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IgG SUBCLASSES IN SYMPTOMATIC IgA DEFICIENCY*

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SUMMARY: Tezcan İ, Ersoy F, Sanal Ö. (Immunology Unit, Hacettepe University Institute of Child Health, Ankara, Turkey). IgG subclasses in symptomatic IgA deficiency. Turk J Pediatr 34:1-4, 1992.

We evaluated IgG subclass levels in 11 symptomatic patients (ages between 3 and 22; mean 7.5 years) with IgA deficiency, seven with selective IgA deficiency, and four with low IgA levels. All patients had experienced three or more episodes of sinopulmonary infections a year. Combined IgG2-IgG4 deficiency was detected in two patients, IgG2 deficiency in one patient and IgG4 deficiency in two patients. Elevated IgG1 and IgG3 levels were detected in most of the IgG subclass deficient and sufficient patients. It is known that gammaglobulin replacement therapy reduces the frequency of infections significantly in IgG subclass deficiency. Although immunization against IgA is a risk in IgA deficiency, these patients can be treated with gammaglobulins containing low IgA. *Key words: IgG subclass, IgA deficiency, recurrent infections.*

IgA deficiency is the most common immunodeficiency disorder. The incidence has been estimated to be between 1 in 500 to 1 in 700 in the normal population[1]. Individuals with IgA deficiency have different clinical presentations; some have recurrent infections and allergic or autoimmune disorders, while others are asymptomatic.

While the factors which play a role in frequent infections are unclear, IgG subclass abnormalities have been demonstrated in some symptomatic patients with IgA deficiency[2-6].

The aim of this study is to evaluate IgG subclass levels in symptomatic IgA deficient patients and plan long-term treatment for the disorder.

Material and Methods

We evaluated 11 patients, 4 females and 7 males with IgA deficiency whose ages ranged between 3 and 22 years (mean 7.5 years). All patients had frequent episodes of sinopulmonary infections which occurred three or more times a year. Serum IgA levels were undetectable in seven patients who were defined as

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selective IgA deficiency. Four patients, whose serum IgA levels were two standard deviations below the age-matched control values, were classified as patients with low IgA levels.

Serum immunoglobulin levels (IgG, IgM, IgA) were measured by nephelometry (Behring, Marburg). IgG subclasses were determined by enzyme-linked immunosorbent assay (ELISA-Serotec, England). IgG subclass levels were compared with the levels of the age-matched healthy controls reported by Oxelius[7]. The values that were two standard deviations below or above the age-matched control levels were considered abnormal.

Results

IgG1 levels were highly elevated in nine out of 11 patients (Table I). Normal values were observed in two patients, one (IA) with selective IgA deficiency and the other (EK) with a low IgA level.

TABLE I: IgG Subclass and IgM Levels in Patients with Symptomatic IgA Deficiency (g/L)

	Age (Yrs)	IgG1	IgG2	IgG3	IgG4	IgM
1. BK	3	13.4[a]	2.8	0.50	0.4	2.0[a]
2. EB	15	>20.8[a]	3.8	1.25	0.5	2.5[a]
3. FA	3	>20.8[a]	0.6	1.35[a]	<0.01[b]	3.3[a]
4. OI	10	>20.8[a]	6.7[a]	2.75[a]	0.09	1.6
5. ES	5	15.6[a]	2.6	1.65[a]	0.04	0.7
6. GD	9	17.5[a]	1.05	1.35[a]	<0.01[b]	1.6
7. IA	12	7.4	<0.42[b]	1.30	0.04	0.6
8. SU*	22	>20.8[a]	<0.42[b]	0.33	<0.01[b]	1.6
9. EY*	3	13.7[a]	0.1[b]	1.80[a]	<0.01[b]	1.2
10. BY*	5	14.2[a]	2.7	0.75	0.7	0.9
11. EK*	5	5.8	5.5[a]	1.75[a]	0.17	1.8

* patients with low IgA levels
a: two standard deviations above the age-matched mean
b: two standard deviations below the age-matched mean

Low IgG2 levels were observed in three patients, one (IA) with selective IgA deficiency and two (SU, EY) with low IgA levels. High levels were detected in two patients (OI, EK).

IgG3 levels were found to be elevated in six patients, while normal levels were found in five patients including two with IgG2 deficiency (SU, IA).

Four patients (SU, EY, FA, GD) had low IgG4 levels, two of whom (SU, EY) also had IgG2 deficiency. The IgG4 level was elevated in one patient (BK).

IgM levels were found to be elevated in three selective IgA deficient patients, one of whom also had IgG4 deficiency.

Discussion

In this study, we found several IgG subclass abnormalities in symptomatic IgA deficient patients. Combined IgG2-IgG4 deficiency was determined in two patients, selective IgG2 deficiency in one patient and IgG4 deficiency in another two patients.

The association of IgG subclass deficiency and recurrent infections has been described in several studies[5,8-10]. Most of the protein antigens induce IgG1 antibodies whereas the majority of antibodies against polysaccharide antigens are in the IgG2 subclass. IgG2 antibody deficiency is one of the factors responsible for increased susceptibility to infections caused by *H. influenza,* pneumococci and other encapsulated microorganisms. IgG subclass abnormalities have been reported in IgA deficient patients[2,3,5]. The incidence of subclass deficiencies in IgA deficient patients with recurrent infections is reported as 20-35 percent, and IgG4, IgG2 and IgG2-IgG4 deficiencies have been found to be the most common deficiency patterns. The incidence of IgG2 subclass deficiency found to be 27 percent in our patients, is consistent with results reported in the literature[3,6]. Several studies on IgG subclass concentrations in healthy children and adults have been reported[7,11,12]. Due to the variability of the age-normal range of immunoglobulins in different populations, a description of age-normal IgG subclass limits is needed in our population in order to determine the real incidence of IgG subclass deficiency[13].

IgG3 deficiency has been reported in a few patients with IgA deficiency[5]. IgG3 deficiency was not detected in our patients. The IgG3 level is the most often conserved, and experimental studies suggest that the expression of this subclass is less T dependent[14].

IgG1 and IgG3 levels were found to be elevated in most of our patients with deficient and normal IgG subclass levels. Increased levels might be related to frequent infections, as a compensatory mechanism. High levels of IgG1 and IgG3 do not always correlate with low IgG2 values in IgA deficiency[2,3,5].

A few reports indicate that panhypogammaglobulinemia may develop in some IgA-IgG subclass deficient patients during the follow-up period[5,6]. Thus, the immunoglobulin levels of patients should be reevaluated periodically.

IgG subclass deficiency is not the only factor responsible for frequent infections in IgA deficiency since recurrent infections also occur in patients with normal IgG subclass values. In recent years, IgA deficient patients with a defective response to polysaccharide antigens, in spite of normal IgG subclass values, have been reported[15].

IgG subclass deficient patients generally respond well to gammaglobulin therapy[4,8,16]. Although immunization against IgA is a risk in IgA deficiency, these patients can be treated with gammaglobulins containing low IgA.

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