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Community Outbreak of Measles in Madrid (Spain) Caused by an Imported Case

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Abstract: *Introduction*: In February 2006, the measles elimination programme of the Epidemiological Surveillance Network of the Community of Madrid (Spain) detected a case of imported, unvaccinated measles which was the index case of a community outbreak whose epidemiological characteristics we describe.

Material and Methods: Descriptive study of the outbreak. Clinical, epidemiological and laboratory information was collected. Measles antibodies (IgM and Ig G) were studied and the virus was isolated and genotyped.

Results: An imported case caused an outbreak of 174 cases (93.1% confirmed). The measles virus was detected by culture in 31% of cases. The genotype was determined in 90.7% of positive samples, all of which were the B3 genotype (subgenotype B3.1), with sequencing in various genes that indicated the same viral lineage. The outbreak lasted 198 days. The age range was 2 months -37 years and 84.6% of cases were Spanish-born. A total of 9.8% of cases presented complications, 37.4% required hospital admission, and 9.2% had a documented history of immunization. Twenty-four clusters were identified in families, health workers and infant schools.

Conclusions: Control measures included advancing the infant MMR vaccination schedule and reinforcement vaccination in health care workers. While the measles virus still circulates, surveillance of suspected cases and maintenance of high vaccination coverages, especially in health care workers, are essential.

Keywords: Case, community, imported, measles, outbreak, Spain.

INTRODUCTION

The possibility of regional elimination of measles and the viability of its eradication remain subject to discussion. Measles elimination is possible due to the characteristics of the virus (the only reservoir is human and environmental survival is poor) and the availability of sufficiently sensitive and specific diagnostic techniques and an effective vaccine. However, paradoxically, large epidemic outbreaks have occurred in different regions after the technical elimination of measles. The transmission of an infectious agent in a population depends on a series of factors whose combination may be summarized by the reproductive rate (R), which is defined as the mean number of secondary cases caused by a typical case in a specific population. When $R<1$ for measles in a specific region, this does not mean that the population is immune to measles, but that the proportion of susceptible people is sufficiently low that sustained transmission is not viable [1].

Epidemiological surveillance through the identification of cases should be able to detect any failure in the elimination strategy rapidly and highlight the interruption of transmission in a region for prolonged periods.

In Spain, measles has been a reportable disease since 1900. Before 1982, the typical prevaccination pattern was observed, with epidemic peaks every two years and an annual mean of 10,464 cases. After 1997, there was a dramatic reduction, partly caused by modification of the reporting method from weekly numerical to weekly with basic epidemiological data [2].

Measles vaccine was introduced into the Spanish immunization schedule in 1981, although high coverages were not

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achieved until 1984-85. In 2006, the infant vaccination calendar of the Community of Madrid introduced the administration of two doses of MMR (measles, mumps and rubella) at 15 months and 4 years of age [3]. Likewise, the option of administering the first dose to children aged 12 months if there was an increased risk of suffering these diseases was included.

In agreement with the 1998 World Health Organization (WHO) recommendations, the Spanish National Measles Elimination Plan was established in 2001 [4-7], with the main objective of collecting and analyzing the epidemiological characteristics of measles to facilitate the continuous adaptation of strategies and activities designed to eliminate it. According to the strategy, measles became an urgently reportable disease in order to facilitate rapid detection of community circulation of the virus. The same year, the Measles Elimination Plan of the Community of Madrid was introduced [8-11] with the general objective of eliminating indigenous measles by 2005, adapting the national strategies to the characteristics of the disease in the Community of Madrid and its health system.

The results of the 3rd Serosurveillance Survey of the Community of Madrid (1999-2000) showed a greater susceptibility to measles in the 16-20 years age group [12]. In addition, according to the Vaccination Information System of the Community of Madrid, in 2006, MMR vaccination coverage was 89.6% for the first dose and 91.7% for the second, lower than the 95% proposed by the WHO for both doses. This indicated that, although the low level of susceptibility in the community was preventing sustained circulation of the virus, there was the possibility that an imported case could give rise to the diffusion of the virus in more-susceptible population groups (cohorts born between 1979 and 1984 and paediatric cohorts with vaccination coverages below those recommended by the WHO).

The Community of Madrid is a mainly urban region with a population of 6,008,183 in 2006, of whom 816,606 were foreign-born. In February 2006, the Epidemiological Surveillance Network detected two epidemiologically-linked cases of measles. In the first case, whose onset was 9 January, the patient had been in the United Kingdom during the incubation period, while the second patient had been in contact with the first in Madrid during the transmission period [13]. The imported case was the index case of a community outbreak whose epidemiological characteristics we describe.

METHODS AND MATERIALS

We Carried Out a Descriptive Study

Information sources: All cases of measles recorded by the reportable diseases system of the Community of Madrid during the outbreak period were included in the study. Clinical, epidemiological and laboratory information was collected for each case using a specific protocol. The information was obtained from the patient's medical record. Data on the vaccination status were obtained from the vaccination register.

Laboratory tests: Health centers were recommended to take samples for confirmation (serum for antibody detection and blood, urine and pharyngeal exudate for viral cultures). Measles IgG and IgM determinations were made using indirect ELISA techniques (Enzygnost; Dade Behring; Germany). These techniques have been used by the National Network of Laboratories of the Spanish Measles Elimination Plan with excellent results [14]. In patients with a clinical suspicion of measles, a differential diagnosis was made by detection of IgM against other viruses producing exanthematic diseases such as rubella (ELISA; Enzygnost, Dade Behring; Germany) and parvovirus B19 (ELISA; Biotrin International, Inc.; Ireland). Isolations in culture, amplification by RT-PCR and subgenotyping of various genes of the virus were made by previously described techniques using samples of blood, urine and pharyngeal exudate [15, 16].

Definitions: A clinical case of measles was considered as a case with maculopapular rash and high fever (≥38ºC) and at least one of the following symptoms: cough, coryza or conjuntivitis.

A cluster of cases was defined as a group of patients who could have shared the place and time of exposure, even when the epidemiological link or the generations of cases that could have occurred in each of them could not be determined accurately.

Analysis: The variables analyzed were age, sex, place of origin, onset of rash, clinical manifestations, severity (complications and hospital admission), vaccination status, degree of diagnostic certainty, virus genotype, source of infection, groups involved in the transmission and history of travel during the incubation period. Denominators to calculate the incidence were obtained from the census of inhabitants.

RESULTS

A community outbreak of measles occurred in the Community of Madrid between 9 January and 25 July 2006. A total of 174 cases were identified, representing an incidence of 2.92 cases per 100 000 inhabitants. A total of 93.1% were confirmed (87.9% by laboratory and 5.2% by epidemiological link) and the remaining 6.9% were classified as compatible (in 3 cases no samples were collected, in 8 serum samples were obtained before the 3 days of onset of the rash and in 1 case two serum samples were taken, both of which gave doubtful results). The measles virus was detected in cultures in the 31% of cases for which adequate samples were available. The genotype was determined in 90.7% of positive samples and was found to be the B3 genotype (subgenotype B3.1) in all, with a sequence in various genes that indicated the same viral lineage. In addition, during the outbreak period, another 81 suspected cases were reported, of which 73 were ruled out, 7 were considered vaccination-related cases and one was a confirmed imported case unrelated to the outbreak.

The number of cases was highest between epidemiological weeks 7 and 10 (12 February-11 March) with 46 cases, and weeks 16 and 20 (16 April-20 May) with 62 cases. The second period coincided with the increase in cases in infants aged < 15 months and detection of the circulation of the virus in infant schools (Fig. **1**). The total duration of the outbreak was 198 days, which includes 11 periods of 18 days (incubation period) during which the imported virus was transmitted in the Community of Madrid.

The male/female ratio was 1:1.02 and the age range was 2 months-37 years. The highest incidence was observed in infants aged < 1 year (35.87 cases per 100 000 inhabitants), followed by the 1-4 years age group (16.23 cases per 100 000 inhabitants). In people aged 20-34 years, the incidence was 5.27 cases per 100 000 inhabitants. A total of 84.6% of cases were from persons born in Spain.

The most common symptoms were rash, fever and cough and 45.7% of cases presented the five clinical manifestations included in the case definition. Complications occurred in 9.8% (17) cases, of which the most common was pneumonia (9 cases) and 37.4% of cases required hospital admission. There was no death.

A documented vaccination history was available in 9.2% (16) cases (2 cases had received two doses and the remaining 14 one dose). In addition, 10 cases reported being vaccinated although this could not be confirmed.

A total of 20.7% (36) cases belonged to birth cohorts who benefited from routine MMR vaccination (children aged > 15 months who were born when high MMR vaccination coverages had been achieved in the Community of Madrid) (Table **1**). Ten of the twenty (50%) of unvaccinated cases in these cohorts came from outside Spain, of which six cases were in Romanian gypsies. Of the unvaccinated Spanish cases, five went to the same school and four were Spanish gypsies.

The first case detected came from the United Kingdom and developed a rash a few days after entering Spain. In 58.6% (102/174) cases, a link with another case was identified; 24 clusters were identified, with a range of 2- 12 cases per cluster (Table **2**).

The clusters were in families (16 with a total of 27 cases), hospitals (8 with a total of 16 cases) and infant schools (4 with a total of 25 cases). Infant schools were involved in two of the three largest clusters.

Transmission of the infection in the eight hospital centers caused 16 cases (13 health workers and 3 community cases). The source of infection was a community case in 13 cases and a health worker in 3 cases. In addition, in five cases in health workers, the source of infection could not be estab-

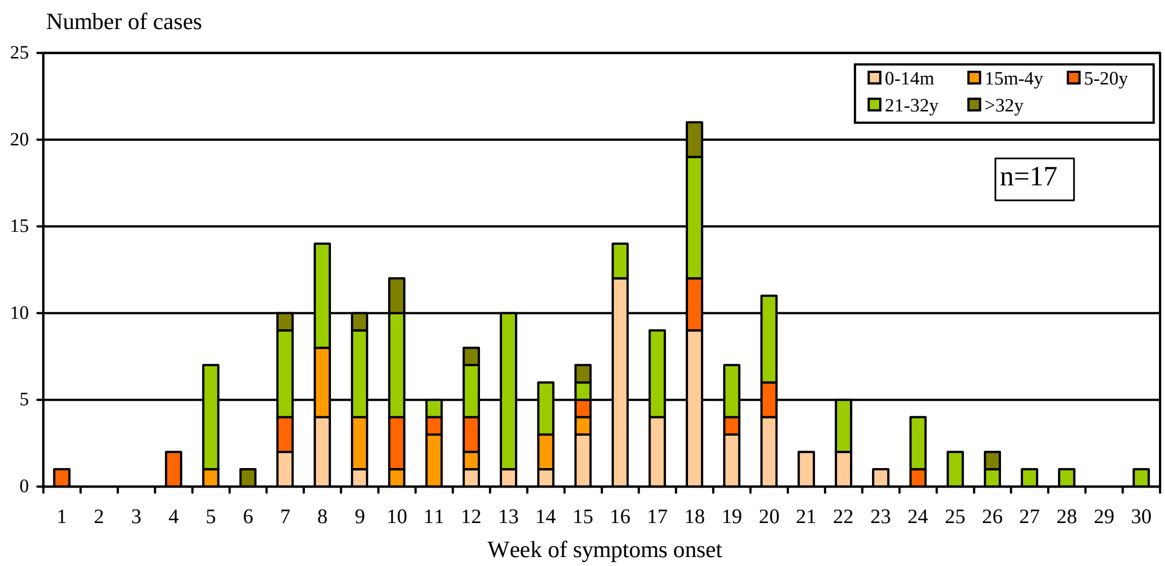

Fig. (1). Community outbreak of measles. Cases per week according to onset of rash and age group. Community of Madrid, 2006.

Table 1. Community Outbreak of Measles. Vaccination Status of Cases Belonging to Birth Cohorts who Benefited from Routine MMR Vaccination. Community of Madrid, 2006

Doses Indicated According to Age	Vaccinated			Non-Vaccinated	Unknown	Total
	Doses Received	Recorded	Not Recorded			
One	One	6*	0	7	0	13
Two	One	3	1	13	4	23
	Two	1*	1			
Total		10	2	20	4	36

*Cases correctly vaccinated for their age.

Table 2. Community Outbreak of Measles. Clusters of Cases Detected. Community of Madrid, 2006

Cluster	Date of First Case	Total Number of Cases	Duration (Days)
1	9 Jan	8	55
2	31 Jan	2	23
3	1 Feb	10	56
4	11 Feb	2	16
5	13 Feb	6	28
6	17 Feb	4	20
7	15 Feb	4	15
8	21 Feb	2	1
9	19 Feb	6	24
10	7 Mar	2	13
11	9 Mar	2	10
12	11 Mar	3	13
13	29 Mar	2	11
14	29 Mar	2	11
15	9 Apr	12	37
16	30 Mar	2	16
17	1 Apr	4	33
18	3 Apr	2	13
19	20 Apr	4	5
20	28 Apr	10	16
21	30 Apr	6	16
22	6 May	3	14
23	23 June	2	9
24	15 July	2	10

lished, except in one case who acquired the infection through a family contact. Therefore, in total, 18 (10.3%) cases occurred in health workers.

Two related outbreaks were detected outside the Community of Madrid: a family outbreak involving two cases in another Spanish region, in which the first case had visited a health center in the Community of Madrid at the same time as one of the cases in the Madrid outbreak, and a community outbreak in Venezuela occurred from an airline pilot who was in Madrid during a week in February [17], both caused by the measles virus B3 genotype.

DISCUSSION

We report a large outbreak of measles in the Community of Madrid with 174 cases. The epidemiological and microbiological data show that the cases derived from a common, imported source of infection. The first case came from the United Kingdom and developed a rash a few days after entering Spain. In the United Kingdom, during the last four-month period of 2005, measles outbreaks were reported in several regions in travellers with low vaccination coverages [18,19]. In Doncaster, the origin of the first case, several clusters of patients infected by strains of the measles virus of the same genotype identified in the Madrid outbreak (B3) were reported [20]. In developed countries, after the elimination of endemic transmission, many outbreaks may have their origin in imported cases [21]. In spite of the marked reduction in the worldwide incidence of measles achieved in recent years [22, 23], increased international travel (50 million passengers are estimated to use Madrid Barajas airport per year [24]), means there is always a danger of introducing imported strains into Spain.

The outbreak mainly affected young adults with low vaccination coverage who reached vaccination age when coverages were low, and also infants aged < 15 months who had not yet received the first dose of MMR. As in other countries [25-28], these two population groups have the greatest risk of infection when an imported case appears.

Some reports [29] suggest non vaccinated people may have a 200-fold higher risk of measles infection compared with vaccinated subjects. However, cases can appear in vaccinated people [30], especially in those who have received only one dose of vaccine [31]. Cases in vaccinated subjects increase with age [32-34].

Measles is a highly-communicable disease whose basic reproduction number can be >15 [22]. Therefore, even when endemic transmission is eliminated, outbreaks in immunologically unprotected groups are possible.

In the outbreak described here, health centres played an important role in the transmission of the virus, due to the greater opportunity of contact between cases and susceptible people. The diffusion of nosocomial measles [35-37] and the occurrence of cases in health workers [38,39] have been documented in some outbreaks. Due to the higher probability of exposure, the relative risk of infection of health workers is 7-45 times higher than that of adults in general [40]. The isolation of cases and control measures for contacts are especially important in the health care setting. In addition, vaccination is recommended in health workers without specific immunity [41].

Transmission of the virus in infant schools is, likewise, very efficient, due to the concentration of children who have not yet received the first dose of MMR. The high risk of complications in small children means isolation of cases and control measures for contacts are very important.

The measles virus is circulating in other European countries. The WHO European region introduced a strategic plan for measles and congenital rubella in 2002: however, several member states have suffered outbreaks since then [42,43]. During 2006, measles outbreaks were detected throughout Europe, including Greece [44], Ukraine [45], Germany [46], Poland [47], Belarus [48], Italy [49], United Kingdom [50], Sweden and Denmark [51]. The WHO estimates that circulation of the measles virus might be eliminated in European region countries by 2011.

With respect to the WHO measles elimination criteria, transmission of the indigenous virus has probably been interrupted in the Community of Madrid, but the outbreak described here underlines the possibility of transmission of imported viruses and highlights the importance of urgent reporting of all suspected cases of measles to the Epidemiological Surveillance Network. Physicians should be highly alert to a patient with fever and rash, whether a child or young adult, in order to adapt the control measures necessary to avoid dissemination of the virus as rapidly as possible.

One key aspect to controlling this outbreak was the temporary modification of the routine vaccination strategy: a recommendation was made to advance the first dose of MMR to 12 months and to administer an additional dose to infants aged 6-11 months. This recommendation was motivated by the high risk of transmission of the measles virus, which caused a large number of cases in infants aged < 15 months in April. The recommendation was temporary (between 12 May and 1 October), and once the high risk situation had abated, the normal schedule (first dose of MMR at 15 months and the second dose at 4 years) was resumed. Other measures adopted were the dissemination of information on the outbreak to the Health Care Network and the surveillance, prevention and control measures introduced.

Clinical alert of cases of rash continues to be essential. The etiologic diagnosis of these cases requires laboratory confirmation. While the worldwide circulation of measles is not eliminated, surveillance of suspected cases and periodic serosurveillance surveys to detect possible susceptible groups and maintain high vaccination coverages are necessary, especially with respect to health care workers and non-vaccinated people from population groups with a lower probability of having benefited from vaccination. Adaptation of the vaccination schedule to the current reality was shown to be a basic tool in controlling the outbreak.

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