Measles and rubella in Croatia

Tatjana Vilbic-Cavlek1, Jelena Ivanice-Jelecki1,2, Dubravko Forcic2,3, Andrea Babic-Enrcg2, Maja Santak2,3, Irena Tabain1, Gordana Vojnovic1, Ljiljana Milasinic3, Snejana Arti3, Bernard Kaic1

1Croatian National Institute of Public Health, Zagreb; 2University of Zagreb, Centre for research and knowledge transfer in biotechnology; 3Center of Excellence for Viral Immunology and Vaccines, CEPiVax

Introduction

In Croatia, measles vaccination was first introduced in the national childhood vaccination schedule in 1968 and was replaced by the combined measles, mumps and rubella (MMR) vaccine in 1976. Vaccine coverage rates for the first MMR dose are more than 94% since 2004, and for the second dose more than 97%.

In the pre-vaccinal period, 5,000-20.000 cases of measles and rubella were notified each year in Croatia. In the last two decades, less than 10 cases have been reported annually, with the exception of three import-related outbreaks (2003/2004, 2008 and 2014/2015). In 2002, four SSPE cases were notified. Regarding rubella, only sporadic cases were reported with an outbreak in 2007 (Fig. 1). There was no reported congenital rubella syndrome. A seroepidemiological study conducted from 2005-2009 showed that 94.6% of the Croatian childbearing-aged women are immune to rubella. However, vaccination coverage has been decreasing since 2012.

2014-2015 measles outbreak

On 1 December 2014, measles was clinically diagnosed in a 6-year-old boy (probably imported from Berlin). His brother developed symptoms on 11 December. Two additional family members with measles represent the first family cluster (4 patients). Until March 2015, 17 clusters (2-15 cases) of measles were identified. Cases were mainly members of Roma community with very low vaccination coverage (<50%) who had numerous contacts with family members from Bosnia and Herzegovina as well as autochthonous cases among members of Roma population. Sporadic cases in non-Roma community also occurred. Six healthcare workers acquired infection at work. Viruses from 30 cases were partially sequenced and all possessed identical or highly similar sequences indicating that the outbreak was caused by a single strain belonging to genotype D8.

Laboratory performance in 2015-2016

- National Measles/Rubella Laboratory, Croatian National Institute of Public Health
  - Measles: virus isolation (B95a; Vero/SH/SAM); RT-PCR; Serology (ELISA IgM/IgG; IFA IgM/IgG; IgG avidity)
  - Rubella: virus isolation (Vero/SH/SAM; Vero); RT-PCR; Serology (ELISA IgM/IgG; IgG avidity)

<table>
<thead>
<tr>
<th></th>
<th>NP swab Tested/Positive</th>
<th>Throat swab Tested/Positive</th>
<th>Urine Tested/Positive</th>
<th>Blood Tested/Positive</th>
<th>Serum Tested/Positive</th>
<th>Total Tested/Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles RT-PCR</td>
<td>83/50</td>
<td>8/7</td>
<td>72/47</td>
<td>1/0</td>
<td>50/0</td>
<td>164/105</td>
</tr>
<tr>
<td>Measles IgM</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>50/0</td>
<td>50/0</td>
</tr>
<tr>
<td>Rubella IgM</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>50/0</td>
<td>50/0</td>
</tr>
<tr>
<td>Measles isolation</td>
<td>7/1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7/1</td>
</tr>
</tbody>
</table>

*Samples from suspected measles cases were tested for rubella

Molecular epidemiology

- University of Zagreb, Centre for research and knowledge transfer in biotechnology

Genetic characterisation of wild type and SSPE strains detected in Croatia is performed since 2003. In-house RT-PCR methods are established for amplification and sequencing of complete measles genome. Sequencing of N450 (450 nucleotides encoding for the last 150 amino acids of the N protein) and genotyping is routinely performed and sequences are submitted to PubMed and MeaNS databases. Similar to contemporaneous epidemiological data from other European countries, strains detected in Croatia belong to genotypes D4 (epidemics in 2003 and 2008), B3 (single imported case in 2014) and D8 (epidemics in 2014/2015, single case in 2016).

Conclusions and future challenges

Due to high vaccination coverage in the past decades, Croatia has interrupted measles and rubella circulation in the population. Only sporadic imported cases of measles occur, with three import-related outbreaks of limited magnitude in the last 15 years. Except one geographically limited outbreak of rubella in 2007, only sporadic imported cases of rubella without secondary cases are noted. The main challenge is to interrupt the decreasing trend in vaccination coverage, observed in the last four years, which represents a threat to population immunity level and can lead to reintroduction of measles or rubella circulation.

Publications


Acknowledgments

This work was supported in part by Croatian Science Foundation, project no. 6255 (to D.S.).