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CASE REPORT

Severe Pneumonitis in Omani Infants During An In-Hospital Measles Outbreak

A report of three cases

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ABSTRACT: Measles is a highly contagious infectious disease. Despite aggressive national initiatives to eradicate measles, outbreaks have occurred in recent years. We report three infants who presented to a tertiary care hospital in Muscat, Oman, in 2019 with measles and then developed pneumonitis, received intensive care treatment and made full recoveries. Infants can have an atypical presentation and develop severe symptoms. Pneumonitis is a serious complication and the management strategies are controversial. The early detection of measles and isolation of affected individuals play major roles in the elimination of measles outbreaks.

Keywords: Measles; Pneumonitis; Infant; Respiratory Distress Syndrome; Vitamin; Case Report; Oman.

Measles is a highly contagious and potentially fatal viral illness that is especially dangerous for infants and malnourished and immunocompromised patients who can develop atypical and severe manifestations.[1] The causative pathogen belongs to the *Paramyxoviridae* family and is mainly transmitted by respiratory droplets. Measles can be prevented by the available vaccine.[2]

The symptoms of measles are often mild; however, infants, malnourished and immunocompromised patients can develop atypical or severe manifestations including pneumonitis, acute disseminated encephalomyelitis and subacute sclerosing panencephalitis.[3] Measles-associated mortality declined following the implementation of vaccination programmes, although outbreaks of cases continue to occur when unvaccinated individuals are exposed to the virus.[2] The incidence of measles in Oman is low (0.53 per 100,000 person-years) and the measles vaccine coverage has been consistently above 95% since 1990.[4] In Oman, the measles vaccine is administered to all children at 12 and 18 months of age, as recommended by the World Health Organization (WHO). However, the Centers for Disease Control & Prevention and WHO guidelines recommend the administration of the measles vaccine at nine months of age during measles outbreaks.[5]

Gulf countries have implemented a vaccination schedule involving two doses of the measles, mumps, and rubella vaccine, with the first dose at 12 months of age. The measles vaccine coverage in Bahrain has been more than 90% and has been sustained at >97% since 2001.[6] Vitamin A supplementation is recommended by the WHO for all children with measles.[7]

Measles-related pneumonia is a life-threatening complication that can lead to severe acute lung injury and acute respiratory distress syndrome. Co-infection with other viruses and bacteria is not uncommon. The treatment for measles-related pneumonia primarily involves supportive care. In this article, we report three infants who developed measles-related pneumonia following exposure of the second and third patients to the index case during a hospitalisation. The early detection of measles, isolation of the affected individuals and performance of sensitive investigations in all contacts are needed to prevent the transmission of measles.

Case One

A previously healthy six-month-old male infant was admitted to a tertiary care hospital in Muscat, Oman, in 2019 with febrile illness and a generalised rash of four days duration. On examination, he was lethargic, dehydrated, febrile and had a normal respiratory rate with bilateral normal breath sounds. He had a maculopapular rash on the face, trunk and extremities. He was admitted to the general ward initially upon suspicion of acute viral fever for hydration with intravenous (IV) fluids. On day three of admission, he became tachypnoeic, tachycardic, febrile with an oxygen saturation of 88–90% in room air; therefore, he was transferred to the high dependency unit for close monitoring and oxygen support via facial mask suspecting acute bronchiolitis.

The patient's complete blood count (CBC) test showed normal white blood cells at 4.0×10^9/L (normal

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Figure 1: Chest X-ray of a six-month-old infant (case one) with measles infection showing bilateral infiltrates.

range: 1.4–9.0 × 10^9/L) with normal neutrophils and lymphocyte count. He received dexamethasone, adrenaline nebulisation and oseltamivir. A nasopharyngeal viral multiplex polymerase chain reaction (PCR) test was reported negative for respiratory viruses including respiratory syncytial virus, influenza A and B, rhinoviruses, parainfluenza, coronaviruses, adenoviruses, bocavirus, enteroviruses, paraechoviruses, human metapneumovirus and *Mycoplasma pneumonia*.

His hospital stay was complicated with the development of respiratory distress and clinical sepsis requiring admission to the paediatric intensive care unit (PICU) on day three and the use of non-invasive ventilation (NIV). A chest X-ray (CXR) showed bilateral lung infiltration [Figure 1]. His vital signs on admission to the PICU showed persistent tachycardia (170 beats/min) with fever (38˚C) and tachypnoea (70 breaths/min) with saturation above 93% on NIV.

On detailed clinical assessment, he was found to have Koplik spots and bilateral conjunctivitis. A nasopharyngeal swab PCR test was reported positive for measles. Measles immunoglobulin (Ig)M antibody test was positive. He required NIV support, which was weaned within one day and he was then transferred to an isolation room. He required oxygen for the subsequent three days and was discharged uneventfully to home on day eight of admission. A detailed examination of this case by infection control specialists did not reveal the source of the infection.

Case Two

A nine-month-old female infant was diagnosed with tracheoesophageal fistula for which she underwent an operation; previously, she had been diagnosed with hypotonia, developmental delay and hypothyroidism. Additionally, she underwent investigations due to the suspicion of a glycogen storage disorder. She was admitted for endoscopic dilatation of the oesophageal stricture during which she was exposed to case one. Ten days after exposure, she developed a high-grade fever with cough and irritability. A maculopapular rash appeared on day two of her illness. Physical examination revealed a generalised maculopapular rash, a pulse rate of 170 beats/min and a blood pressure of 100/58 mmHg with tachypnoea; therefore, she was transferred to the PICU.

Her CXR showed bilateral lung opacities. Her CBC showed leukopenia at 2.9 × 10^9/L and lymphopaenia 0.4 × 10^9/L (normal range: 4–10.5 × 10^9/L) with normal neutrophils. Furthermore, her inflammatory marker levels were high with an erythrocyte sedimentation rate of 72 mm/hr (normal range: 0–20 mm/hr) and C-reactive protein level of 89 mg/dL (normal range: <10 mg/dL). She was started on NIV for respiratory distress. Her pulmonary condition worsened clinically and radiologically with characteristics of acute respiratory distress syndrome (ARDS); therefore, the mode of respiratory support was changed to invasive ventilation. She also required inotropic support with an infusion of adrenaline.

She had persistent fever despite antibacterial treatment and negative blood and tracheal cultures and was, therefore, treated for atypical Kawasaki disease in view of features of prolonged fever, rash for 10-day duration and suspected coronary dilation on the echocardiography. However, a nasopharyngeal swab PCR test revealed a positive test for measles and her measles IgM test was also positive. She received one day of high-dose methylprednisolone. She met the criteria for a diagnosis of ARDS with a partial pressure of oxygen to fraction of inspired oxygen ratio of 122, indicating severe acute lung injury. As part of the management strategy for ARDS, she was treated with a lung-protective ventilation strategy with the airway pressure release ventilation mode for seven days and 80% maintenance fluids. Treatment for measles-related pneumonia included the administration of vitamin A for 48 hours and ribavirin for five days. Over the course of five days in the PICU, she gradually improved, and she was extubated on day seven after admission to the PICU. She was transferred to the paediatric ward, where she stayed for three weeks. She continued to need supplemental oxygen, although that requirement was resolved before discharge.

Case Three

An 11-month-old female infant diagnosed with trisomy 21 who underwent surgery for ventricular septal defects was admitted with acute bronchiolitis

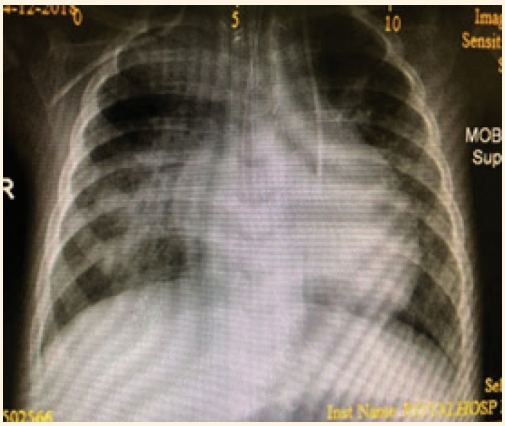

Figure 2: Chest X-ray of an 11-month-old infant (case three) with measles infection showing bilateral chest infiltration two days after paediatric intensive care unit admission.

and needed NIV support. She was discharged home but readmitted with febrile illness, respiratory distress, and maculopapular rash. Her history revealed exposure to case one during hospitalisation 10 days before presentation. On examination, her temperature was 39.3°C, with a blood pressure of 102/62 mmHg, heart rate of 168 beats/minute and respiratory rate of 60 breaths/minute with oxygen saturation of 86% in room air, therefore, she required NIV and PICU care. She had a generalised maculopapular rash with a wheezy chest. Investigations revealed normal CBC and negative blood culture. A CXR revealed bilateral infiltration, and she was, therefore, treated for suspected measles-related pneumonitis or acute viral bronchiolitis [Figure 2]. Nasopharyngeal swab for viral multiplex PCR test was positive for measles and negative for other viruses. Measles IgM antibody test showed a positive result. She required NIV for one day in the PICU due to respiratory distress. She was started on dexamethasone, vitamin A, ceftriaxone and oseltamivir. She gradually improved and showed complete recovery on the third day of admission and was transferred to the paediatric ward isolation room. She was observed in hospital for breathing difficulty and oxygen requirement and was discharged after three weeks stay breathing room air.

Overall, 10 patients were admitted with a diagnosis of measles to the current hospital over a period of seven years from 2013 to 2019. Three required ICU admission (cases one to three), four were discharged from the emergency room and the remaining three were admitted to the paediatric ward for fluid support. The average hospital stay was 2–3 days for those admitted to the general ward.

None of the 10 patients had received the measles vaccine; nine were younger than one year old. There was a history of positive contact with a suspected or confirmed case for eight patients. The diagnosis of measles was made based on the finding of relevant clinical symptoms which was confirmed by positive serological tests, PCR from throat swab samples and the isolation of the virus from urine samples.

This study was approved by the hospital's scientific research committee (SRC#CR26/2020).

Discussion

To the best of the authors' knowledge, this is the first case report from Oman to report three infants with severe respiratory manifestations related to measles [Table 1]. Measles is a highly contagious disease with a transmission rate of at least 90%.[4] It can be prevented by the available vaccine, adherence to infection control measures and careful investigations of all reported measles cases.[4] Oman had measles outbreaks from 1992 to 1993 and 2016 to 2017.[4] These outbreaks were attributed to imported cases leading to infections among the susceptible population, which is mainly composed of unvaccinated persons (unpublished data). To increase awareness, the Ministry of Health introduced many measures aimed

Table 1: Characteristics of cases one to three

Characteristic	Case One	Case Two	Case Three
Age in months	6	9	11
Gender	Male	Female	Female
Comorbidities	None	Tracheoesophageal fistula, suspected glycosylated storage disease, hypotonia developmental delay	Trisomy 21, operated for VSD
Duration of positive pressure ventilation in days (type of ventilation)	1 (NIV)	7 (invasive ventilation)	1 NIV
Length of PICU stay in days	1	10	1
Complications	None	ARDS, secondary bacterial infection	None

VSD = ventricular septal defect; NIV = non-invasive ventilation; PICU = paediatric intensive care unit; ARDS = acute respiratory distress syndrome.

at eliminating measles including introducing the fever and rash surveillance programme in 2004, developing national measles guidelines and conducting training workshops. Widespread catch-up vaccine campaigns were conducted in March 1994 and 2017 that targeted the susceptible population.[4] In their meta-analysis, Nic Lochlainn *et al*. showed that the measles vaccine is safe and effective for children less than nine months of age and that its early administration is an important step to reduce severe manifestations.[8] However, it is challenging to sustain herd immunity in Oman as not all of the population had received the measles vaccine.[4]

Measles-related pneumonia is serious and is associated with high mortality, especially in children less than five years of age as well as malnourished and immune-compromised children.[3] The described lung changes in patients with measles-related pneumonia include congestion, necrosis and exfoliation of bronchial and bronchiolar mucosa. These lung changes lead to increased susceptibility to other forms of viral and bacterial pneumonia, thus increasing the risk of acute lung injury and ARDS.[9]

Coetzee *et al*. reported that the rate of mortality due to severe measles was higher than the rate of mortality due to other causes among a cohort of PICU patients (the measles-related mortality rate was 31% and the non-measles-related mortality rate was 8.8%).[10] The most common cause of measles-related mortality is ARDS with progressive respiratory failure (56%).[10]

In general, the majority of those admitted with severe pneumonia required ventilator support. ARDS and the presence of air leaks such as pneumothorax are associated with worse outcomes.[11] The therapeutic strategies for ARDS include the initiation of lung-protective mechanical ventilation, lung recruitment manoeuvres, fluid management and the appropriate application of muscle relaxants.[12] Case two in this article was treated using lung-protective strategies, lung recruitment and fluid restriction in addition to supplementation with vitamin A and ribavirin. None of the current cases had received the measles vaccine as all were less than one year of age and the immunisation policy of the country is to vaccinate between 12 to 18 months of age.

Two of these cases had underlying chronic complex medical problems. Case one was admitted with a history of fever, rash and conjunctivitis without a history of positive contact with a suspected or confirmed case. As the incidence of measles is low in Oman, measles was not suspected in case one; therefore, he was admitted to the general ward rather than being isolated. As a result, case two and three were exposed to case one. This study emphasises the need to increase awareness of and adherence to infection control measures to prevent an in-hospital outbreak. All of the current cases had to be transferred to the PICU due to hypoxaemia and the need for respiratory support. Case two developed ARDS and required invasive mechanical ventilation while the other two cases had milder forms of respiratory distress and needed NIV support; none of the other cases had air leak syndrome. All patients were treated supportively with vitamin A and appropriate antibiotics, as CXR showed pulmonary infiltration. Case two was initially suspected to have atypical Kawasaki disease based on her history of a prolonged fever lasting 10 days, high levels of inflammatory markers and suspected coronary dilation on echocardiography. However, upon reviewing the echocardiography findings, coronary dilatation was excluded. She showed clinical and radiological improvement one day after starting high-dose IV immunoglobulin (IVIg) and methylprednisolone. However, her improvement could also be attributed to the change in ventilation and fluid restriction.

Despite recent advancements in medicine, the management of measles still relies primarily on supportive care and includes hydration, the administration of antibiotics for secondary bacterial infections and supplementation with vitamin A.[13] A few studies have shown that the use of IV methylprednisolone is associated with improved patient outcomes.[9] However, there have been no randomised controlled trials supporting the use of high-dose methylprednisolone in the treatment of measles-related pneumonia. Meduri *et al*. demonstrated that early use of a low dose of methylprednisolone in patients with ARDS resulted in an improvement in oxygenation and reduction in duration of mechanical ventilation and ICU length of stay.[14]

Infection with measles can lower the immune function. IVIg has been used successfully for measles post-exposure prophylaxis; however, it's effectiveness in the treatment of measles pneumonia has not yet been identified. IVIg may be used for measles pneumonia to boost the body's immune function, inhibit inflammatory reactions and thereby, accelerates the improvement of symptoms.[15]

Conclusion

Healthcare providers need to increase their awareness of the criteria for the diagnosis of the measles, especially in countries where the incidence of measles is low. Measles should be suspected in all unvaccinated infants and children presenting with fever and rash and diagnostic assessments should include surveillance

for the pathognomonic signs of measles. Adhering to the required infection control measures is essential to prevent in-hospital transmission. Unvaccinated infants are prone to developing severe complications of measles; therefore, those with respiratory deterioration need to be transferred to the PICU at an early stage.

AUTHORS' CONTRIBUTION

NAM conceptualised the manuscript. SAH and NAT collected the clinical data. SAH, AE and NAT conducted the literature review. SAH, KAM, SS, AE and NAM drafted the manuscript. KAM, SS and NAM critically reviewed the manuscript and provided intellectual input. All authors approved the final version of the manuscript.

References

1. Sindhu TG, Geeta MG, Krishnakumar P, Sabitha S, Ajina KK. Clinical profile of measles in children with special reference to infants. Trop Doct 2019; 49:20–3. https://doi.org/10.1177/0049475518804695.
2. Uchendu O, Ige O, Adeyera O. Knowledge and home treatment of measles infection by caregivers of children under five in a low-income urban community, Nigeria. Afr J Prim Health Care Fam Med 2019; 11:e1–13. https://doi.org/10.4102/phcfm.v11i1.1744.
3. Misin A, Antonello RM, Di Bella S, Campisciano G, Zanotta N, Giacobbe D, et al. Measles: An overview of a re-emerging disease in children and immunocompromised patients. Microorganisms 2020; 8:276. https://doi.org/10.3390/microorganisms8020276.
4. Ministry of Health, Oman. Public health bulletin: Measles epidemiology and elimination status in Oman. From: www.moh.gov.om/documents/236878/0/Public+Health+Bulletin+%233/db2a8256-b6a5-473d-a30b-b3a3b800ad8f Accessed: Jan 21.
5. Soucheray S. Reviews suggest first measles vaccination typically best after 9 months of age From: www.cidrap.umn.edu/news-perspective/2019/09/reviews-suggest-first-measles-vaccination-typically-best-after-9-months-age Accessed: Jan 21.
6. Jawad JS, Al-Sayyad AS, Sataih F, Naouri B, Alexander JP Jr. Toward measles elimination in Bahrain--A Middle East country experience. J Infect Dis 2011; 204 Suppl 1:S299–304. https://doi.org/10.1093/infdis/jir105.
7. Lindberg C, Lanzi M, Lindberg K. Measles: Still a significant health threat. MCN Am J Matern Child Nurs 2015; 40:298–305. https://doi.org/10.1097/NMC.0000000000000162.
8. Nic Lochlainn LM, de Gier B, van der Maas N, Strebel PM, Goodman T, van Binnendijk RS, et al. Immunogenicity, effectiveness, and safety of measles vaccination in infants younger than 9 months: A systematic review and meta-analysis. Lancet Infect Dis 2019; 19:1235–45. https://doi.org/10.1016/S1473-3099(19)30395-0.
9. Suter C, Buergi U, Eigenmann K, Franzen D. Severe acute measles pneumonitis: Virus isolation in bronchoalveolar lavage fluid. BMJ Case Rep 2015; 2015:bcr2015210826. https://doi.org/10.1136/bcr-2015-210826.
10. Coetzee S, Morrow BM, Argent AC. Measles in a South African paediatric intensive care unit: Again! J Paediatr Child Health 2014; 50:379–85. https://doi.org/10.1111/jpc.12486.
11. Li J, Zhao Y, Liu Z, Zhang T, Liu C, Liu X. Clinical report of serious complications associated with measles pneumonia in children hospitalized at Shengjing hospital, China. J Infect Dev Ctries 2015; 9:1139–46. https://doi.org/10.3855/jidc.6534.
12. Prodhan P, Noviski N. Pediatric acute hypoxemic respiratory failure: Management of oxygenation. J Intensive Care Med 2004; 19:140–53. https://doi.org/10.1177/0885066604263859.
13. Huiming Y, Chaomin W, Meng M. Vitamin A for treating measles in children. Cochrane Database Syst Rev 2005; 2005:CD001479. https://doi.org/10.1002/14651858.CD001479.pub3.
14. Meduri GU, Golden E, Freire AX, Taylor E, Zaman M, Carson SJ, et al. Methylprednisolone infusion in early severe ARDS: Results of a randomized controlled trial. Chest 2007; 131:954–63. https://doi.org/10.1378/chest.06-2100.
15. Chen L, Qi X, Li R, Wang X, Shi B, Meng Q. Injection of immunoglobulin in the treatment process of children with severe pneumonia. Pak J Med Sci 2019; 35:940–4. https://doi.org/10.12669/pjms.35.4.83.