Is it or is it not? Lessons learned from a case of suspected vaccine strain measles

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Abstract

Objective: Measles continues to be a threat to Australia. While post-eradication risks are low, imported measles cases from overseas travellers who are non-immune can cause small outbreaks. This case report discusses the challenge of identifying wild-type measles in an individual who was recently vaccinated with measles-containing vaccine (MCV).

Methods: A positive polymerase chain reaction (PCR) result for measles for an adult who had recently received a measles-containing vaccine was notified. Investigation revealed no known epidemiological link, recent overseas travel or contact with recent measles cases during the incubation period.

Results: The results of the initial sequencing to distinguish between wild-type and vaccine-strain measles were inconclusive. A decision was made to re-run the genotyping, collect additional specimens and quarantine the case until a definitive result was obtained. Sequencing and genotyping revealed that this indeed was a wild-type measles strain.

Conclusions: Changing epidemiology of measles means distinguishing between wild-type and vaccine–strain measles has become a new challenge.

Implications for public health: The reflection of the public health management of this case has provided a valuable teaching tool for public health professionals globally, particularly in low incidence measles countries.

Key words: measles, public health investigation, wild-type measles, vaccine-strain measles

Measles is a highly infectious viral disease that can cause serious illness and complications including encephalitis and death[1,2]. Despite the World Health Organization (WHO) declaring measles to be eliminated from Australia in 2014,[1] there remains a risk of acquiring measles virus (MeV) through importation by susceptible persons (adults born during or after 1966 in Australia and prior to the national measles control campaign in 1988, or immigrants born overseas who are unvaccinated or not fully vaccinated) or foreign visitors where measles is endemic.[2,3] Although Australia has high MeV vaccination coverage, there are low vaccination rates in certain areas, which in conjunction with importation of measles leads to secondary local transmission.[2,4]

In this case report, we describe a metropolitan Public Health Unit's (PHU) challenge in identifying a wild-type measles case in a 32-year-old who was vaccinated with measles-containing vaccine (MCV) seven days prior to presenting with symptoms of measles.

Case presentation

In New South Wales (NSW), measles is a notifiable condition under the *Public Health Act 2010*. Laboratory-confirmed and suspected cases of MeV are required to be reported by laboratorians and clinicians respectively to PHUs. In April 2018, a metropolitan Sydney PHU was notified by the reference laboratory (NSW Health Pathology-Institute of Clinical Pathology and Medical Research [NSWHP-ICPMR], Westmead, NSW) of a positive real-time polymerase chain reaction (PCR) result for MeV on a nasopharyngeal swab collected from a 32-year-old female. Consultation with the case's General Practitioner (GP) identified that the case was overseas-born with uncertain MeV vaccination status. MeV serology was collected for occupational screening, and as results indicated that the case was non-immune (measles-specific IgG and IgM negative), she was vaccinated with MMR-II five days later.

Mild symptoms of self-reported fever, cough and sore throat began two days post vaccination. She presented to her GP seven days post vaccination after she developed a macular rash on the face the evening prior. She did not have fever at onset of rash or when reviewed by her GP. All household members were well and her 13-month-old infant had received a MCV two weeks prior. A thorough investigation by the PHU revealed the case had no known epidemiological link with anyone with measles and no recent overseas travel during her incubation period.

The duplex PCR assay performed at NSWHP-ICPMR simultaneously targets both wild-type and genotype A vaccine strain measles virus (MeVA).[5] MeVA is diagnosed when both targets are detected, whilst detection of MeV only indicates wild-type strain. Initial results indicated infection with wild-type MeV as

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the MeVA target was negative. However, given the recent vaccination, inconsistent clinical symptoms and no identifiable epidemiological link, the case was diagnosed with MeVA following a discussion between the laboratory and PHU, with the suspicion that there was a false negative MeVA result. No contact tracing was undertaken at this stage whilst awaiting definitive genotyping results and repeat testing on additional specimens.

Subsequent sequencing of the 450-nucleotide region coding for the COOH-terminal 150 amino acids of the N gene (by both NSWHP-ICPMR and Victorian Infectious Diseases Reference Laboratory, Melbourne, Victoria) revealed that this indeed was a wild-type strain; genotype D8. This was the same genotype identified in two recently imported measles cases in the Western Sydney region, however, no epidemiological links could be found. The incubation period of MeV would have been exceeded had the index case been exposed to either of these two confirmed cases.

Prompt contact tracing was established following notification of the results and no secondary cases were reported.

Measles vaccine-strain cases in NSW

NSWHP-ICPMR began routinely targeting both wild-type and genotype A vaccine strain measles virus (MeVA) in 2017. This state-wide data on MeV testing demonstrates that MeVA is rare, with the percentage MeVA over all measles PCR testing conducted at NSWHP-ICPMR between 2017 and October 2019 occurring at a rate of 1.0% - 1.4% (Table 1).

Discussion

A change in the epidemiology of measles, especially in low-incidence countries like Australia, means distinguishing between wild-type and MeVA has become a new challenge.[6] However, this is critical in implementing a timely public health response. The WHO indicates that following MCV administration, 5–15% of recipients can experience systemic reactions, including a fever for one to two days, and in approximately 2% a transient rash can occur.[7] In this case, the initial decision to classify this case as MeVA was based on the clinical context and epidemiological risk despite the PCR results. Similarly, the case report by Churchill et al.[6] of MeVA in a Canadian adult suggests where viral genotyping is not readily available to the multidisciplinary public health team, careful consideration and consultation to initiate a public health response should be made based on epidemiological risk and the clinical context.[6] In this case the lack of an epidemiological link created confusion for PHU staff.

Identification of a specific viral genotype is paramount to public health responses. Sporadic cases of wild-type MeV and small outbreaks due to importation and secondary cases linked to susceptible populations are still evident, even in countries like Australia that are recognised to have eliminated measles transmission.[2,3] Individuals recently vaccinated against MeV may already be incubating wild-type MeV. This then becomes a challenge when trying to establish whether the resulting symptoms are caused by the vaccine or MeV infection.[3,4,6] This is clearly demonstrated in this case, whereby the case was evidently incubating wild-type MeV just prior to vaccination.

Choe et al.[8] compared wild-type to MeVA in Korea, finding that respiratory symptoms such as cough, coryza and conjunctivitis were more prevalent in persons with wild-type MeV compared with MeVA.[8] This could potentially reduce the misclassification of cases of wild-type MeV prior to confirmatory genotyping results. Similarly, attenuated MeV infection in individuals with previous MeV vaccination but waning immunity are less likely to develop fever, coryza and cough compared with non-immune persons[9]

A risk analysis by Saunders et al.[10] evaluating the main risks for reintroduction of measles into countries that have reached an elimination status suggests asymptomatic or mild measles infections are possibly circulating in individuals who display immunity to MeV but transmission from these cases is likely to be rare.[10] This notion is worthy of further research and could explain the transmission of MeV in this case, where an epidemiological link was never established. Saunders et al.[10] also propose that although live-attenuated MeV vaccines are safe and effective in the prevention of the transmission of MeV, there may be a possibility of live-attenuated MeV mutating back to wild-type MeV.[10] It is important to note that there are no published data to support this theory.

This case illustrates that even in recently vaccinated individuals exhibiting what appears to be MeVA clinically with no plausible epidemiological link, rapid sequencing and genotyping is imperative, particularly when MeV is known to be circulating in the community. MeVA may be detected as early as one day and up to 784 days in urine and respiratory tract samples, respectively, post vaccination by PCR.[6,11,12] Therefore, in keeping with control guidelines,[13] any individual who was vaccinated with MCV five to 12 days prior to displaying symptoms of measles should not be tested. If these guidelines were strictly adhered to, the GP in the present case would not have requested MeV testing, and this case would never have been identified. This highlights that even in recently vaccinated individuals, there is still a possibility they could be incubating the disease at the time they are vaccinated particularly when MeV is circulating in the community.

The challenge for PHUs is further complicated by atypical presentations of wild-type measles, particularly in those individuals incompletely vaccinated or those with waning immunity, as these individuals present with mild symptoms or symptoms that may be mistaken for other viruses such as parvovirus, adenovirus or enterovirus.

Learning from experience plays a vital role in ensuring that appropriate public health actions are implemented and there is an improvement in the public health response for similar cases in the future. The reflection of the public health management of this case provides valuable teaching points for public health professionals globally, particularly in low incidence measles countries.

Table 1: Results of measles virus nucleic acid testing at conducted at NSW Health Pathology-Institute for Clinical Pathology and Medical Research 2017 – 2019.

Year	Total number of unique measles nucleic acid tests*	Number of positive (%)	Vaccine strain measles (%)	Wild-type measles (%)
2017	574	10 (1.7%)	7 (1.2%)	3 (0.5%)
2018	1263	33 (2.6%)	18 (1.4%)	15 (1.2%)
2019**	3,822	84 (2.2%)	38 (1.0%)	46 (1.2%)

Notes:

**Per individual patient (some patients may have had more than one specimen collected but are counted once only)*

***2019 results are year to date (last test conducted 13 October 2019)*

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