Medical Journal of the
Islamic Republic of Iran

Volume 18
Number 2
Summer 1383
August 2004

MUMPS MENINGOENCEPHALITIS IN PEDIATRIC WARD OF RASOOL AKRAM HOSPITAL IN TEHRAN, IRAN, 1999-2000

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ABSTRACT

To determine the frequency of mumps infection in children hospitalized with aseptic meningoencephalitis (ME), as well as its correlation with parotiditis, this case-series study was conducted in the pediatric ward of Rasool Akram Hospital in Tehran, Iran, from 1999 to 2001.

The blood samples of these patients were tested for specific IgM antibody for mumps by Elisa method. The results of this study showed that 62.7% of children with ME were IgM positive, and the remaining (37.3%) were IgM negative. There was a significant correlation between positive IgM and the presence of parotiditis. However, no correlation was noted between age, sex and season with IGM positivity except for CSF changes (aseptic meningitis) between the two groups. It can be concluded that the presence of neural symptoms (especially aseptic meningitis) in children less than 7 years of age with parotiditis could indicate mumps ME, especially in the spring. Due to a higher percentage of unvaccinated young persons (<15yr old) in Iran, probably the incidence rate of mumps infection and its sequelae are higher compared with its incidence in developed countries before massive vaccination. Therefore with massive vaccination of Iranian young people (< 20yr old), the costs of mumps infection and its sequelae will decrease.

MJIRI, Vol. 18, No. 2, 123-126, 2004.

Keywords: Mumps infection; Meningoencephalitis; Mumps vaccination.

INTRODUCTION

Aseptic meningoencephalitis is an acute inflammatory process involving the meninges and, to a variable degree, brain tissue.[1,2,3] Although the specific etiologic agent is not identified in most cases, clinical and research experience indicate that viruses are usually the responsible pathogens, accounting for seasonal pattern of disease. Enterovirus causes more than 80% of all cases. Other frequent causes of infection include arbovirus and herpes virus. Mumps is a common pathogen in regions where mumps vaccine is not widely used, in the below 15 year old group.[1-8] The malignant form of ME is seen in 1/400-1/6000 cases of mumps, with 1.4% mortality.[1,2,3] Specific IgM antibody for mumps virus is present in more than 75% of patients infected with mumps virus.[1,2,3] There is no comprehensive report on the annual incidence rate of mumps and its role in ME of Iranian children, except for some seroepidemiological studies.[5]

In Iran, like other unvaccinated countries, with the peak incidence in children 5-9 years of age, 85% of infections occur in children <15 years of age, being almost rare in less than 2 yr old children.[1-7]

Mumps infection is endemic in Iran and mumps pa-

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rotiditis is a common disease in Iranian children.[4,5,6] However, in the United States, there has been a dramatic decrease in the incidence of mumps since the introduction of an inexpensive and very effective mumps vaccine in 1968.[1,2,3,9-14]

With regard to the role of this viral infection in affecting children and its consequences as well as the highest cost of hospitalization, the importance of massive vaccination against mumps virus should be recognized and emphasized in our country.[15,16,17,18,19,20] The present study investigated the frequency of mumps infection in children with aseptic meningoencephalitis (ME) admitted to the pediatric ward of Rasool Akram hospital in Tehran, Iran during 1999-2000.

MATERIAL AND METHODS

This case-series study was performed on all children below 15 yr of age who were admitted to the pediatric ward of our hospital based on diagnostic parameters for aseptic ME.

Inclusion-citeria for aseptic ME were fever plus one of the following symptoms (nausa & vomiting, headache, convulsion, confusion), signs of CNS involvement at the time of admission (positive meningeal signs; such as stiff neck, positive Krenig and/or Brudzinski sign), increased ICP, abnormal CSF finding, etc.

Exclusion criteria were positive bacterial culture (blood, CSF or other site of body), or abnormality of CSF supposedly due to bacteral meningitis or another diagnosis except ME (space occupying lesion in brain, intracranial hemorrhage, etc.).

Initially from each patient with ME, a questionaire was completed by the authorized physician, followed by clinical exams in the presence of neural symptoms and parotiditis. Two mL blood was drawn from each patient, blood samples were centrifuged and transferred to the research laboratory. The serum was stored in a -20 degree freezer until the serologic Elisa examination was performed on them.

Serological test

The evaluation of specific IgM antibody for mumps was carried out with commercial Elisa kits (Radim, Italy). The plate was read on an Elisa reader in 450 & 620 nm wave length.The results were interpreted based on the manufacturer's order.

Statistical analysis

In this study, descriptional statistics (Mean, Standard Deviation), comprehensive statistics including Chi-square test for determination of correlation between sex, season, and parotiditis with positive IgM antibody (CI=95%) were used. Also, t-test was used to compare the average age. All the above statistical tests were done via SPSS 9 software.

RESULTS

Sixty-seven patients were studied in two years.The age of patients was between 9 months to 14 years old (mean= 6.61+3.80) with a male to female ratio of 3/1. The highest incidence of ME was seen in the spring (31 cases= 48.8%) and the lowest in the autumn (9 cases= 13.4%). Abnormal CSF findings (aseptic meningitis) were present in 37(55.2%). Specific IgM antibody for mumps was reported positive in 1-13yr olds, mean7.36+3.38, sex ratio: 33/9, thirty three (34.2%) in the spring and the rest were observed in the other seasons. In this group 34(89.5%) had parotiditis and 4(10.5%) did not.

Age of patients in the IgM negative group was between 1-14 years, mean 5.34+4.72,sex ratio: 17/8. Eight cases (25.8%) occurred in the spring and the rest were observed in the other seasons. In this group 4(10.5%) had parotiditis and 21(72.4%) did not.

There was a significant relation between positive IgM and parotiditis in patients (χ^2= 29.93, df= 1, CI=95%, p<0.001) (Table I).

There was no significant difference between positive IgM and the negative IgM group in terms of age (two tail T-test= 1.98, p<0.067, 95% CI:-4.04-0.15); sex(χ^2= 0.92, df= 1, p<0.034) and season (χ^2= 5.11, df=3, p<0.164) (Tables II, III, IV).

Table I. Correlation between parotiditis and specific IgM antibody for mumps.

IgM / Parotiditis	Positive	Negative	Total
Negative	4(16%)	21(84%)	25
Positive	34(80.95%)	8(19.05%)	42
Total	38(100%)	29(100%)	67

χ^2= 29.93, p<0.001

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

Sex	IgM-Positive	IgM-Negative	Total
Female	9(52.9%)	18(47.1%)	17
Male	33(66%)	17(34%)	50
Total	42	25	67

χ^2= 9.92, p<0.34

Abnormal CSF was observed in 81% of positive IgM cases compared with 18.9% in the negative IgM patients (LP was not performed in 3 cases).

There was a significant relation between positive IgM and abnormal CSF (χ^2= 9.288, p<0.002, df=1, CI=95%), (Table IV).

Thirty-four patients (89.4%) with parotiditis (range 1.5-14 year, mean7.92+2.89) were IgM positive, the remaining 4 patients (10.6%) were IgM negative, compared to 9 patients (31%) without parotiditis (age range 1-13 year, mean 4.96+4.29) who were IgM positive and 69% of the rest were IgM negative.

There was a significant age difference between patients with parotiditis and those without parotiditis (two tailed T-test= 3.32, significant=0.001).

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

Season	IgM-Positive	IgM-Negative	Total
Spring	23(74.2%)	8(25.8%)	31
Summer	8(61.5%)	5(38.5%)	13
Winter	8(61.5%)	5(38.5%)	13
Autumn	3(30%)	7(70%)	10
Total	42	25	67

χ^2= 0.92, p<0.34

Table IV. Correlation between CSF changes and specific IgM antibody for mumps.

CSF	IgM-Positive	IgM-Negative	Total
Norm	12(44.4%)	15(55.6%)	27
Abnorm	30(81.1%)	7(18.9%)	37
Total	42	25	64

χ^2= 9.288, p<0.002

LP was not performed in 3 cases.

DISCUSSION

ME is the most frequent complication of mumps infection in childhood.[1,2,3,6,7,8] Its true incidence is hard to estimate because subclinical infection of the CNS, as evidenced by CSF pleocytosis, has been reported in >65% of patients with mumps parotitis.[1,2,3,6,7,8] Clinical manifestations occur in >10% of patients. The incidence of mumps ME is approximately 250/100,000 cases; 10% of these cases occurred in patients >20 years of age.[1,2,3] The mortality rate is about 2%. Males are affected three to five times as frequently as females.[1,2,3] Mumps ME is clinically indistinguishable from ME of other origins.[1,2,3,6,7,8] The mumps vaccine induces antibody in 96% of seronegative recipients and has 97% protective efficacy.[8-14] Maternal antibody is protective in the infant in the first 6 months of life.[1,2]

In the United States, there has been a dramatic decrease in the incidence of mumps since the introduction of the mumps vaccine in 1968. In 1966, 628 cases of encephalitis due to mumps infection were reported with death in 10 cases of mumps. In 1987 there were 683 reported cases of mumps (0.27/100.000 population), a >99% reduction from the 152,209 cases reported in 1968. ME is now the 7th cause of encephalitis in the United States.[1,2,3,5] The malignant form of ME is seen in 1/400-1/6000 cases of mumps, with 1.4% mortality.[1,2,3,8,9,10] Specific IgM antibody for mumps is present in more than 75% of patients infected with mumps virus.[1,2,3,4]

In Iran, due to the absence of mass vaccination of the population, mumps infection is present endemically.[4,5] Previous seroepidemiological studies by Hadian and Bahrami showed that the 0-9 yr old age group was most susceptible to mumps infection; followed by the 10-19 yr old age group. In the year 2000, Vojgani et al. showed that children below 5 yr of age were the most susceptible to mumps (p<0.05) and older than 10 year were the least susceptible group to mumps infection with no sex differences. In general, about 50% of the population have a tendency for mumps infection.[21] Mumps is considered as one of the prevalent and important causes of aseptic ME in children, causing hospitalization in some cases.[5] In another study conducted by Moddares et al., enteroviruses were the causative agent in 15% of viral ME below 1 years old; and mumps in 48% of patients below 14 years of age with the highest prevalence in 5-9yr old children. The lowest incidence of mumps ME was in <1yr of age (2.8%) and the sex ratio was 3/1. The highest seasonal prevalence was in the spring (53.5%), and parotiditis was seen in 79% of patients with mumps ME. The highest incidence of mumps M.E was 250/100,000.

The results of this study, similar to Moddares et al.'s study showed that 62.7% of children with ME (9 mo-14 years, average 6.69 years) were positive for specific anti mumps-IgM (mumps infection). The rest (37.3%)were IgM negative (no mumps infection) probably due to other causes of ME or inadequate antibody response to mumps infection. There is no significant difference of age, sex and season, but a significant difference in CSF

changes between the two groups. So in patients with ME, CSF changes are in favour of mumps ME rather than other viral causes. In this regard due to the similarity between the age distribution of ME patients with parotiditis and seropositive (IgM) patients, it can be concluded that the presence of neural symptoms (especially aseptic meningitis) and parotiditis in parallel in unvaccinated children with average age of~7yr could be indicative of mumps ME especially if it happens in the spring (CI 95%).

The population of children less than 15 years old in Iran is about 24 million. Potentially, they are susceptible for mumps infection and are at risk of CNS involvement. In the presence of mumps ME without parotiditis (which is not always clinically diagnosed as mumps ME), some patients need hospitalization for decreasing their symptoms or definite diagnosis (ruling out bacterial meningitis). It is expected that the yearly incidence of mumps ME would be much higher in Iran compared to developed countries (before vaccination). Moreover, a higher percentage of unilateral sensory hearing loss in children is due to mumps or rubella virus.[1,2,3,22] Considering the days of hospitalization and its costs for diagnosis, treatment, long term sequelae, and probably mortality which burden the health and medical system of our country, this disease is preventable by simple massive vaccination of young people below twenty years of age in Iran.

REFERENCES

1. Lithman N: Mumps virus, In: Mandel GI, Bennet DR, Bauer SG, (eds.), Principles and Practice of Infectious Disease. Philadelphia: Churchil Livingston, 11th edit., pp. 1776-81, 2000.
2. Cherry JD, Mumps virus, In: Feigin RD, Cherry JD, (eds.), Textbook of Pediatric Infectious Disease. Philadelphia: W.B. Saunders, 4th Edition, pp. 757-60, 1998.
3. Maldonador Y: Mumps, In: Behrman, RE, et al. (eds.), Textbook of Pediatrics, Philadelphia: W.B. Saunders, 16th Ed, pp. 954-5, 2000.
4. Hadian B: Seroepidemiological study of mumps. Tehran University MSc Thesis, Tehran, Iran, 1990.
5. Moddares S: Etiology of aseptic meningitis. Iranian J Med Sci 22(3&4):156-60, 1977.
6. Noorbakhsh S, Rimaz SH, Aghahosseini F: Study of clinical course and complicationS of mumps meningoencephalitis. J Iran Univer Med Scien 8(27): 641-8, 2002.
7. Philip RN, Renihard KR, Lackman DB: Observations on mumps epidemic in virgin population. Am J Hyg 69; 91: 111, 1959.
8. Azimi PH, Cramblett HG, Hyanes RE: Mumps meningoencephalitits in children. JAMA 118: 509-12, 1969.
9. Peter G: Preventive measures, In: Behman RE, et al. (eds), Textbook of Pediatrics, 16th Ed., Philadelphia: W.B. Saunders, pp. 1081-9, 2000.
10. Polktin SA, Ornstein WA, (eds): Vaccines, 4th ed., Philadelphia: W.B. Saunders, pp. 1552-90, 1999.
11. Sugiura A, Lyamada A: Aseptic meningitis as a complication of mumps vaccination. Ped Inf Dis J (10): 209-13, 1991.
12. Miller E, Goldacre M, Paugh S, et al: Risk of aseptic meningitis after measles mumps rubella vaccine in UK children. Lancet 341: 979-82, 1993.
13. Wassilak SG, Glasser JW, Chen RT, Hadler SC: Utility of large linked databases in vaccine safety particularly in distinguishing independent and synergistic effects. Ann NY Acad Sci 754: 377-82, 1995.
14. Watson BM, Laufer DS, Kuter BJ, Staehle B, White CJ: Safety and immunogenicity of combined live attenuated measles mumps rubella and varicella vaccine in healthy children. J Inf Dis 173: 731-4, 1996.
15. Saunders WH, Lippy WH: Source of sudden deafness and Bells palsy; a common cause. Ann Oto Laryngo 68: 830-7, 1959.
16. Hyden D, Roberg M, Forsberg P: Acute idiopathic peripheral facial palsy: clinical serological and CSF findings and effects of corticosteroids. Am J Otolaryn 14: 179-86, 1993.
17. Jonville Bera AP, Autret E, Galy E, Chessel L: Thrombocytopenic purpura after measles mumps and rubella vaccination, a retrospective survey by the French regional pharmacovigilance centers and Pastuer-Meriex serums et vaccines. Ped Inf Dis J 15: 44-8, 1996.
18. Drachman RA, Murphy S, Ettinger LH: Exacerbation of chronic idiopathic thrombocytopenic purpura following MMR immunization. Arch Ped J 148: 326-7, 1994.
19. Valcha V, Forman EN, Miron D, Peter G: Recurrent thrombocytopenic purpura after repeated MMR vaccination. Pediatrics 97(5): 738-9, 1996.
20. Peter G: Childhood immunization. N Eng J Med 327: 1794, 1992.
21. Vodjgani M, Hadjati J, Bahrami F: Seroepidemiological study of mumps in 74 children 5-10 years old by complement fixation. Iran J Allergy Asthma 11(1): 33-55, 2000.
22. Vuori M, Lahikainen EA, Pletonen T: Perceptive deafness in connection with mumps, a study of 298 servicemen suffering from mumps. Act Otolaryn 55: 231-6, 1962.