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Measles pneumonitis

The authors declare no financial disclosure

Abstract

Measles is an acute febrile illness, potentially fatal and highly contagious, which is transmitted through the respiratory mode. Fever combined with one of the following: cough, coryza, conjunctivitis are the first manifestations of the disease. Koplik's spots may also appear on the buccal mucosa providing an opportunity to set the diagnosis even before the emergence of rash. Rash typically appears 3–4 days after the onset of fever, initially on the face and behind the ears, and its appearance is associated with the peak of the symptoms. Measles affects multiple systems, including the respiratory system, with pneumonia being one of the most lethal complications. Management involves best supportive care, correction of dehydration and nutritional deficiencies, treatment of secondary bacterial infections and provision of vitamin A. Importantly, given that measles present with lifelong immunity following infection or vaccination, prevention through measles vaccination has a cardinal role for measles' elimination. Indeed, public education and vaccination led to an estimated 79% decrease in global measles deaths from 2000 to 2015. Nonetheless, the last two years have seen a measles outbreak in several countries, partially due to the anti-vaccination movement. This article aims to present two cases of measles in our hospital and highlight the pressing need for vaccination in order to eradicate a potentially fatal disease.

Key words: measles, Koplik's spots, rash, vaccination

Adv Respir Med. 2019; 87: 63–67

Introduction

Measles represents an acute and potentially fatal, febrile illness, affecting not only children but also adults [1]. Measles virus is transmitted through respiratory droplets or small — particle aerosols sustained in the air for up to 2 hours [2]. An incubation period of the disease lasts approximately 10 days, while its first manifestations include fever along with one of the three 'Cs': cough, coryza, conjunctivitis. Koplik's spots may also appear on the buccal mucosa providing an opportunity to set the diagnosis even before the appearance of rash. Rash typically becomes visible 3–4 days after the onset of fever, initially on the face and behind the ears [1]. Measles could also cause life-threatening complications affecting systems such as respiratory and central nervous system [1]. However, deaths due to measles have significantly declined during the last century, mainly through global vaccination measurements as well as improvements in socio-economic status and health care. Of note, before the introduction of measles vaccination in 1963, an estimated 30 million cases of measles occurred each year leading to more than 2 million deaths [3]. Unfortunately, the past few years, diminishment of public awareness and anti-vaccination movements led to recent outbreaks of diseases thought to be eliminated, including measles [4]. Here, we report two cases of measles-associated pneumonia in adults with incomplete measles vaccination, and highlight the pressing need for vaccination.

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DOI: 10.5603/ARM.a2019.0010
Received: 18.11.2018

ISSN 2451–4934

Case 1

A 42-year-old male, active smoker, immunized against measles with only one shot in childhood, was admitted to our clinic complaining about fever up to 39,3° C during the past seven days, cough, exertional dyspnea and diarrhea. Of note, a skin rash showed up at the face and expanded to the upper arms and trunk 24 hours before admission. The patient also complained about sore throat and right earache.

On admission, his vital signs were normal. Arterial blood gases analysis revealed: $pO_2 = 71$, $pCO_2 = 29$, pH = 7,45 and $HCO_3 = 23$. A macerate skin rash was covering the face, trunk and limbs, whereas Koplik's spots were present at the left buccal mucosa (Fig. 1). The blood tests revealed thrombocytopenia (83 000) and elevated levels of LDH (538 U/L). Chest-x-ray showed a consolidative opacity in the right lung, next to the cardiac figure.

Therapeutic treatment was administered, including broad-spectrum antibiotics (piperacillin/ /tazobactam and moxifloxacin), bronchodilation and oxygen therapy. With regards to skin rash and diarrhea, according to the dermatologist's and internist's advice, preservative treatment was provided. Serological testing for measles and other viruses (Hepatitis B Virus, Hepatitis C Virus, Human Immunodeficiency Virus, Herpes simplex virus, Coxsackie, Echo, Cytomegalovirus, Epstein-BarrVirus) antibodies was performed. Testing revealed elevated titers for measles IgM antibodies, and PCR was positive for virus RNA. While hospitalized, the patient developed severe respiratory failure. Chest computed tomography (CT) demonstrated ground glass opacities in both lungs, centrilobular nodules in the upper lobes, mediastinal lymph nodes and minimum bilateral pleural effusions (Fig. 2). No cardiac effusion was present. Brain CT was normal. Treatment remained unchanged. The patient gradually improved and was discharged twelve days later in good clinical condition, without respiratory failure and with normal blood tests.

Case 2

A 52-year-old female, active smoker (40 pack--years), nonimmunized against measles virus, with a history of osteoporosis, hypertension, hyperlipidemia and gastritis, was admitted to hospital due to pneumonia and severe type I respiratory failure.

The patient mentioned that the symptoms had begun three days ago, with dry cough, fever

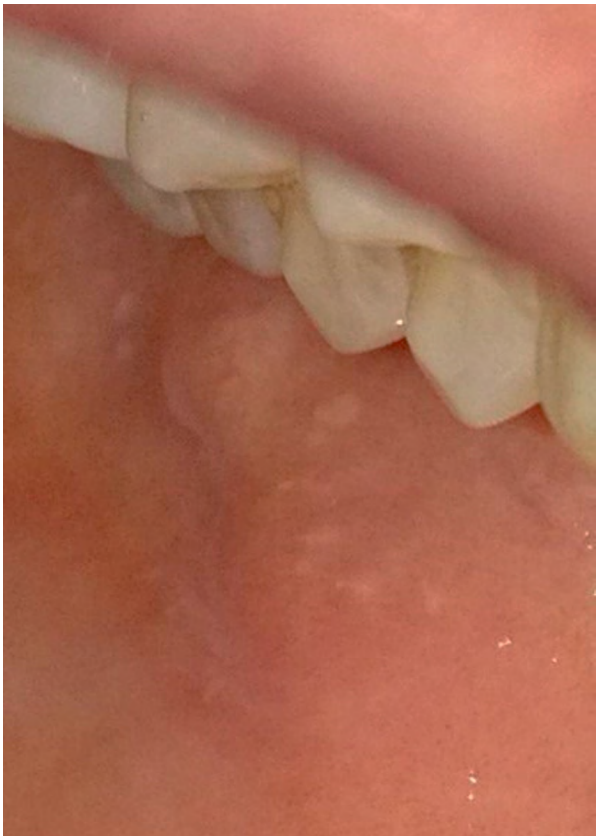

Figure 1. Koplik spots at the left buccal mucosa

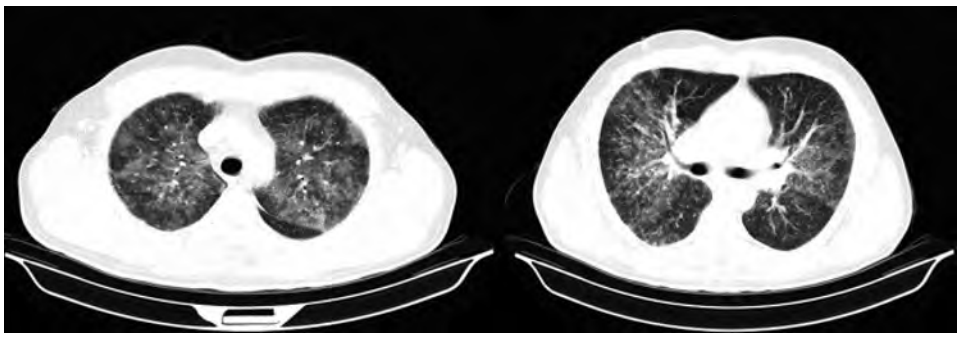

Figure 2. Case 1. Chest CT showing diffuse ground glass opacities in pulmonary parenchyma

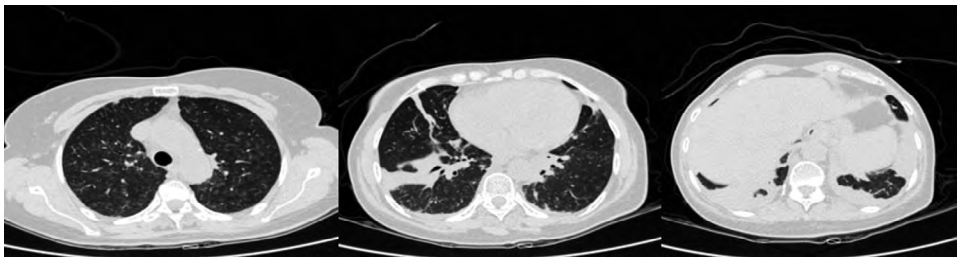

Figure 3. Case 2. Chest CT demonstrating centrilobular nodules, areas of consolidation and atelectasis, as well as bilateral pleural effusion

(40°C) and stomachache. She underwent gastroscopy and the biopsy showed gastritis. Thus, proton-pump inhibitors were prescribed. A general practitioner also examined the patient, ordering cefuroxime. Afterwards, the woman complained about acute abdomen pain, diarrhea and rash, mostly on the face and upper trunk, and she was referred to the emergency department. At the emergency department, the patient had SpO_2 = 90% at FiO_2 40%, 15 breaths per minute, low blood pressure (85/60 mm Hg) and tachycardia (110 beats per minute), as well as an erythematous purulent rash covering the face, trunk and upper limbs. She was immediately resuscitated with crystalloids and treated with oseltamivir and moxifloxacin. The chestx-ray revealed pneumonia bilaterally, while abdominal ultrasound was normal. Chest CT showed consolidation in both lower lobes and middle lobe and centrilobular nodules (Fig. 3). The patient was admitted to the clinic where further blood and pharyngeal tests, including tests for measles and other viruses were undertaken. The woman deteriorated twelve hours after admission and she was intubated and transferred to the Intensive Care Unit. Measles IgM antibodies were isolated and PCR of the pharyngeal smear was positive for virus RNA. The patient recovered and to this day is completely healthy.

Discussion

Measles is a febrile, highly contagious and potentially fatal illness. The Paramyxoviridae virus (genus Morbillivirus) represents one of the most contagious viruses, able to survive for up to 2 hours on fomites, including tabletops and handles. Aerosolized viral particles remain suspended for prolonged periods, and a nonimmunized person can become infected by just walking into a room where an infected individual has recently been. Measles virus is so contagious that an estimated 90% of exposed nonimmunized persons will develop the disease [5].

Prodromal symptoms of cough, runny nose, conjunctivitis, and increasing fever appear after an incubation period of 10 to 12 days. Fever is typically high by the 4th day (39–40.5°C); diarrhea and vomiting may also occur [1]. The characteristic morbilliform rash associated with measles appears about 14 days (range 7–21 days) from initial exposure. The rash begins on the face and spreads downward to the trunk and extremities, lasting for 3 to 7 days and fading in the same directional pattern as it appears. It comes into view initially as discrete red macules that become confluent. Koplik's spots represent 2 to 3 mm bluish-white raised lesions on a red base typically occurring on the posterior buccal mucosa and are pathognomonic to measles. They appear about 2 days prior to the onset of rash and increase in number for about 4 days. Their prevalence in patients with measles ranges between 60% and 70% [6]. The presence of Koplik's spots differentiates measles from similar exanthems such as roseola and rubella. Other symptoms may include abdominal pain, sore throat, mild lymphadenopathy, headache, and iridocyclitis leading to photophobia [7].

Approximately 30% of subjects experience multiple systems complications [8]. Pneumonia is the most common and severe complication, occurring in 3–57% of cases and accounting for most measles-associated morbidity and mortality [5]. It takes two main forms: primary measles virus pneumonia and secondary bacterial/viral pneumonia. The last is associated with immunosuppression caused by the virus itself. Primary measles pneumonia, known as Hecht's giant cell pneumonia, occurs in 3–4% of infected individuals, especially in immunocompromised [9, 10]. Secondary pneumonia is mainly caused by bacterial infections, but viral infections, especially by adenovirus, can occur. It has a later onset and is characterized by sudden exacerbation with symptoms and signs usually beginning 5 to 10 days after the rash [5]. Chest radiographic findings are not disease-specific and include ground glass opacity, consolidation, nodules, micronodules,

and tree-in-bud opacities, interlobular septal thickening, bronchial and/or bronchiolar wall thickening [6]. Atypical measles pneumonia is more severe and presents the patients with lobular or segmental infiltration with hilar lymphadenopathy and frequently pleural effusion [11].

Other complications of the respiratory tract include laryngo-tracheobronchitis (croup) and otitis media [8]. Permanent hearing loss may occur in children who develop otitis as a result of measles. A rare, delayed complication of measles is subacute sclerosing panencephalitis (SSPE), a fatal neurological disease caused by persistence of the virus in the central nervous system. SSPE develops 7 to 10 years after recovery from clinical measles and causes a slow, progressive, demyelination of areas in the brain. The initial signs of SSPE include decreased school performance and behavioral changes. SSPE later progresses to myoclonic seizures and eventually to a vegetative state [7, 12].

Clinical diagnosis of measles is determined by the presence of all of the following: 1) generalized maculopapular rash for 3 days, 2) fever of 38.3 °C, and 3) cough, coryza, or conjunctivitis. Laboratory criteria for diagnosis do not require epidemiologic confirmation and include any of the following: a positive serologic test for measles IgM, documentation of seroconversion by a significant rise in measles IgG level, or identification of measles virus RNA by PCR [7].

Treatment is supportive and includes monitoring and management of fever, dehydration, and other discomforts and complications. Low vitamin A levels are associated with higher rates of complications and increased mortality from measles. Basing on the World Health Organization recommendations, CDC advises treatment with vitamin A for all children with acute measles. Vitamin A should be administered once daily parenterally or for 2 days orally at age-specific doses (50,000 IU for infants < 6 months old; 100,000 IU for infants 6 to 12 months old; 200,000 IU for children 12 months old). A third age-specific dose is recommended 2 to 4 weeks later for children who have clinical signs and symptoms of vitamin A deficiency [9].

Given that measles is highly contagious and potentially fatal, vaccination seems to be crucial. Before the introduction of measles vaccines, the measles virus had been infecting 95–98% of children by the age of 18, and measles was considered an inevitable rite of passage [8]. The measles vaccine was first recommended as a single dose vaccine. However, measles outbreaks among schoolaged children who received one dose of measles vaccine prompted changes in recommendations from a single-dose vaccine to two doses of measles-containing vaccine, preferably Measles-Mumps-Rubella (MMR) vaccine [13]. In 2005, a combined measles, mumps, rubella, and varicella vaccine was licensed as the quadrivalent MMRV [14]. Both contain the same Edmonston-Enders measles vaccine and convey equal immunity against measles. Vaccination with either MMR or MMRV causes a mild infection. The resulting efficacy is 93% to 95% after 1 immunization and 98% to 99% after two doses. Secondary vaccine failure/waning immunity is rare. MMR and MMRV are each licensed for use in infants older than 12 months. MMR may be administered to older adolescents and adults; however, MMRV is only approved up to the age of 12 [14]. Vaccination against measles is not recommended prior to 12 months of age due to poor immune response to the vaccine that may be at least partly owing to interference from circulating maternal antibodies. In outbreak conditions or before international travel, one dose of MMR vaccine may be given to infants prior to travel or within 72 hours of exposure or potential exposure. Any dose of the measles vaccine given before 12 months of age does not count as part of the two-dose series [14].

Despite these recommendations, parental concerns about vaccine safety issues, including a debunked-claim of a connection between vaccines and autism, have led to the anti-vaccination movement. However, there is evidence that MMR does not increase the risk of autism even in high-risk children [15]. On the contrary, there is an urgent need for vaccination, as the virus causes life-threatening complications and is highly contagious. Measles presents even higher basic reproductive numbers for a directly transmitted pathogen than smallpox or influenza and thus it is estimated that there is a need of 89-94% levels of population immunity to achieve significant measles elimination [1]. Increased public awareness and vaccination are indispensable so as to avoid new measles outbreaks.

Conclusion

Measles represents an acute and potentially fatal, febrile illness, affecting not only children but also adults. Vaccination and improvement of health services led to significant reductions in deaths due to measles during the last century. However, the last years have seen the emergence of an anti-vaccination movement. This has led

to measles outbreaks and to the re-emergence of life-threatening complications. Thus, there is a pressing need for public education to increase disease awareness and highlight the importance of vaccination. Measles presents high basic reproductive numbers for a directly transmitted pathogen and thus it is estimated that population immunity should reach levels above 90% to achieve significant measles elimination. It's in clinician's hands to reverse this anti-vaccination movement. Further reports on new measles' cases are needed.

Conflict of interest

The authors declare no conflict of interest.

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