Serum Ig E Concentration In Acute Pulmonary Thromboembolism

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Abstract

Background : Events mediated by immunoglobulin E (IgE) may be related to platelet activation and aggregation, and serum IgE concentrations may increase in various vascular diseases such as previous myocardial infarction, previous stroke and current large-vessel peripheral arterial disease. There may be an association between serum IgE and acute pulmonary thromboembolism (PTE).

Objectives : The aim of the study was to evaluate serum IgE concentrations in patients with acute PTE.

Methods : Twenty-two patients with a diagnosis of acute PTE were included in the study. Serum IgE concentrations were measured by an automated microparticle enzyme immunoassay at the time of diagnosis and 5th, 15th, and 30th days after the diagnosis. Because serum IgE concentrations follow a log-normal distribution, all subsequent analysis were performed on a log transformed scale and geometric mean values were used. The Wilcoxon matched-pairs signed-ranks test was applied for paired analysis.

Results : Serum IgE concentrations (geometric mean ± SEM) were 1.90 ± 0.15, 1.91 ± 0.16, 1.82 ± 0.15, and 1.76 ± 0.15 at the time of diagnosis and 5th , 15th, and 30th days after the diagnosis, respectively. Serum IgE concentrations were not significantly different between at the time of diagnosis and 5th day after the diagnosis. However, serum IgE concentrations were significantly lesser at the 15th and 30th days after the diagnosis than serum IgE concentrations at the time of diagnosis and at 5th days after the diagnosis ($p < 0.001$).

Conclusions : The data evaluating serum IgE concentrations in patients with acute PTE is limited and, to our knowledge, until now there has been only one study. Our study showed that serum IgE concentrations that were detected at the time of diagnosis of acute PTE significantly lessen with treatment at the 15th and 30th days after the diagnosis.

INTRODUCTION

Pulmonary thromboembolism (PTE) is a serious and often fatal condition primarily complicating the course of hospitalised patients. PTE pose a diagnostic challenge to clinicians. The history, physical examination, noninvasive laboratory workup, and basic chest radiography are all nonspecific. Suspicion of the diagnosis, based on the presence of risk factors and frequent, but nonspecific, clinical findings should lead to a thorough diagnostic evaluation that leads to either confirmation or exclusion of PTE [1].

Serum immunoglobulin E (IgE) concentration may increase in various vascular diseases such as myocardial infarction [2], stroke and large-vessel peripheral arterial disease [3]. Events mediated by IgE are related to platelet activation [3, 4] and aggregation [3, 5].

To our knowledge, in only one study [6], acute rise in serum IgE level was reported in acute pulmonary thromboembolism (PTE). Aim of the study was to evaluate serum IgE concentrations in patients with acute PTE and to examine changes in serum IgE concentration with treatment within one month of the diagnosis.

MATERIAL AND METHODS

We conducted a prospective study of patients with a diagnosis of acute PTE at a university hospital between February 1996 and May 1997. Clinically suspected acute PTE was confirmed by ; a) Ventilation/perfusion lung scanning (V/Q scan) that showed a high probability of PTE or b) V/Q scan that showed intermediate probability of PTE and deep vein thrombosis on compression ultrasonography. Patients who met these criteria for inclusion were eligible if the diagnosis was reached within two days. But patients who met these criteria for inclusion were ineligible for the study if they had a documented current or history of atopic diseases such as allergic rhinitis, allergic dermatitis, bronchial asthma, urticaria, and also parasitic diseases.

We examined complete blood count, peripheral blood smear, whole blood chemistry, arterial blood gases, prothrombin time, activated partial thromboplastin time, stool examination for parasites, electrocardiography, chest x-ray and thoracic computed tomography (CT) in all patients.

We used an automated microparticle enzyme immunoassay for measurement of serum IgE levels : 5 ml venous blood was taken from the patients at the day of diagnosis and 5th, 15th, and 30th days after the diagnosis. Each specimen was centrifugated in 2500 revolutions Per minute for 10 minutes and then sera was kept at –70 C until measurement. On measurement day, the sera that was processed with IM x total IgE kit (lot no 23107U101) after solving at room temperature, and the levels of IgE was measured by a spectroflouometry of trade mark IMx.

Because serum IgE concentrations follow a log-normal distribution, all subsequent analysis were performed on a log transformed scale (log IgE) and geometric values were used. The Wilcoxon matched-pair signed-ranks test was applied for paired analysis. Differences were considered significant when the p value was less than 0.05.

RESULTS

The recruitment of patients began in February 1996 and ended in May 1997. A total of twenty-four consecutive patients met the criteria for inclusion, among whom two patients were excluded from the study because they died due to recurences of acute PTE within first week. Of the twenty-two eligible patients, eight (33.3 %) was male. The mean age was 49.5 ± 15.8 years (range : 25-85 years).

All patients underwent ventilation / perfusion lung scanning (V/Q scan) and also compression ultrasonography for both lower extrenmity veins. The results of V/Q lung scans were as follows : Sixteen patients with a high probability of acute PTE and six patients with an intermediate probability. The findings of deep vein thrombosis on compression ultrasonography were positive in twenty-one patients including all the patients with intermediate probability of acute PTE on V/Q lung scans. The localisations of thrombosis were as follows : Bilateral femoral and popliteal veins in eight patients, left femoral and popliteal veins in seven patients, right femoral and popliteal veins in 6 patients.

Serum IgE concentration (IU/ml) of the study group at the time of the diagnosis, and 5th, 15th, and 30th days after diagnosis were shown in table 1. Because serum IgE levels followed a log-normal distribution, all subsequent analysis were performed on a log transformed scale (log[IgE]) and geometric mean values were used. Serum IgE concentration (log[IgE]) (geometric mean ± SEM) were 1.90 ± 0.15, 1.91 ± 0.16, 1.82 ± 0.15, and 1.76 ± 0.15 at the time of diagnosis and 5th , 15th, and 30th days after the diagnosis, respectively, that were shown in table 2.

Figure 1

Table I : Serum IgE levels (IU/ml) at the time of diagnosis (dx), and 5th, 15th, and 30th days after the diagnosis

Patients	at the time of dx	5th day	15th day	30th day
1	472	438	478	299
2	391	423	343	264
3	103	98	90.6	73.2
4	24	22.8	19.8	16.8
5	1904	1649	1438	1144
6	2.4	1.8	1.4	2.6
7	195	256	163	109
8	122	232	96.8	77.6
9	405	471	359	313
10	743	676	643	454
11	17.8	15	7.8	9.2
12	244	380	169	111
13	137	121	131	109
14	85.8	76.8	96	67.4
15	11	10.2	11.4	11.6
16	26.6	38.4	40.8	18.5
17	822	910	628	544
18	35.2	52.8	25.2	21.4
19	255	269	228	196
20	339	527	315	276
21	331	346	305	275
22	45.2	16.4	20	9.4

Figure 2

Table 2 : Serum IgE levels (geometric mean values in log) at the time of diagnosis, and 5th,15th, and 30th after diagnosis

Days	Serum IgE (log[IgE]) (log(IU/ml)
At the time of dx	1.90 ± 0.15
5th day	1.91 ± 0.16
15th day	1.82 ± 0.15
30th day	1.76 ± 0.15
p	p < 0.001

p < 0.05 : statistically significant

Serum IgE concentrations were not significantly different between at the time of diagnosis and at 5th day after the diagnosis. However, serum IgE concentrations were significantly lesser at the 15th and 30th days than that of at the time of diagnosis and 5th day after the diagnosis (p<0.001), that were shown in table 3.

Figure 3

Table 3 : The results of Wilcoxon matched-pairs signed ranks test for serum IgE levels at the time of diagnosis (dx) and 5th, 15th, and 30th days after the diagnosis

	at the time of dx	5th day	15th day	30th day
at the time of dx		p> 0.05	p< 0.01	p< 0.01
5th day			p< 0.05	p< 0.001
15th day				p< 0.001

p < 0.05 statistically significant

DISCUSSION

Although beneficial effects of IgG, Ig A, IgM and IgD are well known, the beneficial role of IgE in health and disease, if there is, is still unknown, except for its larvacidal effect on Schistosoma mansoni that was seen experimentally [7]. Atopic diseases including bronchial asthma, allergic rhinitis, allergic dermatitis, urticaria and parasitic diseases are well known conditions in which serum IgE levels increase. Interestingly the events, increase in serum IgE level, was reported also after myocardial infarction [2, 8, 9], major trauma [10], or surgeries [11], but significance or importance of this event could not be explained. Recently, Takewaka et al [6] reported that serum IgE concentration increased during acute phase (1 to 2 weeks after the onset) and also found that increase in serum IgE levels in severe forms of PTE was more than milder ones, in contrast to previous studies findings in MI patients, in which increase in serum IgE level was found as a good prognostic sign, and Takewaka et al [6] concluded that IgE may be an indicator of the severity of PTE. To our knowledge, this is the second report demonstrating a significant relationship between serum IgE levels and PTE.

The present study showed that the serum IgE concentration increased in PTE, reaching a peak on fifth day and then significantly lessen at the 15th and 30th days after onset. The clinical significance of increment of serum IgE concentrations in early phase of PTE is not known. The proposed possible mechanisms of the early increase in serum IgE concentration in PTE ; 1) an immune response against necrotic tissue in which interleukin- 4 released from CD4 cells specifically induces IgE production by B lymphocytes [12], and 2) a nonallergic response by humoral substances, such as platelet activating factor from emboli or related cells [13].

We do not know exactly what the role or function of IgE is in PTE but possible mechanisms of action of IgE include : (1) IgE-dependent release of a Hageman factor cleaving factor that rapidly cleaves and inactivates the activated factor [14], (2) IgE delays thrombin generation and depresses the clot formation [9], (3) IgE stimulates hypothalamus-adrenal axis and release of glucocorticoids interacting with de novo synthesised interleukin 6 and as a result may act as an acute phase reactant in response to tissue injury [10], (4) IgE mediated heparin release from the mast cells resulting in local tissue anticoagulation [15]. And, lastly, we thought that IgE mediated immune response in association with inflammation reactions may contribute to the clearance of necrotic tissue and/or healing processes.

In our study, with treatment, serum IgE concentrations returned to its basal level that may be due to chemical mediators, such as trasforming growth factor-b, which inhibit IgE synthesis from plasma cells [16] or may be spontenously.

In conclusion, the serum IgE concentration may be an indicator of acute PTE and may be useful for its diagnosis. But, further studies are needed to clarify the mechanism by which IgE level increases and also why serum IgE level increases in acute PTE.

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