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Measles Outbreak in Pediatric Oncology Patients at Hue Central Hospital

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Abstract

AIM: Measles outbreak in the immunocompromised population is a big challenge to interrupt endemic transmission. This study aimed to investigate of measles in pediatric oncology patients and find the reason behind the outbreak.

METHODS: A descriptive study was conducted on 11 pediatric oncology patients with measles. We collected demographic, epidemiological, and clinical data. Most of suspected measles cases were done measles immunoglobulin M test and clinical data were followed up and analyzed by SPSS.

RESULTS: From April 20, 2018, to July 10, 2019, a total of 11 patients with malignancies were notified to develop measles in Hue. Of these 11 patients with the median age of 4.0 years (range: 1–9 years), two patients had not received any dose of measles vaccine, five patients received two doses, and four patients had received 1 dose of measles vaccine; all patients had fever with the median fever of 39°C (range: 38.5–39.5), the median fever duration was 7 days. All patients had cough and rash, three patients had pneumonia complication and two patients had elevated liver transaminase levels. All patients had hospital visits or were hospitalized before measles onset, with the median time: 10 days (range: 7–24 days); all patients were likely to expose each other. All 11 patients recovered.

CONCLUSIONS: The measles outbreak was occurred among children with cancer, especially for children without prior measles vaccine or without two prior doses. Moreover, even children received two prior dose vaccine, their immunocompromised status caused them to be infected. There was not a different area for outpatient and inpatient in the hospital, so measles transmission occurred.

Introduction

Measles is a viral infection that starts in the respiratory system. It is a highly contagious, serious disease and can be spread by direct contact, droplets, or airborne transmission. Measles symptoms appear 7–14 days after contact with the virus and typically include high fever, cough, coryza, and conjunctivitis as well as a characteristic rash. Measles still remains a significant cause of death worldwide, despite the availability of a safe, effective vaccine [1].

There were about 110,000 global deaths related to measles in 2017, most of them in children under the age of 5, according to the World Health Organization source.

In Vietnam, there were 1,177 confirmed measles cases in 2018, twice as many cases as in 2017. Most of the measles cases related to the lack of vaccination due to parents deciding to delay vaccination of their children. In late 2018, the Ministry of Health launched an additional measles-rubella vaccination campaign for 4.2 million children aged between 1 and 5 in vulnerable areas in 57 cities and provinces [2]. UNICEF called on parents to make an extra effort to consult health official to ensure that their children's immunization status is up to date to protect their children against the disease. UNICEF also advocated health authorities to sustain investment to build trust among the population and to focus on reaching the poorest, most marginalized communities, including internal migrant populations. Unexpected, measles outbreak occurred in immunocompromised children in some hospitals all over the world [3]. The immunocompromised children are not only at high risk of developing the severe vaccine-preventable infectious disease but may also serve as a reservoir for the transmission of pathogens in the susceptible population. In this study, we described the epidemiological features, clinical manifestation, and outcomes of 11 children with malignancies.

Patient and Method

Patients

All 11 measles children with malignancies were treated at Pediatric Center, Hue Central Hospital, Vietnam. Measles case was diagnosed based on both clinical manifestations and laboratory confirmation with the presence of measles-specific

immunoglobulin M (IgM) in serum, or possibly diagnosed based on clinical manifestations and measles endemic.

The present study was approved by the Hue Central Hospital Review Board and conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Laboratory investigations

For all patients, the serum samples were collected at the time of clinically suspected of measle and these samples were delivered to the Department of Biochemistry of Hue Central Hospital. IgM antibody against measles virus was tested by enzyme-linked immunosorbent assays.

Furthermore, during the time patients were suffered from measles in hospital, all of the patients developed bacterial infection, especially respiratory infection, so each patient received a comprehensive laboratory investigation, including complete peripheral blood cell count, C-reactive protein (CRP), and chest X-ray.

Data collection

Data were prospectively collected which were based on the medical record during hospitalization, and data analysis was performed anonymously. We collected demographic features, vaccination status, clinical symptoms and signs, laboratory findings, treatment, and outcome.

Pneumonia was diagnosed based on both respiratory symptoms and chest X-ray images; the magnitude of aminotransferase alteration was defined based on the criteria [4]; neutropenia was diagnosed when the absolute neutrophils count (ANC) of peripheral blood was <0.5 × 109/l.

Statistical analysis

Data were analyzed with SPSS v.18.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequency and continuous variable was computed for a median and a range.

Results

Epidemiology characteristic

From April 20 to July 10, in 2019, a total of 11 oncology children were diagnosed measles with the median age of 4.0 years (range: 1–9 years), of these, there were 7 girls and 4 female/male = 1.74/1. The first case was a 13-month-old boy who was undergoing chemotherapy and irradiation and did not receive measles vaccine since he developed malignancy at the age of 8 months. There were seven patients appeared measles symptoms when they were in hospital, and they had been possibly exposed to each other. The other four measles children also visited the hospital for medical care 7–21 days before measles onset. Most of the patients (10/11) were admitted hospital and transferred to the pediatric infection department when they were suspected measles cases.

Measles vaccination status

Measles vaccination status was available in nine patients; two patients had not received any previous measles vaccine. Among the 9 vaccinated children, 4 cases had received one dose of vaccine and 5 cases had received two doses of vaccine. The interval between vaccination and onset of measles was more than 6 months.

Clinical characteristics

All of 11 patients had a fever with the median fever of 39°C (range: 38.5–39.5), the median fever duration was 7 days (range 3–13 days); 11 patients had cough; nine patients had coryza; seven patients had conjunctivitis; two patients had Koplik's spot; and 11 patients had rash (Table 1). The median time to appear rash since onset was 4 days. Most of the patients, the appearance and sequence of rash were typical.

Table 1: Symptoms of measles

Clinical signs	Frequency
Fever	11
Cough	11
Rash	11
Conjunctivitis	7
Coryza	9
Koplik's spot	2

The types of underlying diseases included acute lymphoblastic leukemia in seven patients, neuroblastoma in one patient, and Wilms tumor in three patients. Nine patients developed measles when patients were ongoing chemotherapy, irradiation, or just completion of chemotherapy, and the remaining two patients did not receive chemotherapy during recent 1 month.

Of the 11 patients, there was one outpatient with very typical clinical manifestation; we did not check IgM antibody, five patients were positive for measles-specific IgM antibody. One patient had neutropenia during the illness. The median WBC and ANC were

2.08 × 10^9/l and 1.27 × 10^9/l, respectively. The median CRP was 12.2 mg/dl (Table 2).

Table 2: The result of blood tests

Laboratory investigations	Median	Range
CRP	12.2 mg/dl	2.2–171.0 mg/dl
WBC	2.08×10^9/l	0.67–6.04×10^9/l
Neutrophile	1.27×10^9/l	0.07–3.51×109/l
Hb	10.0 g/dl	7.4–12.2 g/dl
PLT	150×10^9/l	100–460×109/l

CRP: C-reactive protein, WBC: White blood cell, Hb: Hemoglobin, PLT: Platelet.

Treatment and outcomes

Of the 11 patients, three patients had pneumonia, eight patients had bronchitis, one patient had diarrhea, and two patients had marked increase in aminotransferase level. Only one patient had neutropenia, and ANC recovered slowly due to she got pneumonia and had to use antibiotics combined with antifungal. All of the patients used antibiotics, in which there were two patients who received oral antibiotics. All of the patients recovered.

Discussion

In our study reported the measles outbreak in pediatric patients with malignancies during the measles epidemic in Vietnam. Similarly, Ge described the measles outbreak in pediatric patients with malignancies and post-HSCT during the measles epidemic in China [3], Nakano and Kaplan described clinical features of measles in immunocompromised children [5], [6]. Our first case was the same first case in Ge's research: Both cases were undergoing chemotherapy and did not receive the measles vaccine since they developed malignancy at a very young age before the age to receive the measles vaccine [3]. The rate of vaccinated patients (1–2 doses of measles) was 9/11, which was smaller than the rate of vaccinated patients in Ge's research: 95.6%. This was a factor make our patients to be easier to expose measles. Chemotherapy-induced immune suppression may result in significant loss of pre-existing protective antibodies against vaccine antigens due to long-term impairment of humoral immunity in cancer patients and other immunocompromised populations [7], [8], [9]. At present, it is recommended that cancer patients could be immunized or reimmunized at appropriate intervals to reduce the risk of vaccine-preventable infection [10], [11]. However, live vaccines administrations are usually contraindicated to cancer patients during chemotherapy and are recommended to be administered to cancer patients 3–6 months after cancer chemotherapy. Hence, it is difficult to balance the risk and benefit of revaccination for patients during chemotherapy in an outbreak setting and no existing evidence can be used to guide this practice [10], [11]. The immunocompromised children are not only at high risk of developing severe vaccine-preventable in infectious disease but may also serve as a reservoir for the transmission of pathogens in susceptible populations. This can explain the transmission in our patients; at the beginning, there was one patient with measles, then there were 10 other patients exposed measles. Similarly, Ge showed that 20 patients were likely to be exposed to each other [3].

The median age in our patients was 4 years old (range: 1–8 years) which was smaller in Ge's research: The median age was 5.5 years (range: 11 months–14 years) [3]. Half of our patients were positive for measles-specific IgM antibody which was smaller than that in Ge's research (95.7%) [3]. It can be explained the time we did the test too earlier, at the early stage of appearing rash, and we did not do the second measles-specific IgM test again if the first time test was negative. Some previous literature documented that the measles-specific IgM response may be either short lived or absent in vaccinated person [12], [13]. However, we could probably diagnose measles based on clinical symptoms and measles endemic. All of our patients had rash, fever, and cough; most patients had coryza, conjunctivitis, and a small patient had Koplik's spot. Similarly, Ge showed that 43.5% of breakthrough measles in vaccinated immunocompromised children did not present Koplik's spot [3]. All of our patients recovered without any death. Contrast to us, Ge showed 21.7% of patient died [3], Nakano reported one patient died [6]. It could be explained that in our research, these patients did not receive intensive chemotherapy before the measles attack and we followed up the patients carefully; in Ge's research, those fatal patients received more prolonged and intensive chemotherapy for relapsed leukemia before measles attack.

Conclusions

The measles outbreak was occurred among children with cancer, especially for children without prior measles vaccine or without two prior doses. Moreover, even children received two prior dose vaccine, their immunocompromised status caused them to be infected. There was not a different area for outpatient and inpatient in the hospital, so measles transmission occurred. Following this measles outbreak, a designated outpatient area was established to limit inpatient exposures and hospital transmission.

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