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Measles outbreak in a French Roma community in the Provence-Alpes-Côte d'Azur region, France, May to July 2017

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ABSTRACT

Objectives: To analyse a measles outbreak in a Roma community.
Methods: We describe a community-wide outbreak of genotype D8 measles that took place in southeastern France, between May and July 2017, along with the control measures adopted.
Results: We identified a total of eighteen cases, between six months and 24 years old. All cases were unvaccinated or incompletely vaccinated and belonged to a sedentary French Roma community. Most of them (67%) were hospitalised, with three cases (17%) of severe measles including one death of a 16-year-old girl who had previously received oral corticosteroids. The latter was the only lethal case notified in France during the year 2017. Control measures included intensification of surveillance, isolation of cases, and a large vaccination campaign in this Roma community. During the outbreak period, there was no case of healthcare-associated measles transmission. A broad adherence to vaccination through the mediating role of both the chief of the community and the pastor allowed reaching completed vaccination coverage of 90%.
Conclusions: Efforts should be concentrated to enhance access to health services for minorities such as the Roma community characterized by low vaccination coverage. A trustful relationship with leaders of the community is essential to ensure adherence to vaccination. In France, attributable mortality to measles is low and concerns mainly unvaccinated and immunodepressed patients.

Introduction

Measles remains an important cause of global child mortality although it is decreasing, with 89,780 deaths recorded worldwide in 2016 (WHO, 2018a). The Expanded Program on Immunization and the wide use of a first, then a second dose of the measles-containing vaccine (MCV) has made world incidence decrease from 850 000 in 2000 to 250 000 annual cases worldwide in 2015 (Moss, 2017). In Europe, according to the European Centre for Disease Prevention and Control, Romania, Italy and Greece had by far the highest incidence in 2017, with respectively 281.3, 89.6 and 82.4 cases per million inhabitants, while in France it was of 7.7 (Monthly measles and rubella monitoring report, 2018).

France faced an important measles outbreak in 2010–2011 with nearly 15 000 cases. At the beginning of this large outbreak, the Regional Health Agency of Provence-Alpes-Côte d'Azur (RHA-PACA) reported 310 cases in specific groups such as Roma communities, characterized by low vaccination coverage. Healthcare workers represented 9% of the patients. Most patients were unvaccinated (82%) or had received a single dose of vaccine (15%) (Six et al., 2010).

Severe measles is a rare complication that should be distinguished from secondary infections (Bichon et al., 2017). The largest series of severe measles (N = 36) has been recently reported in adults hospitalized in Intensive Care Units (ICUs) in France (Rafat et al., 2013). Severity was due to measles-associated pneumonia and consequent acute respiratory distress syndrome (ARDS), or

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encephalitis. Atypical presentation with no evidence of exanthema or Koplick's sign during or before hospitalization was reported in 4 immunodepressed cases (11.1%). Risk factors for severe measles-related complications include immunodepression, pregnant women, extreme ages, individuals with poor nutritional status and vitamin A deficiency (Moss, 2017).

We describe here the fatal case of a 16-year-old girl admitted to the ICU for acute respiratory distress syndrome that was subsequently diagnosed as atypical and severe measles. We also report results of our investigation of the associated outbreak within French Roma families settled in southeastern France.

Materials and methods

Case descriptions and outbreak investigation

Data on patients diagnosed with measles during the outbreak were collected from mandatory notifications transmitted to the RHA-PACA and then to the world health organization (WHO) Regional Office for Europe. Patients were ambulatory or hospitalised in the paediatric ward and adult intensive care units in the hospitals of Toulon and Marseille, between May and July 2017. Information was completed by interviews of patients' families and the review of the hospitalised patient's medical file.

Clinically suspected cases were defined as having fever ≥ 38.5 °C, maculopapular rash, and at least one of the following signs: conjunctivitis, coryza, cough, Koplik's sign. Laboratory-confirmed cases were clinically suspected cases with microbiological confirmation: specific IgM detected in saliva or serum and/or seroconversion with at least a four-fold increase of IgG titres and/or positive polymerase chain reaction (PCR) for measles virus. Epidemiologically-confirmed cases were defined as clinically suspected cases who reported a contact with laboratory-confirmed cases 7–18 days before the onset of symptoms (WHO, 2018b).

Patients were systematically put under airborne precautions when they were hospitalised until four days after onset of rash.

Measles outbreak was defined as the occurrence of at least two or more laboratory-confirmed cases which were temporally related (with dates of rash onset occurring between 7 and 18 days apart) and epidemiologically or virologically linked, or both (Anon, 2013).

Outbreak control measures were taken according to the most recent WHO European region guidelines: (i) intensification of surveillance, (ii) isolation of cases when they were hospitalized, (iii) contact management, (iv) vaccination campaign, and (v) advocacy and communication to ensure effective community involvement and public awareness (Anon, 2013).

According to the French recommendations, we proposed a systematic vaccination of all case contacts, if they did not receive the complete two-doses vaccination schedule (Calendrier des vaccinations et recommandations vaccinales, 2018).

The resolution of the epidemic was considered in the outbreak community until 21 days after the onset of rash in the last case of measles (end of August).

The term 'Roma' used here refers to diverse range of nomadic or sedentary ethnic groups, who have migrated within Europe. In this outbreak, the population of concern is a sedentary French Roma community.

Virological analysis

For all tested samples, qualitative RT-PCR Measles virus was performed as previously described (Hummel et al., 2006). IgM and IgG specific for Measles virus were tested using commercial ELISA tests (Diasorin Inc., Saluggia, Italy). RNA extracts positive for measles were sent to the National Reference Laboratory for measles in France. The WHO recommendations were applied for measles genotyping (Anon, 2012). To determine the genotype, a phylogenetic tree was constructed including all known measles genotypes.

Results

Case report

A 16-year old girl was admitted on June 5th 2017 in the respiratory intensive care unit in Marseille, France. She had no previous medical history and was unvaccinated. The patient's family settled in Nice and belonged to a sedentary French Roma community. She first presented with acute rhinopharyngitis and was treated since May 25th with oral corticosteroids and josamycin. Neither erythema nor Koplik's sign were observed during and before hospitalization. On June 4th, she consulted the emergency medical ward for persistent fever and consciousness disorder. She was referred to Nice university hospital and then presented in septic shock with acute respiratory failure and underwent mechanical ventilation. She received hemodynamic support, and antibiotic treatment with cefotaxime and levofloxacin. She developed severe acute respiratory distress syndrome (ARDS) and needed a veno-venous extracorporeal membrane oxygenation (ECMO) for refractory hypoxemia. She was then referred to an ECMO centre in Marseille. Search for immunodeficiency was negative: immunoglobulin dosage and lymphocyte subpopulation counts were normal; HIV tests were negative. Microbiological analysis performed on broncho-alveolar lavage (BAL) showed no evidence of bacterial infection but a positive Polymerase Chain Reaction (PCR) for Measles. Measles serology was also positive (IgM and IgG). The patient was placed on airborne precautions. Antiviral therapy with ribavirin 10 mg/kg/j was initiated. Blood vitamin-A dosage was low (0.20 mg/l, reference 0.41-0.49 mg/l) and a supplementation with intravenous vitamin A 200,000 UI single dose was performed. Despite this, the patient died of refractory ARDS.

Outbreak description and analysis

On July 5th 2017, the RHA-PACA was notified of a cluster of cases of measles in two nearby cities of the region. The measles outbreak has been confirmed. The first cluster was located in Nice, in the department of Alpes-Maritimes where five cases occurred in a single family (father and 4 children) with one case who required hospitalisation for transient monitoring in Marseille and one death in the ICU because of refractory ARDS (as described in the case report). The second cluster was in Pignans, a municipality in the department of Var, where five cases occurred in three families (Figure 1). After this first notification, according to the WHO European Region guidelines, several measures were taken. First, surveillance was intensified to ascertain the size and geographic extent of the outbreak. An official communication from the public health authorities to health care workers was done. Medical practitioners and laboratories working in the concerned municipalities were informed about the outbreak. Subsequently, eight other cases belonging to the same community were notified in Pignans and Gonfaron, a nearby village, until the end of July (Figure 1). Second, we conducted a case investigation and found evidence of repeated gatherings between families, all belonging to a single sedentary French Roma community settled in southeastern France. Third, case isolation was recommended when feasible. Patients were systematically put under airborne precautions when they were hospitalised. The rate of hospitalisation tended to increase after the public health authorities alert in early July (5/10 *vs.* 7/8; $p = 0.13$). Fourth, we performed contact management. None of the cases among children used to go to school. None of the contacts belonging to the same Roma community were completely vaccinated. Fifth, a vaccination campaign was launched for

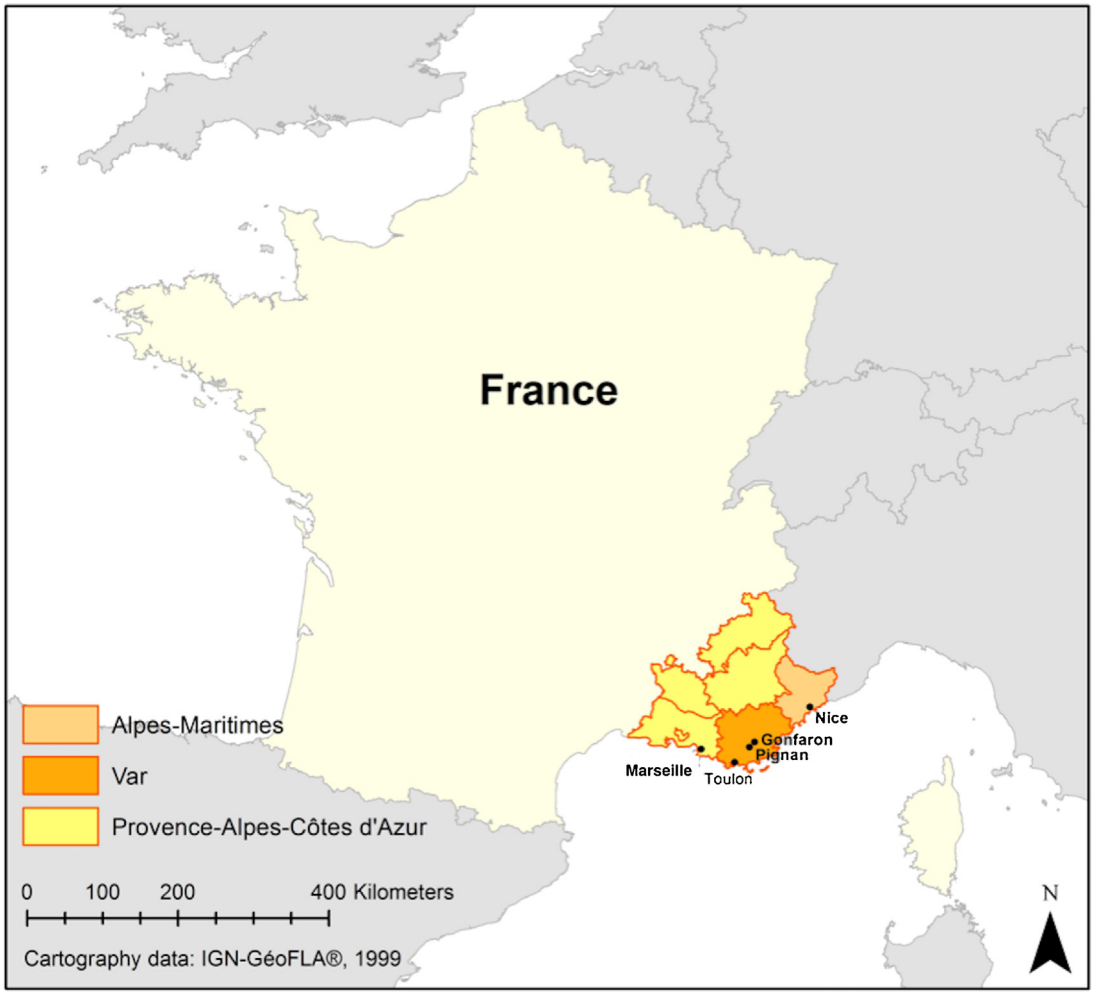

Figure 1. Geographical localization. All cases occurred in a single French Roma community settled in Nice, Pignans and Gonfaron. Patients were hospitalised in Nice, Marseille and Toulon.

relatives who were in contact with cases or their families. For this, a dialogue was established with both the chief of the community and the pastor to convince families to quickly get a vaccination against measles by their family doctor. After the measles vaccination campaign, two-doses coverage in these families was estimated at 90%.

Overall, from May to July 2017, eighteen cases were notified (Figure 2). All cases occurred in a single sedentary French Roma

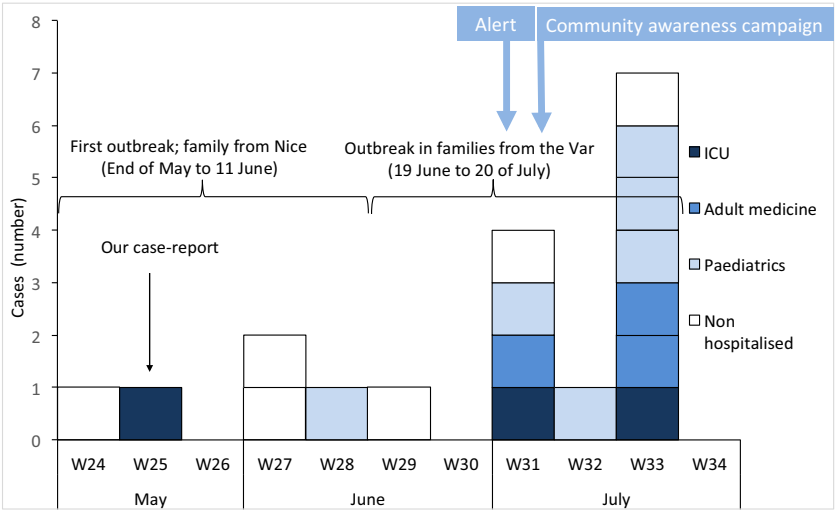

Figure 2. Outbreak Timeline. Measles cases were represented by squares.
W = week; ICU = Intensive Care Unit.

community settled in Nice, Pignans and Gonfaron. According to the case definition, fifteen (83%) cases were laboratory confirmed (PCR) and three (17%) were epidemiologically confirmed. Fifteen cases (83%) were not previously immunized (unvaccinated) and three (17%) were vaccinated with the first dose of measles-containing vaccine just a few days before the onset of the disease. Cases were between 6 months and 24 years old including twelve cases aged less than 15 years old (six between 0–3 years old and six between 4–13). Among cases under 15 years old, seven (58%) were hospitalised, mainly for deterioration of the general status and dehydration. Two of them developed pneumonia, including a 6 month-old infant hospitalised in ICU. Five of the six cases (83%) over 15 years old were hospitalised, including a 23 years old young man with hepatitis, a 16 years old young man under close surveillance in ICU for pneumonia, and our reported case. During the outbreak period, there was no case of healthcare-associated measles transmission.

Virological analysis

In our case report, measles virus RT-PCR was positive in BAL fluid, pleural fluid, pharyngeal swabs and plasma EDTA (Cycle Threshold = 19, 33, 23 and 35 respectively).

All other strains from patients positive for measles by RT-PCR in this outbreak (N = 14) belonged to the same D8 genotype (data not shown). The N-450 sequence of our MVs/Marseille.FRA/23.17(D8) strain isolated from our case report was compared to 27 sequences representing all known genotypes (Figure 3).

Discussion

In this study, we investigated a measles outbreak involving eighteen related cases in a French Roma community settled in southeastern France. Although very heterogeneous, Roma

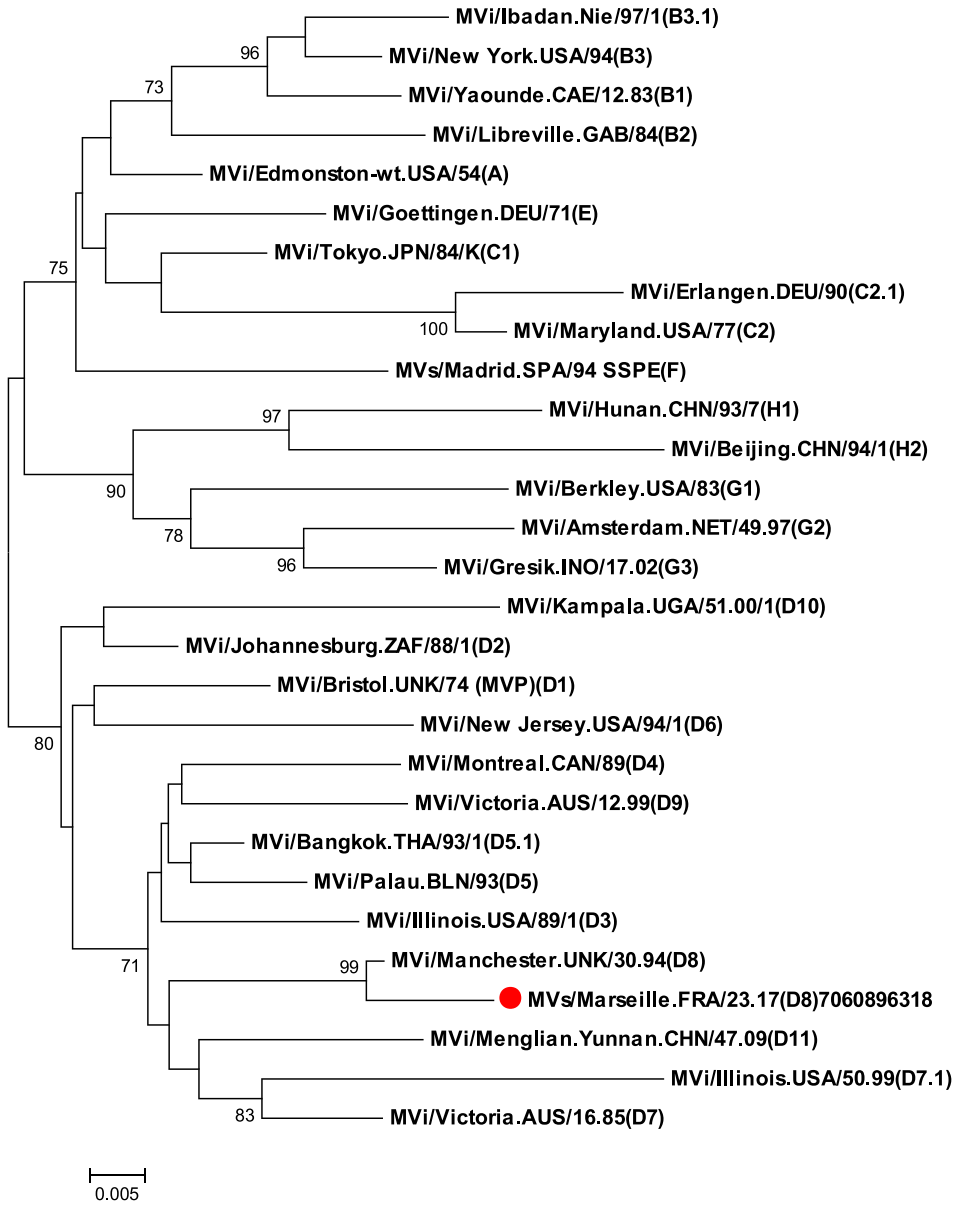

Figure 3. Phylogenetic analysis of the N-450 sequences comparing the sequence of our MVs/Marseille.FRA/23.17(D8) strain isolated from our case report to 27 references representing all known genotypes.
The sequence of the MVs/Marseille.FRA/23.17(D8) was deposited to the GenBank under accession number MG837007.
The tree was constructed using Mega 6 software by NJ method K2 parameter.
A red circle points out the Marseille sequence situation in this tree.

communities, Europe's largest minority of about six million people (European Centre for Disease Prevention and Control, 2013), harbours several risk factors for severe measles outbreaks. First, vitamin A deficiency is associated with higher rates of lower tract infection and has been reported as a risk factor for severe measles (Stevens et al., 2015). This diet deficiency associated with poor nutritional status has already been described in the European Roma community measles outbreak in 2008–2010 (Melenotte et al., 2012). Second, vaccination coverage has been reported to be particularly low in the Roma community. Notably, a polish study showed a coverage of 37% in this specific population while the country displays high (97%) double-dose vaccination coverage in national statistics (Stefanoff et al., 2010). This low vaccination coverage may be related to barriers in access to health services. Recent measles outbreak control in the Roma community showed that vaccination is accepted if it is made accessible, and when leaders and health mediators belonging to this community are involved (European Centre for Disease Prevention and Control, 2013). In this outbreak, none of the cases among children used to go to school. The successful and rapid control of this outbreak may be in part attributed to the mediating role of both the chief of the community and the pastor that helped to convince families to quickly get a vaccination against measles by their family doctor. Third, by sequencing all Measles strains isolated in this outbreak, we showed that they all belonged to the same D8 genotype. In France as well as other European countries, two main genotypes circulated in 2017: genotype B3, mainly reported in Northern and Eastern Europe; and genotype D8 (Santibanez et al., 2017), also implicated in outbreaks in the north of Italy (Amendola et al., 2017). The geographical proximity with Italy that experienced a high incidence of measles in 2017 and the high mobility of Roma communities may have been determining factors that contributed to this measles outbreak.

We described here a fatal case of a 16-year old girl with a diagnosis of atypical and severe measles. In France, one death attributable to measles (our patient case) has been notified in 2017 (Anon, 2018). Rafat et al. reported in their study over three years (between 2009 and 2011) describing cases of severe measles hospitalised in ICUs in France, that five patients (13.8%) died, all of them were immunodepressed (Rafat et al., 2013). Although considered as immunocompetent, our patient had been treated with oral corticosteroids before the worsening of symptoms. This may have played a role in the atypical presentation and the severity of this case. Although often prescribed, clinical practice guidelines do not recommend systemic steroids in the treatment of acute respiratory tract infections (ARTIs) (Waljee et al., 2017), adverse events among which infection susceptibility can develop within 30 days of short-term steroid use, which raises concern about the safety of systemic steroids for ARTIs (Waljee et al., 2017).

In conclusion, suboptimal vaccination coverage rates in some areas and in minority populations as well as immunity gaps in the population remain the primary cause of continued measles transmission (García Comas et al., 2017).

Funding sources/Conflict of interest

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Ethical approval

Not provided.

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