Short Communication

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Serum Immunoglobulin Levels in Splenectomized and Non-Splenectomized Patients with Major Beta-Thalassemia

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Abstract

Objective: Thalassemia is a common disease in many countries, in which several complications such as infections can occur. Although aberration in the function of the immune system could be a reason for such complication, a little is known about the status of humoral immune system in major beta thalassemia. In this study we measured serum immunoglobulins level in a group of patients with major beta thalassemia.

Methods: Ninety nine patients with major beta thalassemia were enrolled in this study divided into two groups of splenctomized and not splenctomized patients. Serum IgG, IgM and IgA levels of these patients were measured and analyzed.

Findings: Serum mean levels of IgG and IgM in patients of all ages in both groups were normal. The mean serum IgA level in the group of not splenectomized patients aged less than five years as well as in the splenectomized patients aged more than twenty years was increased. However, it was normal in other age groups.

Conclusion: Although this study could not show any defect in the humoral immune system, evaluation of immunoglobulins could be useful to understand the relmarkable high rate of infection in the patients with major beta thalassemia.

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Key Words: Humoral Immune System; Immunoglobulins; Major Beta-Thalassemia; Splenectomy

Introduction

Major beta thalassemia is one of the most prevalent disorders in Mediterranean regions, caused by mutations in the gene responsible for producing beta globin chain on the chromosome 11[1]. The disease in the affected patients can progress to a number of complications such as

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cardiac failure, infection, leukemia and lymphoma, which consequently is associated with higher rate of mortality. Infection is considered as the second cause of mortality in these patients[2]. There are various causes of infection including blood transfusion, splenectomy, iron overload in the body, and aberration of function in immunity system[2].

Aberration in the immunity system could increase the risk of leukemia and lymphoma. A number of studies revealed various qualitative and quantitative defects in the production of the immunoglobulins, T and B lymphocytes activities, number and function of microphages and neutrophils including chemotaxis and phagocytosis and also aberrations of complement system[3-5].

Some studies have revealed an increased activity, number and differentiation of B lymphocytes[3,4,6,7]. However, other studies reported normal levels of these figures[5]. In different studies, IgA and IgG serum levels have been reported normal[3-5,8] to high[9-12], whilst IgM level was normal[2,7,8] or decreased[4].

Considering the high prevalence of major beta thalassemia in the Mediterranean countries, we investigated a part of the humoral immune system as a probable cause of increased risk of infection in these patients.

Subjects and Methods

This cross-sectional study was performed on patients with major beta thalassemia, referred to Thalassemia Center of Qazvin's Qods Children's Hospital in 2007. During the study, none of the patients was affected by any kind of infection. This study was approved by local Ethics Committee of the Hospital. From 106 patients cared for by this center, 99 volunteers were enrolled in the study after obtaining informed consent.

Six clotted venous blood samples of each patient were centrifuged in fast spin and the gathered serum was kept in -20˚C till the time of assay.

The serum levels of the immunoglobulins IgA, IgG and IgM were detected by immunoturbidometry, using special kits (Pars Azemoun Company, Iran) according to the international standards. In this method, serum immunoglobulins form an immune complex with polyclonal antibodies existing in the solution and cause turbidity of the solution. The intensity of turbidity resulted has direct relation with the level of immune globulin. The light passing through this suspension is refracted in proportion with protein concentration of the test sample (here immunoglobulin) which is detected by the photodiode apparatus.

The demographic and specific (removing the spleen) information about the patients has been gathered in questionnaires and patients' files. The mean serum immunoglobulin levels of all patients (either splenectomized or not splenectomized) were compared with normal ranges of each age group.

Findings

Ninety nine patients (48 males and 51 females) with major beta thalassemia were studied. Mean age of the patients was 12 (range 2 to 32) years. Seventy (70.7%) patients were in the age groups of less than 20 years (Table 1). Twenty two (22.2%) patients underwent therapeutic splenectomy.

The mean serum levels of IgG and IgM were normal for all age groups (Table 1) compared to normal levels. However, the mean serum level of IgA in the non splenectomized patients under five years old and also in the splenectomized patients above twenty years old were increased (Table 1).

Discussion

Evaluation of serum immunoglobulin level in those patients who did not undergo splenectomy revealed that the mean levels of IgG and IgM were normal, but there was increased serum IgA level in those under five years old.

The mean serum levels of IgG, IgA, IgM were normal in major beta thalassemic patients aged 5

Table 1: Serum immunoglobulin levels according to age segregation

Groups	Serum Ig (g/L)	Age range (years) 1-5	6-10	11-15	16-20	>20
Splenectomized	# cases				7	15
	IgG	-	-	-	12.1±3.2	15.3±5.5
	IgM	-	-	-	1.57±0.4	1.63±0.93
	IgA	-	-	-	2.6±0.77	4±1.8
Not splenectomized	# cases	10	15	20	18	14
	IgG	10.22±2.5	10.24±3.2	11.47±2.9	14.9±6.9	14.6±3.2
	IgM	1.13±0.4	1.37±0.41	2.1±3.6	1.58±0.55	1.64±0.48
	IgA	1.4±0.6	1.9±1.13	2.3±1.3	2.7±1.03	3.3±1.4
Normal range	IgG	34.6-139.4	60.8-157.2	63.9-134.9	63.9-134.9	63.9-134.9
	IgM	4.3-20.7	5.2-24.2	5.6-35.2	5.6-35.2	5.6-35.2
	IgA	1.4-15.9	3.3-23.6	7.0-31.2	7.0-31.2	7.0-31.2

to 10 years, which is in contrast to previous study in Shiraz that indicated increased levels of IgG and IgA for this age group[12]. However, in another study in Turkey there was no significant difference in the immunoglobulin levels for splenectomized and not splenectomized patients with an average age of 12 years[8], which is in agreement with our study. It is noteworthy that in three age groups in our study, there was no splenectomized patient. It seems that proper follow up of these patients could have resulted in spleen salvage.

In our study, the mean serum levels of IgG and IgA in splenectomized and not splenectomized patients aged 15 to 20 years, were normal. This is in concordance with the study reported from Greece, where levels of IgG and IgA were normal, but the IgM level was low after splenectomy[4].

In the age group above twenty with patients classified into splenectomized and not splenectomized, the mean serum levels of IgG, IgA and IgM in the latter group were normal, whereas in the first group the mean serum level of IgA was higher than normal. In the study in Shiraz, serum levels of IgG and IgA in the splenectomized patients were increased, while serum level of IgM showed a decrease, compared with those not splenectomized[12].

It seems that differing immunoglobulin serum levels in major beta thalassemic patients could be due to heterogeneity of different studies in aspects including age groups, race, socioeconomic status, nutrition, and difference in the care provided for the patient to control anemia and varied measures of ferritin, ignorance of the patients' simultaneous affliction with hepatitis C and the failure to divide them into two groups of splenectomized and not splenectomized patients. According to the studies, the mean serum levels of immunoglobulins are different between the splenectomized and not splenectomized patients.

Another study in the Indian beta-thalassemic patients, IgG and IgA levels in both splenectomized and not splenectomized groups did not show a significant difference compared with the control group[8]. This result is in concordance with our study.

Spleen acts as a large lymphoid organ to remove infectious agents from the blood, its removal may lead to activation of the secondary lymphoid organs and will compensate immunoglobulin synthesis.

Considering the fact that humoral immune system and sufficient amount of immunoglobulins are the main components of the immune system to prevent infections in patients with beta thalassemia, it seems that a decrease in immunoglobulin levels of these patients is one of the major factors increasing the risk of infection. On the other hand, the patients' contact with viral and bacterial infections caused by frequent blood transfusions makes the immune system constantly

stimulated to produce more amounts of immunoglobulins.

Conclusion

Although this study cannot show the defects of the humoral immune system, surveying functions of immunoglobulins and other components of the immune system seems necessary to understand the remarkable high rate of infection in these patients.

Conflict of Interest: None

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