

IgG SUBCLASS DEFICIENCY IN CHILDREN WITH RECURRENT INFECTIONS*

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SUMMARY: Tezcan İ, Ersoy F, Sanal Ö, Göçmen A, Yeniay İ. (Immunology Unit, Hacettepe University Institute of Child Health, Ankara, Turkey). IgG subclass deficiency in children with recurrent infections. Turk J Pediatr 33: 163-166, 1991.

IgG subclass levels were studied in 12 children, aged between 2.5 - 12 years with recurrent respiratory tract infections. They did not have low IgG levels or IgA deficiency. We found combined deficiency of IgG2 - IgG4 in one patient and selective IgG2 deficiency in another (16.6 % of patients). These two patients had bronchiectasis due to recurrent severe pneumonia, however one patient with bronchiectasis had normal IgG subclass concentrations. Our IgG subclass - deficient patients who did not respond to prophylactic antibiotic therapy were given gammaglobulin therapy. IgG subclass deficiency should be considered in children with unexplained recurrent infections even in the presence of normal serum immunoglobulin levels. *Key words:* IgG subclass deficiency, recurrent infections, gammaglobulin.

IgG subclass deficiency has been described in patients with selective IgA deficiency, ataxia telangiectasia, common variable hypogammaglobulinemia, allergic diseases, autoimmune disorders and in individuals with recurrent infections¹⁻⁸. Although the actual incidence of IgG subclass deficiency is unknown, it is probably one of the most common humoral immunodeficiency disorders.

We studied IgG subclasses in 12 children with recurrent respiratory infections who did not have IgA deficiency and whose total IgG levels were not less than two SD below the age-matched control values.

Material and Methods

We examined 12 children, ages 2.5 - 12 years (mean: 5.5 years), who were referred to the Immunology Unit of Hacettepe University Children's Hospital for

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evaluation of recurrent infections. They did not have low total IgG levels or IgA deficiency.

Eleven patients had a history of recurrent episodes of pneumonia, three of whom had bronchiectasis and one recurrent otitis media with purulent drainage.

Serum IgG, IgA and IgM values were measured using the radial immunodiffusion method (Behring - Werke Inst.). IgG subclasses were determined by the ELISA technique (Serotec, England).

The IgG subclass values obtained were compared with the normal ranges reported by Oxelius⁹. A subclass deficiency was established in a patient if the IgG subclass value was two standard deviations below the mean for the age-matched control.

Results

Increased IgG1 levels were found in seven patients including two with IgG2 deficiency (Table 1). Two patients (NB, OS) who had recurrent pneumonia and

TABLE 1: Immunoglobulin Levels in Children with Recurrent Infections

Patient	Age (yrs)	Diagnosis	Serum Immunoglobulin Levels (g / l)					
			IgG1	IgG2	IgG3	IgG4	IgM	IgA
1.DD	3	R.P.	7.6	1.45	0.55	0.52	2.08 ^a	0.77
2.BB	2.5	R.P.	9.42 ^a	0.42	0.17	0.18	1.23	0.70
3.SK	7	R.P.	15.2 ^a	1.15	0.30	0.64	1.23	0.77
4.CH	4.5	R.O.M.	7.3	1	0.35	0.08	1.38	0.42
5.SO	4	R.P.	12.4 ^a	0.8	0.27	0.13	1.45	0.42
6.SY	4	R.P.	14.8 ^a	0.42	0.27	0.07	0.59	0.42
7.NI	3	R.P.	7.9	0.8	1.05 ^a	0.04	1.76 ^a	1.35 ^a
8.MD	7	R.P.	9.1 ^a	0.95	1.15	0.08	2.80	1.09
9.NB	12	R.P.+B	16.3 ^a	< 0.01 ^b	0.85	UD ^b	3.70 ^a	0.62
10.BA	5	R.P.	7.6	1.35	1.38 ^a	0.17	2.55 ^a	0.52
11.OS	9	R.P.+B	8.7 ^a	< 0.42 ^b	0.65	0.06	9.43 ^a	0.66
12.AY	7	R.P.+B	5.9	1.85	2.10 ^a	0.06	0.86	0.90

Abbreviations used in Table:

R.P : Recurrent pneumonia.

ROM : Recurrent otitis media.

B : Bronchiectasia.

UD : Undetectable.

a : Two standard deviations above the mean values of the age-matched control.

b : Two standard deviations below the mean value of the age-matched control.

bronchiectasis had very low IgG2 concentrations. Ten patients had normal IgG2 levels and one had bronchiectasis.

Increased IgG3 was found in three patients. IgG4 was undetectable in one patient (NB) with IgG2 deficiency. Thus, of 12 children with recurrent respiratory tract infections, one had combined deficiency of IgG2 - IgG4 and one had selective IgG2 deficiency.

Serum IgM levels were elevated in five patients including two IgG2 - deficient patients.

Discussion

In two of 12 children with a history of recurrent respiratory tract infections, we discovered combined deficiency of IgG2 - IgG4 in one, and selective IgG2 deficiency in the other.

The association of IgG subclass deficiency with infections (particularly sinopulmonary infections) was first reported by Schur et al⁵. IgG2 - deficient patients with recurrent infections tend to show a defective humoral immune response to bacterial polysaccharide antigens¹⁰. It appears that patients with low IgG2 levels are susceptible to infections caused by encapsulated bacteria (e.g. pneumococci, *H. influenzae*). Since serum IgG4 levels vary widely in the normal population, selective IgG4 deficiency is difficult to interpret.

The real incidence of IgG subclass deficiency is unknown. Shackelford et al¹¹ reported IgG2 deficiency in seven of 30 children who had recurrent respiratory tract infections, some of whom also had IgA deficiency. Stanley et al¹² studied 100 adults with recurrent or chronic respiratory tract infections and found that seven of them were IgG2 - deficient. In our study, IgG2 deficiency was found in 16.6 percent of patients with recurrent infections and normal IgA levels, which is a higher rate than Stanley's. Aucouturier et al¹³ reported that IgG subclass deficiency was detected in one fourth of children and adults studied with abnormally frequent infections, and that isolated IgG2 deficiency and combined deficiency of IgG2 - IgG4 were the most common, which is consistent with our findings.

Shackelford et al¹¹ emphasized that their IgG2 - deficient patients had more severe infections than the patients prone to infections who had normal immunoglobulin levels. Our two IgG2 - deficient patients had chronic lung disease due to recurrent severe infections. However, in one patient with bronchiectasis and severe recurrent pneumonia, we found the IgG subclass levels to be within the normal range. Patients with normal IgG subclasses and severe recurrent infections may have an inability to produce specific antibodies to several antigens (e.g. IgG2 antibody to polysaccharide antigens) in spite of normal IgG subclass levels¹⁴.

Elevated IgG subclasses and IgM levels were found in some of our patients which might have resulted from chronic antigenic stimulation.

Gammaglobulin replacement therapy is beneficial for IgG subclass deficient individuals^{8, 10, 15, 16}. Most authors advise prophylactic antibiotic therapy prior to gammaglobulin treatment. In general, patients who do not respond to prophylactic antibiotic therapy, are treated with gammaglobulin. Our patients who did not respond to antibiotic prophylaxis were administered gammaglobulin therapy.

IgG subclass deficiency should be considered and screened in children with unexplained recurrent respiratory tract infections, even in the presence of normal serum total immunoglobulin levels.

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