Specific Anti Mumps Antibodies (IgG & IgM) in Cerebrospinal Fluid of Mumps Meningoencephalitic Children

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Abstract- Mumps infection is endemic in Iran. Our objective was to evaluate the presence of anti mumps antibodies (IgM & IgG) in cerebrospinal fluid in mumps meningoencephalitic children. A prospective/cross-sectional study was performed in Tehran, Iran (2003 to 2004) and serum anti mumps antibodies (IgM) were detected (quantitive; ELISA) in meningoencephaltis patients. Specific anti mumps antibodies (IgM & IgG) were detected in cerebrospinal fluids of mumps meningoencephalitis cases. 43 meningoencephalitic patients were tested (59.2% male and 40.8% female). The age of patients was 79.96 ± 4.7 month. 23 (78.7%) cases had specific mumps IgM in serum. None of cases had IgM antibodies in CSF. Anti mumps IgG antibody was detected in CSF of 7.5% (2/23) cases. We detected lower than expected frequency of local immunity to mumps virus in CSF of our cases. For better serologic diagnosis we recommend more sensitive methods like virus detection (PCR) or short-term culture of lymphocytes from cerebrospinal fluid in future studies.

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Key words: Mumps, meningoencephalitis, cerebrospinal fluid

Introduction

Like other unvaccinated countries (1-4), mumps infection is endemic in Iran (5-10). Meningoencephalitis is the most frequent complication of mumps infection in childhood (7, 8). The mumps vaccine induces antibody in 96% of seronegative recipients and has 97% protective efficacy (1, 2).

Specific IgM antibody for mumps virus is present in more than 75% of patients infected with mumps virus (3).

Local immunity in mumps meningitis reported in recent years. These results could be attributed to antibody synthesis, particularly IgG, in the CNS (11-13). This might be considered as direct evidence that specific antibodies are produced within the CNS in inflammatory nervous system diseases.

The aim of study was to evaluate the presence of local immunity to mumps (IgM and IgG) in cerebrospinal fluid in confirmed cases of mumps meningoencephalitis.

Patients and Methods

This prospective/cross-sectional study was carried out in the pediatric infectious diseases department of Hazrat Rasoul Hospital in Tehran Iran (2003-2004). The protocol of the study was approved by the ethical committee in Iran medical university. Patients were visited by an expert pediatrician and suspected cases of aseptic meningoencephalitis (less than 14 years old) were selected by simple sampling. Initially a questionnaire was completed by an authorized physician for each case, followed by complete clinical exams (including neurologic exams and inspecting the presence of parotiditis in admission) and daily follow up visits. Lumbar puncture was done in cases with clinical indications only by authorized physicians. We excluded all cases of meningoencephalitis without lumber puncture. Diagnostic parameters for meningoencephalitis were based on clinical and physical examination with abnormal CSF changes with or without (+/-) imaging changes (CT scan or MRI).

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Inclusion criteria were: 1. Clinical diagnosis of meningoencephalitis, 2. Positive CSF finding for aseptic meningoencephalitis (negative smear and culture for bacterial pathogens, negative latex agglutination test in CSF, normal protein and sugar, predominancy of lymphocytes for WBC of CSF.) added to suitable imaging (CT scan or MRI).

Exclusion criteria were confirmed other causes of central nervous system involvement including: metabolic disorders, poisoning, head trauma, CNS malformation, brain tumor, hemorrhage, abscess and other infectious causes of meningoencephalitis (Measles, chicken pox, herpes, *etc.*) by extensive laboratory and imaging techniques.

Blood samples (2 ml) were taken from each patient, centrifuged. The remaining samples of Cerebrospinal fluid for each selected patient were transferred to research laboratory. The serum and CSF samples were restored in –20 degree freezer until the serologic Elisa examination was performed on them.

We screened all serum samples for anti mumps IgM antibody by ELISA methods. Detection of specific anti mumps antibodies (IgG and IgM) in CSF samples were done only for cases with confirmed acute mumps infection with positive anti mumps IgM antibody in their serum.

Serological test: The specific anti mumps antibodies (IgM and IgG) were detected quantitatively by ELISA method with commercial kits (Radim, Italy). Results were interpreted as instructed by the manufacture.

Statistical analysis

The Student's t-test was used to determine significant differences in means for all continuous variables. Chi-square values (CI 95%, $P<0.05$) were calculated for all categorical variables. All analyses were conducted using SPSS.13 (SPSS Inc., Chicago, IL) and EPI 6 software.

Results

Sixty seven cases with aseptic meningoencephalitis were admitted in our center. 43 cases had specific IgM antibody for mumps in their serum (Table 1). The highest incidence of mumps infection was seen in spring and the lowest rate in summer.

We studied 43 aseptic meningoencephalitis cases which had mumps meningoencephalitis based on positive anti mumps-IgM in their sera.

Only 23 from 43 cases (53%) needed lumbar puncture. 59% were male and were 41% female (Table 2).

Table 1. Correlation between different seasons and serum specific IgM antibody for mumps

Season	IgM-Pos	IgM-Neg	Total
Spring	23	8	31
Summer	8	5	13
Winter	9	5	14
Autumn	3	7	10
Total	43	25	68

P=0.4

Table 2. Correlation between different sex and serum specific IgM antibody for mumps

Sex	IgM-Pos	IgM-Neg	Total
Female	5	6	11(41%)
Male	18	14	32 (59%)
Total	23	20	43 (100%)

P= 0.07 NO significant between 2 sexes.

Age of patients was between 10 and 180 months (mean 79.6 ± 4.78 months). 4 % (1) of patients were less than 1 year old, 26% (6) between 1 and 3years old, 35% (8) between 4 and 7 years old and 35% (8) were more than7 years old (Table 3).

Clinical signs and symptoms: 30% (7 of 23) of cases was febrile, 89.5% had parotiditis, convulsion, and loss of consciousness were seen in 13% (3) of cases.

Normal imaging in CT scan or MRI was observed in 85% (19 of 22) of cases.

There was a significant relation between the positive IgM in serum and parotiditis in Patients. (Chi2=29.93, df=1, 95% CI, $P<0.001$).

There was no correlation between positive mumps serology (Mumps-IgM) and age, sex, convulsion, level of consciousness, Fever and imaging results (Table 4).

Table 3. Age groups in mumps meningoencepthalitis cases

Age	Total
< 1 years	1(4%)
1-3 years	6(26%)
4-7 years	8(35%)
>7 years	8(35%)
Total	23(100%)

P=0.8

No significant different between age groups

Table 4. Frequency of clinical sign and symptoms in cases

Clinical signs	Positive	Negative	*P-value*
Loss of conscious	3	20	*1*
Convulsion	3	20	*0.4*
Fever	7	2	*0.4*
Parotiditis	20	3	*0.001*
Abnormal Imaging (CT/MRI)	3	19	*0.4*
Convulsion	3	20	*0.4*

P= 0.08 (between age groups)

None of mumps meningoencephalitis cases had anti mumps-IgM in their CSF.

Local Specific anti mumps-IgG antibody were weakly positive in CSF of only 2 (7.5%) suspected mumps meningoencephalitic cases (with anti mumps-IgM in serum).

Discussion

Mumps infection is one of the most common etiologies for aseptic meningoencephalitis among the unvaccinated children in Tehran (7,8). In this study we observed that mumps meningoencephalitiis is clinically indistinguishable from meningoencephaliti of other origins.

We detected local immunity (CSF) to mumps virus (IgG) in 7.5% (2 of 23) of mumps infected patients. It is lower than the study of Kacprzak-Bergman *et al* (2001) in which the antibody to mumps virus was found in 11 of 15 CSF samples (11). Evaluation of the CSF-serum ratio for antibodies to mumps viruses showed a substantially higher ratio for antibody to mumps virus. The ratio of IgG/IgM antibody activity to mumps virus was greater in CSF than in sera (11).

The lower frequency of local immunity to mumps virus in CSF of our cases may be due to the lower age of patients or the delay in CSF sampling in our cases. Mumps-IgG in CSF increased rapidly, reaching to a peak four to ten days from onset of meningitis, and quickly decrease thereafter (11-13).

Use of less sensitive methods in present study is one of the causes for lower than expected results. CSF- lymphocytes usually produce higher amounts of antibodies than the corresponding number of peripheral blood lymphocyte (PBL) in all patients with mumps meningitis (13). This method had higher specificity and sensitivity and gave more precise information about the antibody response in infections of the nervous system (13).

To summarize the limitation of this study we should note that we detected lower than expected frequency of local immunity to mumps virus in CSF of our suspected cases. The probable causes for this discrepancy might be the lower age of patients, use of less sensitive methods, delay in CSF sampling or other unknown ethiologic factors.

In conclusion, isolation of the virus in cell culture, detection of viral antigen by direct immunofluorescence, or identification of nucleic acid by reverse transcriptase polymerase chain reaction are the optimal methods for confirmation the mumps in suspected meningoencephaltis cases, but these are expensive and need longer time for diagnosis.

For better serologic diagnosis we recommend more sensitive methods like Short-term culture of lymphocytes from cerebrospinal fluid in future studies. This method provides higher specificity and sensitivity and gave more precise information about the antibody response in infections of the nervous system.

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