumonitis, and idiopathic hypereosinophilic syndrome (1, 2) that usually involves multiple organs. Eosinophile counts in patients with these diseases range widely from 1 to $10 \times 10^9/l$. Although some reports have focused on the degree of eosinophilia among cases of different diseases (3–9), a definite difference in the eosinophile count between patients with disorders associated with considerable hypereosinophilia and those with symptoms generally referred as “atopic diseases” has not yet been determined. Wardlaw classified eosinophilia into mild (1.0 – $1.5 \times 10^9/l$), moderate (1.5 – $5.0 \times 10^9/l$) and high (more than $5.0 \times 10^9/l$) levels, and reported, without presenting any actual data, that atopic diseases were associated with the mild level, whereas idiopathic hypereosinophilic syndrome, drug reaction and eosinophilic pneumonia were associated with the moderate or high level (3). In contrast, the range of eosinophile count in

healthy individuals was determined to be 0 – $0.65 \times 10^9/l$ (3, 7, 9–11).

Based on our experience, it is noteworthy that a less severe eosinophilia was observed in cases with symptoms generally referred as “atopic diseases”, which include asthma, atopic eczema/dermatitis syndrome (AEDS) and allergic rhinitis or conjunctivitis (Asthma/AEDS) (12). On the other hand, a very high eosinophile count of more than 3 – $4 \times 10^9/l$ was exclusively observed in patients with pathological conditions other than those described above, even if those may be present as complications. Thus, firstly, we attempted to compare the eosinophile count under two pathological conditions, namely bronchial asthma, as a representative of Asthma/AEDS, and conditions highly associated with eosinophilia other than Asthma/AEDS, in order to determine the threshold eosinophile count that differentiates these two conditions.

Furthermore, the entire data obtained from the blood samples sent to the laboratory centre in our hospital for white blood cell (WBC) count measurement were screened for eosinophilia on a serial basis without regard

to diagnoses. Clinical features of all patients with considerable eosinophilia were investigated. This study focused on whether some relationships exist between the degree of eosinophilia and the incidence of a disease.

Material and methods

Patients with bronchial asthma

Blood samples from 101 consecutive patients with bronchial asthma, who were admitted to our hospital from 1990 to 1996, were analysed with respect to the maximum peripheral blood eosinophile count, WBC count, serum IgE level, and total dose of steroid administered per body when the eosinophile count peaked. The diagnosis of bronchial asthma was based on the International Consensus Report on Diagnosis and Management of Asthma in 1992 (13). Our patients included those with both allergic and nonallergic asthma.

Patients with hypereosinophilia-associated diseases (HEADs)

Twenty-five consecutive patients with hypereosinophilia-associated diseases (HEADs; defined below) who were admitted to our department from 1983 to 1998, were studied with respect to the peripheral blood eosinophile count, WBC count when eosinophile count peaked, serum IgE level, and organ involvement.

With some modifications to the criteria of Chusid et al. in 1975 (1) and those of the National Institute of Health in 1982 (2), we defined HEADs in this study as pathological conditions with the following.

- 1 An eosinophile count of more than $1.5 \times 10^9/l$, even for cases of less than 6 months duration.
- 2 Involvement of at least one organ system suspected of being associated with eosinophilia.
- 3 When a patient has a known cause of eosinophilia including parasitic infection and Asthma/AEDS, the presence of signs or symptoms other than those explainable by it, but suggestive of being associated with eosinophilia.
- 4 Cases of allergic granulomatous angiitis, drug reaction associated with eosinophilia, and episodic angioedema associated with eosinophilia (14) were included.

Eosinophile count of serial blood samples determined in our hospital

The eosinophile counts were determined in consecutive blood samples sent to the laboratory centre of our hospital, during the period from May 21 to Nov. 30, 1997, for a total of 125 days except weekends and national holidays. The diagnoses based on the clinical records of patients with an eosinophile count of more than $1.0 \times 10^9/l$ were classified into six groups: HEADs, Asthma/AEDS, malignancies, infections, autoimmune diseases, and others.

Measurement methods of eosinophile count and IgE level

WBC and eosinophile counts were determined using SE-9000 (Sysmex, Kobe, Japan). The peripheral venous blood was diluted 250 times with an erythrocyte-lysing solution, and the number of cells per 250 μl was counted by the direct current detection method. If there was any morphological abnormality or an extreme abnormality in WBC differentiation, light microscopy was performed to confirm findings.

The serum IgE level was measured by enzyme immunoassay using an AIA-21 kit (Toso, Tokyo, Japan). Its normal range was deter-

mined to be 11–580 IU/ml using blood samples from 150 healthy workers in our hospital.

Statistical analyses

For the analysis of asthma and HEADs patients, the comparison of the counts and levels was analysed using Welch's *t*-test, the threshold counts were determined using the receiver operating characteristic analysis, and the correlations were analysed by regression analysis.

For the analysis of consecutive blood samples sent to the laboratory centre, Fisher's protected least significant difference was used to compare the eosinophile counts among the different diagnostic groups. For the comparison of percentage of the count of more than the threshold level, the chi-squared test was used.

Results

Clinical features of patients with bronchial asthma and HEADs admitted to our department

Among the 101 patients with bronchial asthma, 48 were male and 53 were female, with a mean $\pm$ SE age of 49.1 ± 1.6 years. The dose of prednisolone administered was 1.2 ± 0.3 mg/day.

The sex, age, diagnoses and organs involved in 25 patients with HEADs are presented in Table 1. The number of organs involved in a patient ranged from 1 to 5, and the mean was 2.44. Fifteen patients responded well to steroid therapy, six patients recovered spontaneously, two patients who exhibited a drug reaction recovered after withdrawal of the drug, one patient with eosinophilic pneumonia recovered by treatment with suplatast tosilate, and Case 11 with allergic granulomatous angiitis died of acute cardiac failure.

Thresholds of eosinophile count, eosinophile percentage, and serum IgE level to differentiate HEADs from bronchial asthma

The eosinophile counts were $0.574 \pm 0.045 \times 10^9/l$ (range: $0-2.457 \times 10^9/l$) in cases of asthma, and $10.967 \pm 1.680 \times 10^9/l$ ($1.536-30.312 \times 10^9/l$) in cases of HEADs ($P < 0.0001$). The threshold eosinophile count differentiating the two groups was $2.052 \times 10^9/l$, with a sensitivity of 98.0% and specificity of 100%. Only one among 101 asthmatic patients had a count of more than the threshold level. Conversely, only one patient with a drug reaction had a count below $2.052 \times 10^9/l$ among the 25 with HEADs.

The WBC counts were $6.926 \pm 0.240 \times 10^9/l$ ($3.4-16.3 \times 10^9/l$) in patients with asthma and $17.459 \pm 1.890 \times 10^9/l$ ($6.4-42.1 \times 10^9/l$) in those with HEADs ($P < 0.0001$). The eosinophile percentages with respect to the total WBC were $9.0 \pm 0.7\%$ ($0-32.0\%$) in those with asthma and $55.8 \pm 4.1\%$ ($21.0-84.5\%$) in those with HEADs ($P < 0.0001$); the threshold value was 27.0% (sensitivity: 97.1% specificity: 96.0%). The serum IgE levels were 902 ± 248 IU/ml ($3-23\ 179$ IU/ml, $n = 99$) in

Table 1. Clinical features of patients admitted with hypereosinophilia-associated diseases

Diagnosis	Patient		Age (years)	WBC* ($\times 10^9/l$)	Eosinophile†		Organs involved
	No.	Sex			($\times 10^9/l$)	(%)	
Idiopathic	1	F	45	11.2	4.779	43	Skin
hypereosinophilic syndrome‡	2	F	50	13.0	9.880	76	Gastrointestinal tract, pericardium
	2	F	72	31.0	24.490	79	Skin, lung, heart
	4	F	27	9.2	2.944	32	Skin, joints, bronchi
	5	M	47	23.0	18.630	81	Skin, lung, heart, joints
	6	F	59	9.5	5.605	59	Skin, joints
	7	M	33	10.9	6.758	62	Skin, vessel
	8	M	58	18.1	9.593	53	Lung, heart
	9	F	25	23.5	12.220	52	Skin
Allergic	10	F	60	13.2	6.204	47	Skin
granulomatous	11	M	58	42.1	30.312	72	Bronchi, lung, PNS§, heart, skeletal muscle, liver (autopsy)
angiitis	12	F	72	15.8	12.956	82	Bronchi, kidney, PNS§
	13	M	53	28.7	24.000	85	Bronchi, lung, PNS§, heart, skeletal muscle
	14	M	39	21.4	5.778	27	Skin, bronchi, PNS§, gastrointestinal tract, peritoneum
	15	F	54	19.1	11.210	59	Bronchi, PNS§, skeletal muscle, gastrointestinal tract
Eosinophilic	16	M	57	22.9	16.259	71	Peritoneum
petitonitis	17	M	26	31.3	23.006	74	Bronchi, peritoneum, pleura
Eosinophilic	18	M	30	8.1	4.860	60	Gastrointestinal tract
gastroenteritis							
Eosinophilic	19	F	65	7.3	3.431	47	Bronchi, lung
pneumonia							
Drug reaction	20	F	52	6.4	1.536	24	Kidney
(to bucillamine)	21	F	27	7.2	3.312	46	Skin, lung
Others	22	M	54	26.7	22.161	83	Skin, bronchi, lung
	23	F	27	9.8	2.058	21	Bronchi, liver, CNS¶
	24	F	26	7.6	2.052	27	Skin, bronchi
	25	F	17	19.5	10.140	52	Bronchi, lung
Mean $\pm$ SE			45.3 $\pm$ 3.3	17.459 $\pm$ 1.890	10.967 $\pm$ 1.680	56.6 $\pm$ 4.0	

* The count when eosinophile count peaked.

† Maximum count during the disease course.

‡ Defined based on the criteria of Chusid and National Institute of Health.

§ PNS: peripheral nervous system.

¶ CNS: central nervous system.

those with asthma and 3047 ± 1680 IU/ml (3–20 304 IU/ml, $n = 24$) in those with HEADs ($P = 0.0037$); the threshold level was 909 IU/ml (sensitivity: 78.6% specificity: 52.0%). The WBC count, eosinophile percentage and serum IgE level were all significantly higher in patients with HEADs than in those with bronchial asthma.

In the case of HEADs, the eosinophile count correlated significantly with the eosinophile percentage ($P < 0.0001$), but not with the serum IgE level. In the case of asthma, the correlations were similar.

Eosinophilia among serial samples sent to the laboratory

Among 43 805 blood samples (for which a differential count was requested) out of 58 989 sent to the laboratory centre for WBC count measurement, 273 blood samples (0.6%) obtained from 165 patients had an eosinophile count more than $1.0 \times 10^9/l$, and the mean $\pm$ SE was $1.624 \pm 0.067 \times 10^9/l$ (1.000 – $8.080 \times 10^9/l$). The number of samples with the eosinophile counts in

increments of $0.5 \times 10^9/l$ were: 175 (for 1 – $1.5 \times 10^9/l$), 52 (1.5 – 2), 18 (2 – 2.5), 10 (2.5 – 3), 6 (3 – 3.5), 6 (3.5 – 4), 1 (4 – 4.5), 2 (4.5 – 5), 3 (< 5). There were 41 (0.1%) samples from 24 patients with an eosinophile count more than the threshold level ($2.052 \times 10^9/l$) that differentiated HEADs from bronchial asthma.

Diseases with eosinophile count of more than $1.000 \times 10^9/l$

The maximum eosinophile counts for each of the 165 patients with eosinophile counts of more than $1.000 \times 10^9/l$ during the follow-up period are shown in Table 2, with the respective diagnoses. Thirty-eight patients with Asthma/AEDS included 23 with bronchial asthma, 15 with atopic dermatitis, and six with allergic rhinitis or conjunctivitis (some patients had more than one of these). Sixty-five patients with malignancies included 59 with solid tumours (one had cancers both in the breast and stomach), two with lymphoma, and five with acute myelocytic leukaemia. Among these 65

Table 2. Eosinophile counts and diagnoses of the patients who provided blood samples with eosinophile counts of more than $1.000 \times 10^9/l$

Max. eosinophile count ($\times 10^9/l$)	Diagnosis*†						Total
	Hypereosinophilia-associated diseases	Asthma/AEDS‡	Malignancy	Infection	Autoimmune diseases	Others	
1–1.5	1 (0.9)	22 (21.6)	44 (43.1)	14 (13.7)	8 (7.8)	39 (38.2)	102 (100)
1.5–2	2 (5.6)	11 (30.6)	10 (9.8)	4 (3.9)	0 (0)	14 (38.9)	36 (100)
2–2.5	2 (16.7)	4 (33.3)	5 (41.7)	1 (8.3)	0 (0)	5 (41.7)	12 (100)
2.5 <	6 (40.0)	1 (6.7)	6 (40.0)	0 (0)	0 (0)	6 (40.0)	15 (100)
1 < (total)	11 (6.7)	38 (23.0)	65 (39.4)	19 (11.5)	8 (4.8)	64 (38.8)	165 (100)
Mean $\pm$ SE of eosinophile count	3.310 $\pm$ 0.592§	1.518 $\pm$ 0.079	1.551 $\pm$ 0.085	1.377 $\pm$ 0.076	1.186 $\pm$ 0.050	1.653 $\pm$ 0.103	1.600 $\pm$ 0.054

* Diagnoses are multiple in some patients.

† In parentheses, percentage of total patients with the eosinophilia of each increment.

‡ Asthma/AEDS: asthma, atopic eczema/dermatitis syndrome, and allergic rhinitis and/or conjunctivitis.

§ $P < 0.001$ vs. other diseases.

patients with malignancies, a remission of more than 5 years was noted in four, and 21 died by Oct. 1998; about one-third were considered to be at the terminal stage at the time of sampling. Among 19 patients with infections, seven outpatients were asymptomatic carriers of the human immunodeficiency virus, seven had type C viral hepatitis, two had type B viral hepatitis, and one each had measles, herpes zoster, and *Loa loa* parasitic infection. HEADs were noted in 11 patients: five had idiopathic hypereosinophilic syndrome; three had a drug reaction induced by ranitidine hydrochloride, minocycline hydrochloride, and ciprofloxacin hydrochloride; and one each had eosinophilic pneumonia, Kimura's disease and eosinophilic gastroenteritis. Eight patients with autoimmune diseases included two each with systemic lupus erythematosus, rheumatoid arthritis and hyperthyroidism, one each with Sjogren's syndrome, chronic thyroiditis, and primary biliary cirrhosis; one patient had overlapping diseases. For the 64 remaining cases, the diagnoses included 91 diseases, which have been previously thought not to be associated with peripheral blood eosinophilia, and the diagnosis in one was not determined, and one case visited our hospital only for a vaccination.

Although the diagnoses were mostly diseases other than HEADs, the higher the eosinophile count, the higher the incidence of HEADs. The eosinophile count in patients with HEADs was $3.310 \pm 0.592 \times 10^9/l$, which was significantly higher than those in patient groups with any other diseases, as determined by the analysis of variance ($P < 0.001$) (Table 2).

Diseases with eosinophile count of more than $2.052 \times 10^9/l$

Among the 24 patients with eosinophile counts of more than $2.052 \times 10^9/l$, four had Asthma/AEDS; however, among them, only one had bronchial asthma only; one had breast cancer and two had HEADs, in addition to

Asthma/AEDS (Table 3). Consequently, eight had HEADs and 10 had malignancies; these 18 comprised 75% of patients with eosinophile count of more than $2.052 \times 10^9/l$. Cases with the eosinophile count of more than $2.052 \times 10^9/l$ occurred at a significantly higher incidence among HEADs, than among those of malignancies ($P < 0.001$) or others ($P < 0.001$), among patients with the eosinophile count of more than $1.000 \times 10^9/l$. Although four patients (Nos 4, 11, 14, 20) had no known eosinophilia-associated disease, no further investigation concerning their eosinophilia was carried out. The maximum count obtained with respect to the total samples was $8.080 \times 10^9/l$ in a patient with eosinophilic gastroenteritis.

Discussion

In this study, the criteria for HEADs included a wider scope than those for hypereosinophilic syndrome criteria established by Chusid et al. (1) and the National Institute of Health (2). These conventional criteria excluded disorders generally referred to as atopic diseases. However, a patient with such a disorder could potentially suffer from another disease associated with eosinophilia. We thought that it was reasonable to include these cases in the HEADs group. The conventional criteria also excluded cases of eosinophilia of less than 6 months. However, sometimes we have no choice but to start therapy. We also thought it was reasonable to include cases in whom therapy was started within 6 months, and cases in whom the time when eosinophilia had developed was unclear. Furthermore, allergic granulomatous angiitis and drug reaction with eosinophilia should be included with HEAD in this study, in order to determine the level of peripheral blood eosinophile count in disorders, the pathogenesis of which is strongly associated with eosinophilia.

Table 3. The diagnoses in 24 patients, who provided the samples with eosinophile counts of more than $2.052 \times 10^9/l$

No.	Eosinophile count ($\times 10^9/l$)	Hypereosinophilia-associated diseases	Asthma/AEDS*	Malignancy	Infection	Others
1	2.090			Lung cancer†		
2	2.090		Asthma			Hypertension, Mitral regurgitation
3	2.100			Lung cancer		
4	2.130					Vertigo
5	2.146			Melanoma†		
6	2.170			Lung cancer		Diabetes mellitus
7	2.300	Idiopathic HES§	AEDS			Emphysema
8	2.340				HIV¶	
9	2.490	Eosinophilic pneumonia	Asthma			
10	2.520	Idiopathic HES§				
11	2.592					Cataract, Sclerotic retinopathy
12	2.620			Gastric cancer Breast cancer		
13	2.730			Lung cancer†		
14	2.856					Diabetes mellitus, Hypertension, Gout, Old myocardial infarction
15	2.930			Gastric cancer†		
16	3.150		Allergic rhinoconjunctivitis	Breast cancer		
17	3.480	Idiopathic HES§				
18	3.560	Drug reaction**				Bronchiectasis
19	3.770	Kimura's disease				
20	3.870					Membranous glomerulonephritis
21	3.936			Acute myelocytic leukaemia		
22	4.674			Gastric cancer‡		Prostatic hypertrophy
23	5.320	Drug reaction††				Gastric ulcer
24	8.080	Eosinophilic gastroenteritis				
Total numbers of patients		8	4	10	1	10

* Asthma/AEDS: asthma, atopic eczema/dermatitis syndrome, and allergic rhinitis and/or conjunctivitis.

† Died within 1 year after sampling.

‡ Good prognosis after curative operation.

§ HES: hypereosinophilic syndrome.

¶ HIV: human immunodeficiency virus infection.

** Caused by ciprofloxacin hydrochloride.

†† Caused by ranitidine hydrochloride.

This study was conducted to determine whether there was a clear difference in the eosinophile count between cases of HEADs and disorders generally referred to as atopic diseases, which to date has not yet been determined. The results showed the threshold count that differentiates these two disorders to be $2.052 \times 10^9/l$.

Eosinophilia has been defined as a pathophysiological condition with an eosinophile count of more than $1.5 \times 10^9/l$ (1,2); the normal upper range was generally considered to be less than $0.5 \times 10^9/l$. Thus, to determine the incidence of eosinophilia, we studied the percentage of samples with eosinophile counts of more than $1.0 \times 10^9/l$. The analysis of serial samples in our general hospital revealed that 0.6% had a count of more than $1.0 \times 10^9/l$. However, most of the samples had a count of less than $2.0 \times 10^9/l$, and a count of more than $2.052 \times 10^9/l$ was observed only rarely in 0.1% of the total serial samples.

Although Asthma/AEDS were diagnosed in about one-fourth of 165 patients with eosinophile counts of more

than $1.0 \times 10^9/l$, most of them had counts below $2.052 \times 10^9/l$. Rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis and systemic sclerosis may be sometimes complicated with eosinophilia (15,16). In this study, eight patients with collagen diseases exhibited eosinophilia, but the counts were less than $1.5 \times 10^9/l$. The relationship between human immunodeficiency virus infection and blood eosinophilia or skin diseases, particularly eosinophilic folliculitis, and the relationship between the terminal features and eosinophilia have been reported (17–19). In the present study, only one out of seven patients with human immunodeficiency virus infection had eosinophile counts of more than $2.052 \times 10^9/l$; all the infected patients, including the one with a count of more than $2.052 \times 10^9/l$, were outpatients with well-tolerated infection. Previous studies reported that some eosinophilic patients had malignancies (20–26), and if the patients, including those who underwent irradiation (20), had blood eosinophilia, they would have a good prognosis (19–22). In the present

study, malignancies were diagnosed in more than one-third of the 165 patients, and 10 exhibited counts of more than $2.052 \times 10^9/l$. However, few had a good prognosis; many were at the terminal stage at the time of sampling, and about one-third died within one year after sampling.

When discussing the relationship of blood eosinophilia with pathological conditions in this study, we must consider that our general hospital has considerable experience in handling malignancies and infectious diseases including human immunodeficiency virus infection. The comparative ratios of diagnoses of the hospitalized patients determined by a one-day study by the Metropolitan Government showed that the ratios of malignancies and infectious diseases were much higher in our hospital than in other hospitals run by the Government (27). The bed use in our Department of Allergy and Immunological Diseases was only 3.3% of the total 801 beds. However, the higher the eosinophile count, the higher the HEAD incidence; the mean count of $3.310 \times 10^9/l$ in cases of HEADs was more than two times higher than that for any other cases of diseases with eosinophile counts of more than $1.0 \times 10^9/l$. Nevertheless, it should be noted that some patients with malignancy may exhibit hypereosinophilia, but milder.

Among the 24 patients with an eosinophile count of more than $2.052 \times 10^9/l$, those with malignancies comprised the largest number. However, the incidence of counts greater than $2.052 \times 10^9/l$, even among the samples with counts of more than $1.0 \times 10^9/l$, was significantly higher in patients with HEADs than in those with malignancies. This suggests that an eosinophile count of more than $2.052 \times 10^9/l$ is strongly suggestive of HEADs.

Since no study has reported a threshold count which could differentiate HES or HEADs from disorders referred to as atopic diseases and some other diseases associated with eosinophilia, we propose $2.052 \times 10^9/l$ as the threshold count. The maximum eosinophile count obtained during the serial sample analysis for six months was $8.080 \times 10^9/l$ in a patient with eosinophilic gastroenteritis. On the other hand, the maximum count in each of the 25 patients with HEADs treated in our department was much higher, being more than this

value in 13 patients, reaching $30.312 \times 10^9/l$. HEADs are very rare. In contrast to Asthma/AEDS, which are usually limited to the bronchus, skin and mucosa, the organs involved in 25 HEAD patients included organs other than the three; up to five organs were involved in one patient.

Although the pathogenesis for the increase in blood eosinophile count in patients with HEADs has not yet been clarified, some immunological mechanisms have been suggested. A history of allergy has been confirmed in the case with allergic granulomatous angiitis; antineutrophil cytoplasmic antibody and/or rheumatoid factor was often found; and surface receptor abnormalities of peripheral blood lymphocyte and a high level of immune-complex were reported (28). The serum IgE level was reported to be higher than the normal upper limit in 38% of patients with idiopathic hypereosinophilic syndrome, and a relatively good prognosis was suggested in patients with a high serum IgE level (28). In this study, a patient with the highest eosinophile count, and a serum IgE level of 3682 IU/ml died; others with various serum IgE levels either had spontaneous remission or recovered after steroid treatment (data not shown). Although both the eosinophile count and serum IgE level were higher in cases of HEADs than in those of asthma, no statistically significant correlation was found between the count and level in either disorder. The mechanisms underlying the increases may be different.

In conclusion, HEADs are associated with a very high peripheral blood eosinophile count, which is observed rarely. When a patient is found to have a much higher count than the threshold, that is, $2.052 \times 10^9/l$, determination of the organs involved in association with eosinophilia would be necessary, irrespective of whether the patient has an Asthma/AEDS or not. A simultaneously observed high serum IgE level is also suggestive of HEADs.

Acknowledgments

The authors thank Ms Keiko Miyahara for her help.

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