

## BRIEF COMMUNICATION

### ASEPTIC MENINGITIS IN A LARGE MMR VACCINE CAMPAIGN (590,609 PEOPLE) IN CURITIBA, PARANÁ, BRAZIL, 1998

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#### SUMMARY

The aseptic meningitis after Measles-Mumps-Rubella vaccine (MMR) is a well recognized complication, and different incidences have been observed in several studies. We retrospectively analyzed forty cases of aseptic meningitis, during a large public immunization campaign (1998) in Curitiba, Southern Brazil (590,609 people), admitted in our Service. The vaccine utilized was Leningrad-3-Zagreb mumps strain, Edmonston-Zagreb measles strain, and RA 27#3 rubella strain. In all county, a total number of 87 cases were reported, resulting in a incidence of 1.7 cases per 10,000 given doses. The mean age was  $23.7 \pm 12.8$  years. The female:male ratio was 1.35:1. Severe headache with meningismus (92.5%), fever (87.5%), nausea/vomiting (82.5%) were the most common clinical findings. Three cases (7.5%) developed mild mumps. All patients underwent cerebrospinal fluid (CSF) tap with the following findings: mononuclear pleocytosis from 100 to 500 cells/mm<sup>3</sup> in 17 cases (42.5%;  $257.5 \pm 260.6$  cells/mm<sup>3</sup>); increased protein 28 cases (67.5%;  $92.1 \pm 76.9$  mg/dL); glucose was normal in all cases ( $56.8 \pm 11.2$  mg/dL) except in 4 (10%) cases, which presented less than 44 mg/dL. All serological tests (latex to bacterial meningitis, *Cryptococcus*, cysticercosis, VDRL) and bacteriological cultures were negative. Virus identification were also negative in 8 samples. None of the patients had neurological deficits or related symptoms after one year of onset. We believe the benefit of vaccination clearly outweighs the incidence of benign vaccine-associated meningitis.

**KEYWORDS:** Aseptic meningitis; MMR vaccine.

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Aseptic meningitis (AM) is a well-recognized complication of mumps vaccine typically occurring 2-4 weeks after immunization and resolving without sequelae. North American studies have shown a risk of post-vaccinal meningitis between 0.4 and 10 per million doses with the use of Jeryl Lynn strain<sup>1</sup>. In Japan, a higher rate of AM with Urabe Am9 strain was reported<sup>2,3</sup>.

We report the findings of aseptic meningitis during a large vaccination campaign (MMR) in Curitiba, Southern Brazil, in 1998.

#### METHODS

From October 24, 1998 to November 30, 1998, 590,609 people with ages from 1 to 39 years-old and living in Curitiba, Southern Brazil ( $25^{\circ}25'40''S$ ;  $49^{\circ}16'23''W$ -GR), were vaccinated with Leningrad-3-Zagreb mumps strain, Edmonston-Zagreb measles strain, and RA 27#3 rubella strain (Measles, Mumps and Rubella Vaccine Live, Attenuated (Freeze-Dried – Serum Institute of India Ltd, India). The reason for this campaign was an alarming increase of measles cases during 1998.

The estimated 1998 Curitiba population in this age interval was 1,102,578 people. Notification of all cases of aseptic meningitis to the County Health Secretary is obligatory by law.

A total number of 87 cases was reported, giving an incidence of vaccine-associated meningitis in our study of 1.7 per 10,000 doses. Forty patients out of the 87 cases of post-vaccination AM were admitted to our Service, giving an annual prevalence rate of 29/1,000 cases, in comparison with an average annual rate of 5/1,000 rate in other years (from 1994 to 1997).

The mean age of our patients was  $23.7 \pm 12.8$  years. The female:male ratio was 1.35:1. Signs/symptoms of meningitis occurred between 11 and 20 days after vaccination in most cases (60%) (mean  $21 \pm 8.7$  days). Severe headache with meningismus (92.5%), fever (87.5%), nausea/vomiting (82.5%) were the most common clinical findings. Three cases (7.5%) developed mild mumps. All patients underwent cerebrospinal fluid (CSF) tap within 48 hours of onset, with the following findings: mononuclear pleocytosis from 100 to 500 cells/mL in 17 cases (42.5%;

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257.5 ± 260.6 cells); increased protein 28 cases (67.5%; 92.1 ± 76.9 mg/dL); glucose was normal in all cases (56.8 ± 11.2 mg/dL) except in 4 (10%) cases, which presented less than 44 mg/dL. All serological tests: latex to bacterial meningitis (latex detection of soluble antigens: *N. meningitidis* A., C., Y/W135., B.; *E. coli* K1, *H. influenza*, *S. pneumoniae*, *Streptococcus* B. – PASTOREX MENINGITIS, Bio Rad, France), *Cryptococcus* (Cryptococcal Antigen Latex Agglutination – Meridian Diagnostics, Inc. USA), cysticercosis (immunoenzymatic test for neurocysticercosis in cerebrospinal fluid – Biolab-Mérieux S.A., Brazil) and VDRL (Syphilis serological antigen screening – Laborclin, Brazil) and bacteriological cultures were negative. Eight samples were sent for detection of mumps virus and were negative (Adolfo Lutz Institute, São Paulo). Symptomatic treatment with parental hydration, anti-emetics, analgesics, and bed rest was effective in all cases.

Most patients (38) were completely asymptomatic after 30 days. After one year, all forty patients were reviewed and were in good health without noticeable sequelae.

There was a marked drop of cases of measles during the following two years after this campaign.

#### COMMENTS

There was a relatively high incidence of post-vaccination AM with the use of Leningrad-3-Zagreb strain (1.7 per 10,000 doses), but lower to other reported series (9-10 per 10,000 doses)<sup>4,5</sup>. The Urabe strain was also associated with a higher risk of AM when compared to the Jeryl-Lynn strain in UK<sup>6</sup>, and gave numbers very close to ours (risk estimate of 1 per 11,000 doses). Comparative data of these 3 mumps strains on long-term antibody persistence and protective efficacy are still lacking. We believe the benefit of vaccination clearly outweighs the incidence of benign vaccine-associated meningitis.

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Competing interests: None declared.

#### RESUMO

##### Meningite asséptica na campanha de vacinação pública tríplice viral (590.609 indivíduos) em Curitiba, Paraná, Brasil, 1998

A incidência de meningite asséptica após vacina tríplice viral (MMR) é diferente em diversos estudos. Analisamos retrospectivamente quarenta casos de meningite asséptica, relacionados a uma campanha de vacinação pública para cobertura tríplice viral em Curitiba, PR, Brasil, ano de 1998. A vacina utilizada foi a Leningrado-3-Zagreb para caxumba, Edmonston-Zagreb para sarampo e RA27#3 para rubéola. Um total de 87 casos foram relatados, resultando em uma incidência de 1,7 casos por 10.000 doses. A idade média dos pacientes foi 23,7 ± 12,8 anos. A relação feminino/masculino foi 1,35:1. Cefaléia intensa com sinais meníngeos (92,5%), febre (87,5%), náuseas e vômitos (82,5%) foram os achados clínicos mais comuns. Três casos (7,5%) desenvolveram caxumba branda. Todos os pacientes foram submetidos a punção lombar para obtenção de líquido, com os seguintes achados: pleocitose mononuclear de 100 a 500 células em 17 casos (42,4%; 257 ± 260,6 células/mm<sup>3</sup>); proteínas aumentadas em 28 casos (67,5%; 92,1 ± 76,9

mg/dL) e glicose (56,8 ± 11,2 mg/dL). Os testes sorológicos (látex para meningites, *Cryptococcus*, cisticercose, sífilis) e culturas bacteriológicas foram negativas. Identificação viral também foi negativa em 8 casos. Nenhum dos pacientes desenvolveu déficits neurológicos ou sintomas relacionados após um ano do início do quadro. Acreditamos que o benefício da vacinação claramente supera os eventuais efeitos da meningite asséptica após vacinação MMR devido ao seu caráter e evolução benignos.

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