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Mumps outbreak and laboratory diagnosis

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ABSTRACT

Background: Several mumps outbreaks have been reported in Europe and in the United States among highly vaccinated populations. Biological diagnosis is classically based on the detection of mumps-specific IgM, but the ability of serological tests to confirm mumps infection seems to be limited among vaccinated patients.
Objectives: We aim to report a mumps outbreak in an engineering school in Grenoble, France, from February to June 2013 and results of the biological testing.
Study design: WHO definitions were used to define cases. Mumps – specific IgM and IgG were assessed by a commercially available EIA. Mumps RNA detection by real time reverse transcriptase polymerase chain reaction tests (RT-PCR) and mumps genotyping were performed by the French National Reference Centre for Paramyxoviridae.
Results: Sixty two mumps patient-cases were identified using WHO case definitions, 20 being biologically explored, of which 17 were confirmed by biological tests. Vaccination status was documented for 27 patients/62: 4 (14.8%) patients had received one dose of MMR vaccine, and 23 (85.2) two doses of MMR vaccine. Among the biologically explored patients, 83% had a positive RT PCR at the first sampling whereas only 45% had positive or equivocal IgM. All the genotyped strains were genotype G.
Conclusions: Mumps laboratory diagnosis in a highly vaccinated population is challenging. Serological tests among vaccinated patients should be interpreted cautiously and confirmed by RT-PCR tests at the beginning of a mumps outbreak.

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1. Background

Mumps is an acute viral infection presenting with parotitis, sometimes associated with complications such as meningitis, pancreatitis or orchitis (web reference). Mumps immunization was implemented in France in 1986 as a single dose of measles–mumps–rubella (MMR) vaccine for 1-year-old children. A second dose was added in 1996 for children between 11 and 13 years old (now recommended between 16 and 18 months). After the implementation of vaccination, the incidence of mumps disease decreased from 859 to 9 cases per 100,000 inhabitants/year between 1986 and 2011 [1]. Surveillance is realized by the French General Practitioners Sentinel network and the National Institute for Public Health Surveillance (InVS). Several mumps outbreaks have been reported in Europe [2,3] and in the United States [4,5] among highly vaccinated populations, raising the question of whether mumps vaccines are effective enough to prevent outbreaks [6–8]. Biological diagnosis is classically based on the detection of mumps-specific IgM, but the ability of serological tests to confirm mumps infection seems limited among vaccinated patients [5,9].

2. Objectives

In February 2013, the student health department of an engineering school was informed of cases of mumps: we aimed to report this

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outbreak investigation and the results of serological and virological testing in a globally vaccinated population.

3. Study design

3.1. Case definitions

WHO definitions were used: a clinical case was defined by an acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary gland, lasting 2 or more days and without other apparent cause, a biologically confirmed case met the clinical case definition and was biologically confirmed (isolation of mumps virus or mumps RNA from an appropriate clinical specimen or seroconversion or significant (at least fourfold) rise in serum mumps IgG titer as determined by quantitative serological assays (i.e. immunofluorescence assay) or positive serological test for mumps-specific IgM antibodies) and an epidemiologically confirmed case met the clinical case definition and was epidemiologically linked to a biologically confirmed case (web reference).

3.2. Characteristics of the patients

For each case, date of birth, sex, clinical data, place of living, vaccine status and exposure to another patient with a clinical presentation suggestive of mumps were collected. For the patients who documented having been vaccinated, the number of received doses and the dates of vaccination were recorded. Patients whose immunization registry could not be consulted were considered as "unknown vaccination status".

3.3. Biological testing

At the beginning of the outbreak, serological tests were performed at the University Hospital in Grenoble (France) and the molecular assays for mumps detection and genotyping were performed by the French National Reference Centre for Paramyxoviridae. The samples for molecular detection were freezed at −80 °C and shipped to the laboratory on nitrogen gaz. Later, as the diagnosis of mumps is highly probable in case of parotitis during an epidemic, the diagnosis was no more biologically confirmed in symptomatic patients who reported a link with engineering school. Marketed enzyme immunoassays were used, according to the manufacturer's recommendations, for detection of mumps IgG and IgM antibodies (Enzygnost® quantitative anti-parotidis-virus/IgG and Enzygnost® anti-parotidis-virus/IgM, Siemens, Marburg, Germany). The absorbance values (ΔA) were automatically deducted from the absorbance values of the sera tested with mumps virus antigen minus the absorbance values of sera tested with control antigen. According to the manufacturer's recommendations, IgG and IgM were reported as negative if ΔA were <0.100, positive if >0.200 or equivocal if $0.100 \geq \Delta A \leq 0.200$. A real time RT-PCR (RT-PCR) targeting the nucleoprotein gene was performed as previously described (10) for mumps RNA detection on saliva specimens, parotid duct swabbing or urine samples. A molecular sequencing of the short hydrophobic gene (SH gene) was carried out after the RT-PCR amplification of this gene, for genotyping.

4. Results

4.1. Chronology of the outbreak

After the identification of the first four cases in February 2013, the outbreak was investigated by the student health center and the regional health agency. All first cases were students in an engineering school (University A) counting 5300 students, in Grenoble, France. On 29 March 2013, oral information to the students was given by physicians about mumps transmission, prevention and symptoms. Students were encouraged to monitor themselves for the symptoms, and symptomatic students were encouraged to go to student health services for diagnosis. The case finding was based on the students' self reporting of symptoms to the student health services. Isolation of patients for 5 days after symptoms onset and monitoring of contacts for symptoms were recommended; students without proof of immunity were offered vaccination.

Between February and June 2013, 62 cases of mumps were reported: 17 were biologically confirmed and 45 were epidemiologically confirmed cases (Fig. 1). The first case presented with bilateral parotitis on 6 February 2013. The attack rate was 1.2% among the students. No more cases of mumps were notified after 16 June 2013.

Table 1
Clinical presentations of mumps cases.

	No of patients ($n = 62$)	%
Male	40	64.5
Age (median [range])	21.6 [18–25]	
Clinical presentation		
Fever	20	32.8
Parotitis	58	93.5
Unilateral parotitis	43	69.4
Bilateral parotitis	15	24.2
Orchitis	1	1.7
Oophoritis	0	0
Meningitis	0	0
Hospitalization	0	0
Exposure to another case of mumps disease	44	71.0
University campus		
University A	56	90.3
University B	5	8.1
University C	1	1.6
Place of living		
University room	25	40.3
University room with roommates	7	11.3
Own apartment with roommates	20	32.3
Alone in their own apartment	13	21.0
Unknown place of living	4	6.5
Measles–mumps–rubella vaccination status		
Unknown vaccinal status	35	56.5
Known vaccinal status	27	43.5
1 dose	4	6.5
2 doses	23	37.1

4.2. Characteristics of the patients, vaccination status

Clinical presentations, vaccination status, university campus and place of living of the 62 patients are described in Table 1. Fifty eight students (93.5%) presented with parotitis and 4 did not: 2 of them only presented with sub maxillary gland inflammation, the third had unilateral orchitis and the last patient had only fever. Among the University A students, eighteen of the cases belonged to the same master's program, thirteen to another program; three other programs included seven, six and five students. We do not know the program of the remaining seven students, neither the relationship with the students from Universities B and C.

Vaccination status was confirmed by the immunization registry in 27 cases/62 (4 cases with one dose of MMR vaccine, and 23 with two doses). Among them, the delay since vaccination ranged from 1 to 21 years (median: 14 years; interquartile range 11–15). The presumed index case was a male, aged 22 years, which immunization registry could not be consulted.

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