Re-emergence of another vaccine-preventable disease?—Two cases of rubella in older adults

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ABSTRACT

Unlike its devastating teratogenic effects, post-natal infection with rubella typically causes subclinical or inapparent illness. While rubella has been largely eliminated from the United States following the introduction of an efficacious live-attenuated vaccine in 1969, a small proportion of the population remains susceptible. Recent declining vaccination rates have resulted in a rising incidence of sporadic and outbreak-associated measles, reminding us that an increasing proportion of the population is also susceptible to, and may be reservoirs of transmission for, rubella. We describe two rare adult cases with no clear exposure. These cases serve as a reminder that clinicians should remain vigilant and consider rubella infection in susceptible patients, including older adults, presenting with febrile rash illness.

1. Why these cases are important

While the teratogenic effects of rubella infection in pregnant women are a major public health concern, post-natal infection typically causes mild disease of little clinical significance. Since the introduction of an effective vaccine and national vaccination rates >90%, rubella has been largely eliminated from the US. This report describing two cases of acute rubella in older adults serves as a reminder that rubella continues to circulate in many parts of the world and that a small proportion of the US population remains susceptible.

2. Case descriptions

Case 1: A previously healthy 60-year-old female presented with complaint of myalgias for 1 week, fevers to 102 °F for one day, and development of a diffuse, erythematous, mildly pruritic rash on her abdomen, which progressively spread up her torso and to all four extremities on the day of admission. The patient had returned 1 week prior from a 3 week vacation to east Africa, France and England. She could not recall ill contacts. The patient had never received measles mumps rubella (MMR) vaccine or had a rash illness suggestive of rubella.

In the emergency room the patient had a temperature of 101.8 °F with otherwise normal vital signs. Her physical exam was notable for right occipital, pre-auricular and anterior cervical lymphadenopathy and a diffuse, non-pruritic, morbilliform, blanching rash on the face, abdomen and extremities. Her routine laboratory tests were normal except for a hematocrit of 33.7%, platelets of 87 cells × 10^3/μl and white blood cell count of 2.4 cells × 10^3/μl (57% neutrophils, 26% lymphocytes, 11% monocytes and 4% eosinophils) and slide review identifying >20% bands. The patient was briefly hospitalized for evaluation. Microbiologic testing, including for parasites, arboviruses, bacteria and rickettsia, was unrevealing; subsequent serologic results were negative for measles (IgG and IgM), but positive for rubella IgM.

Case 2: A previously healthy 61-year-old female employed as an international travel agent presented with a history of severe diarrhea and abdominal pain, and two days of fever to 101 °F, sore throat and an erythematous rash on the face, chest and legs. Symptoms resolved after 5 days, but were followed by severe joint pain of the wrists, knees, hips and ankles. The patient denied recent travel, but reported recently hosting well visitors from England and France in her home and attending an "international" luncheon with 40 guests. She had a well housekeeper of Hispanic descent; country of origin and place of birth were unclear. The patient was born in England, and had not ever had a rash illness consistent with rubella or received MMR vaccine.

Her physical exam was remarkable for pharyngeal erythema, bilateral enlarged, tender posterior occipital and supraclavicular lymphadenopathy, a fading maculopapular rash on her back,

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and bilateral erythema, tenderness and effusions of the carpal, knee and ankle joints. Her hip joints were tender to palpation, and she had difficulty rising to her feet due to pain. She was prescribed oral steroids for acute serum sickness. Complete blood count and chemistries were normal. Four days later, the patient reported improved arthralgias, although she still felt weak with difficulty ambulating. Her fading rash had become intensely pruritic and scaly, requiring topical steroids for relief. Laboratory results included a negative bacterial throat culture, negative serology for parvovirus B19 and positive rubella IgG and IgM.

Because rubella is a reportable disease, confirmatory testing was performed for both cases at the California Department of Public Health Viral and Rickettsial Disease Laboratory; results of an in-house developed Enzyme Immunoassay showed IgM and IgG indices of 3.09 and 3.61 in the first case, and 2.69 and 2.54 in the second case, respectively. An index of $\geq 1.0$ indicates the presence of rubella-specific antibody.

3. Other similar and contrasting cases in the literature

Rubella in the US remains rare. While a review of the literature over the past two decades reveals infrequent reports of outbreaks in the US occurring in unvaccinated populations, none of these reports provide detailed clinical descriptions.4-6 Our cases are unique in that they occurred in presumably immune, older adults without clear exposure to ill contacts.

4. Discussion

Prior to introduction of vaccine, rubella was endemic worldwide with peak incidence in pre-school and school-aged children.1,2 Periodic epidemics caused major morbidity and mortality; for example, a US epidemic in 1964–1965 resulted in an estimated 12.5 million cases of infection, over 20,000 cases of congenital rubella syndrome (CRS) and 11,000 fetal deaths.1 Following licensure in 1969, rubella vaccination was widely incorporated into national childhood immunization campaigns in the 1980s, including current recommendations that all children receive two doses of MMR vaccine at 12–15 months and 4–6 years.2 These collective efforts resulted in a decline in rubella incidence of $\sim 99\%$, such that since 2003 <20 cases have been reported annually in the US.2–3,7–9 Similar dramatic declines were observed in Western Europe.10

The current live-attenuated rubella vaccine, using strain RA 27/3, appears to be efficacious and provide lifelong immunity. Following a single dose at $\geq 12$ months of age, an immunologic response is induced in $\geq 95\%$ of recipients.2,7 Roughly 90% of persons have protection against clinical rubella and viremia for at least 15 years following immunization, and antibody titers persist up to 20 years.2,7,11 While titers of vaccine-induced rubella antibodies may decline with time, re-infection following vaccination appears rare.1 The routinely recommended second MMR dose provides an added safeguard against primary vaccine failures. Non-pregnant women of child-bearing age without evidence of immunity are also targeted for vaccination. Our cases, born in 1947 and 1948, could not recall ever receiving MMR vaccination, and while current US strategies are based on the general assumption that persons born before 1957 have acquired natural immunity, such individuals are not guaranteed to be immune.2 Seropositivity among adults (20–49 years of age) surveyed between 1988 and 1994 was 88.4%.12 The cases described herein fall within this age cohort.

Acute rubella infection can be difficult to recognize. Symptoms are usually mild; 25–50% of cases are asymptomatic.12 Adults may experience a 1–5-day prodrome with low grade fever, malaise, and upper respiratory symptoms preceding the rash. The classic rubella rash is a generalized, erythematous, maculopapular rash that begins on the face and moves down, lasts 3–5 days and is occasionally pruritic. Lymphadenopathy may begin a week after the rash, commonly affecting the suboccipital, postauricular and cervical nodes, and lasting several weeks. Polyarthritis and polyarthralgias can last up to 4 weeks; up to 70% of adult women are affected. Encephalitis and severe thrombocytopenia are rare sequelae.2,7 Infection in pregnant women can result in miscarriage, fetal death or severe anomalies in the infant with CRS.2 Acute infection is frequently confirmed serologically by detecting either rubella-specific IgM or a fourfold rise in acute and convalescent IgG titers.

The sources of exposure in our cases are unclear, as neither could recall contact with ill persons within the probable exposure period (12–23 days before rash onset). Our first case was likely exposed during international travel. In many developing countries, particularly Africa and Southeast Asia, rubella remains endemic; for example in sub-Saharan Africa, where our first patient traveled, no countries include rubella in their national immunization programs and little surveillance data is available.13–14 Our second case did not travel, but had contact with visitors from England and France and possibly other countries. While the reported numbers of rubella cases remain low in Western Europe, recent declining MMR vaccination rates due to poor vaccine acceptance have resulted in a rising incidence of sporadic and outbreak-associated measles in that region, reminding us that an increasing proportion of that population is also susceptible to, and may be reservoirs of transmission for, rubella.7

In conclusion, these cases serve as a reminder that non-immune individuals who were not vaccinated within the framework of national immunization programs initiated over the past two decades, either because they were not eligible or were missed, remain at risk for rubella infection. Interestingly, a recent increase in the number of rubella cases reported nationally has been observed (17 in 2008 compared to 12 or less reported annually in 2003–2007); similar to our second case, more than half of cases reported in 2008 had no history of travel9 (personal communication—Al Barskey, CDC). While our cases presented with hallmark symptoms that alerted astute clinicians to their diagnosis, rubella can often present with a mild, uncharacteristic clinical picture and may easily be missed. Surveillance for rare diseases like rubella is hampered by loss of awareness and diagnostic skills, and asymptomatic transmission may be more common than suggested by the low numbers of reported cases. Given this, clinicians should remain vigilant and consider rubella infection in susceptible persons, especially older adults, presenting with febrile rash and characteristic symptoms. Prompt reporting of confirmed cases to public health authorities, in conjunction with ongoing monitoring of the immune status in different age groups and populations, is critical to inform current and future vaccination strategies.

Conflicts of interest

None declared.


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