Increased Immunoglobulin E and Interferon- γ in Patients with Malignant Lymphoma

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In recent years, there have been several reports of increased concentrations of cytokines as well as other indicators of immune activation, e.g. soluble interleukin-2 receptor or neopterin, in patients with lymphoma [1-7]. Among other immunological disturbances, increased immunoglobulin E (IgE) levels have also been reported [8]. IgE synthesis is known to be induced by interleukin-4 (IL-4) and inhibited by interferon- γ (IFN- γ) [9], and elevated IL-4 levels have been reported in some conditions characterized by increased IgE concentrations, e.g. atopic disorders [10]. A rise in serum IL-4 has also been described in other disorders, notably in cutaneous T cell lymphoma [11].

We assayed plasma concentrations of IL-4, IFN- γ and IgE in 14 patients with a histologically confirmed diagnosis of lymphoma (mean age 42 ± 17 years, table 1) and in 15 healthy controls (10 males and 5 females, mean age 48 ± 20 years, range 21-75). All patients had active disease and were either newly diagnosed or untreated for at least 4 weeks. A plasma sample was obtained and kept frozen at -45°C until assayed. IL-4 and IFN- γ were determined using commercial ELISA kits (Quantikine human IL-4, R&D Systems, Minneapolis, Minn., USA, and Endogen human IFN- γ , Boston, Mass., USA) according to the manufacturer's instructions. IgE was measured with a nephelometric method using a commercial kit (Behring, Marburg, Germany). The limits of detectability were 10 pg/ml for IL-4 and IFN- γ and 33 IU/ml for IgE. The results were expressed as mean, standard deviation and range of values, the statistical comparison was performed with the Mann-Whitney U test and the correlations were studied with the Spearman rank coefficient. Significance was based on the $p = 0.05$ level.

Table 1. Patient characteristics
Patient Sex

Age years
Diagnosis
Stage
IgE IU/ml
IFN- γ pg/ml

I
f
19
HD, nodular sclerosis
II
248
53.3
2
m
47
HD, mixed cellularity
IV
440
44.4
3
f
22
HD, mixed cellularity
III
363
73.6
4
f
40
HD, mixed cellularity
III
305
63.3
5
f
39
HD, nodular sclerosis
IV
127
57.5
6
f
30
HD, nodular sclerosis
IV

44
82.4
7
f
21
HD, mixed cellularity
IV
221
0
8
m
33
HD, nodular sclerosis
II
878
0
9
m
38
HD, lymphocyte-depleted
III
298
0
10
f
61
NHL, lymphocytic
IV
189
51.5
11
m
78
NHL, lymphocytic
IV
112
20.1
12
m
63
NHL, lymphocytic
III
95
0
13
m

44

NHL, centroblastic-centrocytic

IV

243

25.1

14

m

54

NHL, centroblastic-centrocytic

IV

103

20.2

HD = Hodgkin's disease; NHL = non-Hodgkin lymphoma.

Table 2. IFN- γ and IgE levels in lymphoma patients and controls

IL-4 was not detectable in any of the studied subjects. On the other hand, IFN- γ and IgE were significantly elevated in patients with Hodgkin's disease and in the whole group of patients with lymphoma (table 2). No significant correlation was observed between IFN- γ and IgE in lymphoma patients ($r_s = -0.027$, $p = 0.928$) and in patients with Hodgkin's disease ($r_s = -0.339$, $p = 0.372$).

These results are in accord with a previous report of increased IgE concentrations in Hodgkin's disease [8]. More recent studies have found an elevation in circulating levels of a variety of cytokines, including interleukin-6, interleukin-8, interleukin-10 and interleukin-2 [1-3, 7]. High levels of interleukin-6 have been linked to the presence of symptoms and poor prognosis in Hodgkin's disease [2]. On the other hand, negative results have been reported regarding serum concentrations of both IL-4 and IFN- γ [1,2, 7]. Contrary to these reports, we found a significant elevation of IFN- γ in patients with lymphoma. However, an increase in IFN- γ activity is known to be associated with elevated levels of neopterin [12], and neopterin concentrations in patients with lymphoma are known to be significantly increased, which could also indicate enhanced IFN- γ activity [5, 6].

IL-4 and IFN- γ are thought to be produced by different subsets of CD4 lymphocytes, Th2 and Th1 lymphocytes, and have opposing effects on IgE synthesis [9, 13]. Despite the fact that IgE was significantly higher in patients with lymphoma we were unable to detect plasma IL-4 in any of the patients. In contrast, the circulating levels of IFN- γ , a known inhibitor of IgE synthesis, were elevated in these patients. The present findings could indicate the activation of ThO CD4+ cells, which are known to produce both IL-4 (high IgE in this group) and IFN- γ [13].

In conclusion, both IFN- γ and IgE seem to be elevated in malignant lymphoma. There seems to be no apparent link between plasma IgE and IFN- γ concentrations in lymphoma patients.

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168

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IgE and Interferon- γ in Lymphoma