IMMUNOLOGICAL ASPECTS OF SECRETORY OTITIS MEDIA IN IRANIAN CHILDREN, IMMUNOGLOBULIN AND COMPLEMENT CONCENTRATION IN SERUM AND GLUE

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ABSTRACT

Otitis media with effusion (OME) is very common in pediatric patients. Immune reactions in serum and middle ear system play roles in the etiology, pathogenesis and prevention of otitis media. Immunologically active antigens interact with immunocompetent cells in the lamina propria of the middle ear to produce a local immune response.

In this investigation, 32 sera and 50 middle ear fluid samples from children (ranged 1 to 10 years) with secretory otits media were analyzed for IgA, IgM, IgG, C3 and C4 by single radial immunodiffusion (SRID) and IgE by enzyme linked immunosurbent assay (ELISA) techniques. Our results indicated a highly significant increase in IgA and a decrease in IgM, IgG, IgE, C3 and C4 in secretion as compared to serum concentrations. The ratio of IgA/IgG, a valuable index of local immune response, was higher in the middle ear than in serum. These data support the hypothesis that there is an independent mucosal immune response in the middle ear mucosa to different stimuli.

Keywords: Immunoglobulin (IgG, IgA, IgM, IgE), Compelement (C3, C4), Otitis media

INTRODUCTION

Otitis media with effusion (OME) is a very common pediatric disease with unknown etiology which sometimes leads to chronic recurrent OME. Immune reactions in serum and in the middle ear system play roles in the etiology, pathogenesis, and prevention of otitis media. The middle ear mucosa has a secretory immune system similar to those of other areas of the respiratory tract, except that it does not have lymphoid follicles (1).

Immunologically active antigens interact with the immunocompetent cells in the lamina propria to produce a local immune response. The middle ear effusion that results from acute or chronic infection or environmental antigens contains the major classes of immunoglobulins, complements, inflammatory cells, immune complexes and various chemical mediators of inflammation (2). The immune responses in the serum and middle ear to various antigens may prevent subsequent infection, assist in the clearance of the middle ear effusion, or contribute to the accumulation and persistence of fluid in the middle ear cavity (3). Immunological studies of otitis media in the human are based on assay of serum, middle ear effusion obtained by needle aspiration through tympanic membrane and middle ear mucosa obtained by biopsy (4). Secretory otitis media has been reviewed by different investigators. Jeep et al. from university Clinikum Rudolf Virchow has studied 90 secretions of 61 children with OME for correlation of IgA, E, G, M, the complement system and mediator of the inflammation. He showed that IgA and IgG significantly increased whereas IgM and IgE decreased in the secretion as compared to serum concentration (5). Mogi and his colleagues have investigated 400 OME patients. They showed that proteins found in the effusion were derived for the most parts from the serum. Quantitative analysis of sIgA revealed the existence of appreciable amounts of sIgA in both serous and muciod effusion (6). Sun and colleagues have shown that C3, C4 and C5 concentrations were significantly lower and Bf (B factor) and immune complexes higher than those in serum of patients with OME (7). Havada and Ogino investigated complement anaphylatoxins activity in the middle ear effusion and showed an extremely high value of C3a and C5a in the middle ear fluid that was indicative of a local intensive inflammatory reaction (8).

MATERIAL AND METHOD

Patients

In this study, 32 children (ages ranged 1 to 10 years) with otitis media suffering from loss of hearing and snoring were selected. The major problem in these patients was the hearing loss, and their audiological studies showed type B tympanogram and they had been candidate for ventilation tube (VT) insertion.

Samples

After having performed the myringotomy in the preferred region, middle ear content was aspirated and collected in a special micro tube designed for this purpose. By this method we were able to collect 0.2 to 0.8 ml of middle ear effusion. We also collected 5 ml of peripheral blood from each patient for serum studies.

Test Procedure

The amount of IgM, IgG, IgA, C3 and C4 in serum samples and middle ear effusion were measured by single radial immunodiffusion (SRID), and IgE concentration was detected by the Enzyme linked immunosorbent assay (ELISA) method. Effusion samples were cultured on desirable media for the bacteriological studies.

The results were analyzed using student T test for the comparison between concentrations of immunoglobulins and complements of middle ear effusion and serum samples.

RESULTS

The results of this study indicated that the mean IgA concentration in the right and left middle ear effusion (220.95 & 229.17 mg/dl respectively) was significantly higher than serum IgA concentration mean (135 mg/dl) P value < 0.01, Fig. 1.

Mean of serum IgM, IgG and IgE cocentrations were higher than the middle ear effusion (table 1, Fig. 2, 3, 4). IgE concentration of serum and middle ear content in most of our patients was higher than the normal control and is indicative of an allergic background in the studied patients.

C3 and C4 concentrations of the middle ear content were approximately half of the serum concentration which is indicative of complement activation and an inflammatory response in the middle ear (Fig. 5 & 6).

IgA / IgG ratio in serum, left and right middle ear effusion were 0.13, 0.35 and 0.23 respectively, this indicated of a local immune response in the middle ear mucosa.

Table 1. Comparison of serum IgG, IgA, IgM, IgE, C3 and C4 and middle ear effusion

Samples	N	M (mg/dl)	SD	SE	P
Serum IgG	32	1012.5	344.76	60.95	
Left ear IgG	20	625.98	592.05	132.39	P=0.005
Right ear IgG	21	993.32	957.82	209.01	P=0.2
Serum IgM	32	168.75	95.4	16.86	
Left ear IgM	26	75.75	72.9	14.3	P=0.0001
Right ear IgM	22	80.04	84.29	17.97	P=0.0006
Serum IgA	32	135	63.25	11.18	
Left ear IgA	26	220.95	206.8	40.56	P=0.047
Right ear IgA	24	229.17	246.44	50.3	P=0.017
Serum C3	32	121.81	18.83	3.33	
Left ear C3	24	60.94	40.31	8.23	P=0.01
Right ear C3	22	55.76	37	7.89	P=0.01
Serum C4	32	32.84	10.55	1.86	
Left ear C4	24	15.8	11.14	2.27	P=0.01
Right ear C4	23	12.85	10.42	2.17	P=0.01
Serum IgE (iu)	32	379.5	391.57	69.22	
Left ear IgE (iu)	27	153.85	532.84	102.52	P=0.07
Right ear IgE (iu)	24	128.47	319.09	65.13	P=0.01

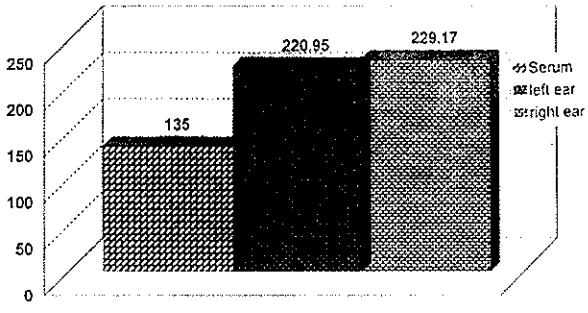

Fig. 1. The amount of IgA in middle ear effusion and serum in patients with otitis media

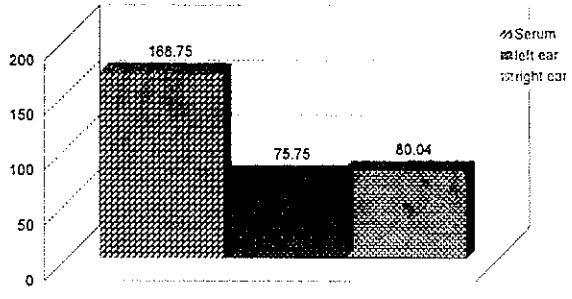

Fig. 2. The amount of IgM in middle ear effusion and serum in patients with otitis media

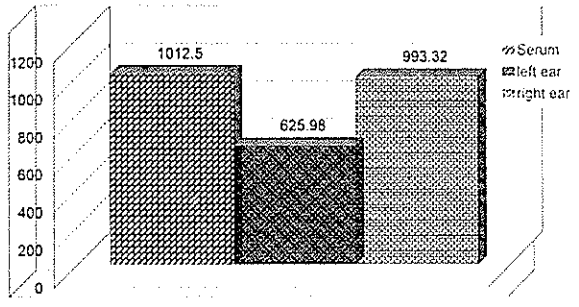

Fig. 3. The amount of IgG in middle ear effusion and serum in patients with otitis media

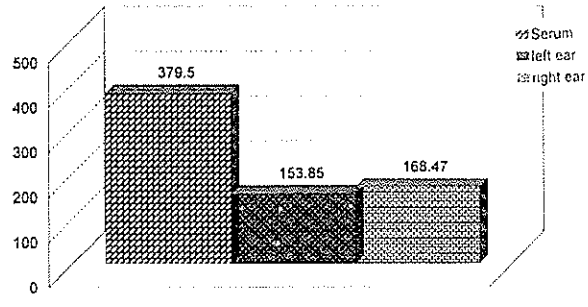

Fig. 4. The amount of IgE in middle ear effusion and serum in patients with otitis media

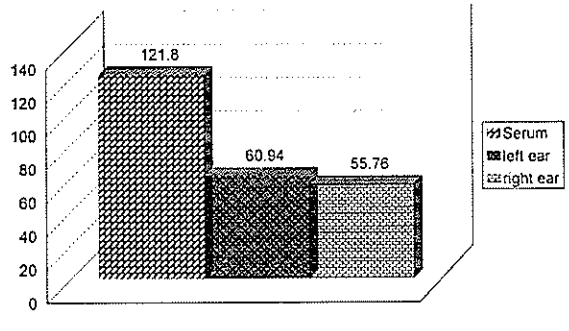

Fig. 5. The amount of C3 in middle ear effusion and serum in patients with otitis media

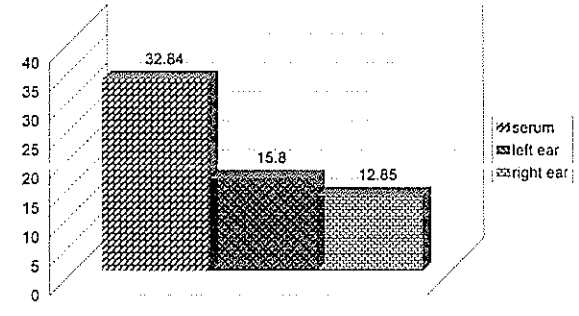

Fig. 6. The amount of C4 in middle ear effusion and serum in patients with otitis media

Bacteriological studies revealed that H. influenza was the most frequent pathogen in the middle ear effusion of our patients followed by the Pneumococci and B. catharalis.

DISCUSSION

Different studies have suggested that the middle ear is a potential site of Immunological regulation and that the middle ear mucosa constitutes a part of the mucosal immune system. Suenage and colleagues flow cytometric analysis of middle ear effusion showed the existence of about 15% gamma delta T and IgA specific producing cells and Th2 type cytokines such as IL-5 and IL-10 (9). Our study and studies by other invstigator have confirmed that IgA is the predominant Immunoglobulin in the middle effusion and is approximately twice of the serum concentration (220.9 mg/dl and 229 mg/dl in the left and right ear to 135 mg/dl in the serum) table 1 and Fig. number 1. Kuronoy and Moji have shown that sIgA and fibronectin significantly increase in otitis media with effusion and influence adherence of the H. influenza to middle ear mucosa (10). Our bacteriological studies have also shown H. influenza as the most frequent bacteria infecting the middle ear followed by the peunomococci and B. catharalis. Specific IgA can interfere with adhesion of bacteria to mucosal membrane and neutralize viruses such as adeno viruses, respiratory syncytial virus (RSV) and para influenza viruses, sIgA and IgG coated bacteria are important factors in preventing attachment of microorganism to mucosal cells in the middle ear. IgA / IgG ratios in predicting local synthesis of IgA is a valuable index in mucosal immunity and usually is higher in the middle ear effusion than serum, in most patients with otitis media. IgA / IgG ratio in our patients left middle ear effusion was 0.35 and in the right ear was 0.23 and in the sera of these patients was 0.13 and these data are compatible with previous studies by Jeep S. (5) and faden H. (11) Jeep S. showed a highly significant correlation between the IgG / IgM, IgG / IgA, IgA / IgM, IgG / kinin of the effusion to serum index especially in serous secretions. IgM and IgG present in the effusion of patients with both acute and chronic otitis media in a concentration about half of the serum concentration (table 1, Fig. 2 and 3)

suggesting local development of IgM and IgG in the middle ear. These data are compatible with Frejd A. et al. (12). But Jeep S. (5) showed a highly significant increase in IgA and IgG and a decrease in IgM and IgE in the secretions as compared to the serum concentration. As both otitis media with effusion and allergic rhinitis symptoms are common among young children, these disorders are occasionally seen in the same patients. Clinical study of Mogi G, and colleagues revealed that the ratio of complications of nasal allergy in 222 secretory otitis media children is 42%. Animal studies have also shown that the eustachian tube is involved, both functionally and morphologically in type I allergic reactions of the nose (12). The mean concentration of serum IgE in our patients was 379.5 IU which is 3 fold higher than the serum concentration of normal individuals (about 10-100 IU) and this is indicative of an allergic background in our OME patietns, However many clinical and experimental studies have denied the allergic etiology of OME. Although type I allergic reactions in the nose leads to tubal obstruction, it remains for a short time and does not induce middle ear effusion.

Clinical and experimental study showed the efficacy of allergic treatment in patients or animals having both diseases. It is recommended that allergy and OME be treated simultaneously (13).

Complements concentration of the middle ear effusion in our patiets was about half of the serum complement level (table 1, histogram 5 and 6) and it is compatible with lin chuang (7) and Harada T. (8) studies. The capacity of complement system in clearing the immune complexes in the middle ear was very low and therefore, the immune complex may deposit in the mucosa of the middle ear causing complement activation following by decrease in complement concentration and increasing anaphylatoxin (C3a, C5a) hence the permeability of capillary will increase and the middle ear effusion occurs. Bacterial and viral infection of middle ear lead to complement activation and finally to serous collection or mucosa in the middle ear. In conclusion our data in consistent with others showing active mucosal immunity in the middle ear to invading bacterial or viral infection and allergic background leading to effusion in the middle ear, and the therapeutic strategy should consider both antibiotic, anti-inflammatory and anti-allergic therapy.

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