MEASLES OUTBREAK IN PEDIATRIC ONCOLOGY PATIENTS AT HUE CENTRAL HOSPITAL, VIETNAM

Nguyen Thị Kim Hoa[1], Tran Kiem Hao[1], Tran Thi Kim Cuc[1],
Truong Thị Kim Yen[1], Nguyen Hoang Son[1]

ABSTRACT

***Background**: Measles outbreaks in 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 and prospective study on 11 paediatric oncology patients with measles. We collected demographic, epidemiological, and clinical data. Most of suspected measles cases were done measles IgM test and clinical data were followed up and analysed by Medcalc software.*

***Results**: From April 20 to July 10 in 2019, a total of 11 patients with malignancies were notified to develop measles in Hue. Of these 11 patient with the median age of 4.0 years (range: 1 year to 9 years), 2 (18.2%) hadn't received any dose of measles vaccine, 5 (45.5%) received 2 doses and 4 (36.4%) had received 1 dose of measles vaccine; all patients had fever with the median fever of 39 degrees Celsius (range: 38.5 – 39.5), the median fever duration was 7 days, 100% had cough and rash, 3 (27.3%) had pneumonia complication, 2 (18.2%) had elevated liver transaminase level. 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 exposed each other. 100% patient recovered.*

***Conclusions**: Children with cancer is very easy to exposed measles to each other. Getting vaccinated is the best way to prevent measles, and improved infection control was crititcal for the prevention of measles in malignancy patients.*

***Key words**: Children; Measles; Oncology.*

I. 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 airbone transmission. Measles symptoms appear 7 to 14 days after contact with the virus and typically include high fever, cough, coryza, and conjunctivitis as well as characteristic rash. Measles still remains a significant cause of death worldwide, despite the availability of safe, effective vaccine[3].

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 was 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

1. Hue Central Hospital

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- Corresponding author: Nguyen Thi Kim Hoa
- Email: kimhoa.fmi@gmail.com; Tel: 0935645836

57 cities and provinces. 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[4], . The immunocompromised children are not only at high-risk of developing severe vaccine-preventable infectious disease but may also serve as a reservoir for transmission of pathogens in susceptible population. In this study, we described the epidemiological features, clinical manifestation, and outcomes of 11 children with malignancises.

II. PATIENT AND METHOD

2.1. 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 IgM in serum, or possibly diagnosed based on clinical manifestations and meales endemic.

Pneumonia was diagnosed based on both respiratory symptoms and chest X-ray images; the magnitude of amiotransferase alteration was defined based on the criteria[5]; Neutropenia was diagnosed when the absolute neutrophils count (ANC) of peripheral blood was <0.5x109/l

2.2. Methods

A prospective and descriptive study. 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.

Statistical analysis: Data were analyzed using Medcalc program.

III. RESULTS

3.1. Epidemiology characteristic

From April 20 to July 10 in 2019, a total of 11 children at were diagnosed measles with oncology center the median age was 4.0 years (range: 1 year to 9 years), of these there were 7 girls and 4 boys the ratio female/male was female/male = 1.74/1. The first case was a 13 month old boy who was undergoing chemotherapy and irradiation and had not received measles vaccine since he developed malignancy at the age of 8 months. 7 patients (63.6%) appeared measle 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 patients (10/11, 90.9%) were admitted hospital and transferred to Pediatric infection department when they were suspected measles case.

3.2. Measles vaccination status

Measles vaccination status was available in 9 patients (81.8%), 2 patients hadn't received any previous measle vaccine. Among the 9 vaccinated children: 4 (4/11, 36.4%) had received one dose of vaccine, 5 (5/11, 45.4%) had received 2 doses of vaccine. The interval between vaccination and onset of measles was more than 6 months.

3.3. Clinical characteristics

All of 11 patients (100%) had fever with the median fever of 39 degrees Celsius (range: 38.5 – 39.5), the median fever duration was 7 days (range 3-13 days); 11 (100%) had cough; 9 (81.8%) had coryza; 7 (63.6%) had conjunctivitis; 2 (18.2%) had Koplik's spot; 11 (100%) had rash (table 1). The median time to appear rash since onset was 4 days. Most of patients, the appearance and sequence of rash were typical.

The types of underlying diseases included acute lymphoblastic leukemia in 7 (63.6%) patients, neuroblastoma in one patient (1.1%), and Wilms tumor in three patients (27.3%). Nine (81.8%) patients developed measles when patients were ongoing chemotherapy, irradiation or just completion of chemotherapy, and the remainning

two patients did not receive chemotherapy during recent 1 month.

Of the 11 patients, there was one outpatient with very typical clinical manifestation, we didn't check IgM antibody, 5 (5/10, 50%) were possitive for measles-specific IgM antibody. 1 (9.09%) patient had neutropenia during the illness. The mean WBC and ANC were 2.97 ± 1.69 x $10^9/_1$ and 1.55 ± 0.93x$10^9/_1$ respectively. The mean CRP was 31.6 ± 48.4 mg/dl (table 2).

Table 1: Symptoms of measles

Variables	Quantity	%
Fever	11	100
Cough	11	100
Rash	11	100
Conjunctivitis	7	63.6
Coryza	9	81.8
Koplik's spot	2	18.2

Table 2: The result of blood tests

Variables	Mean	Range
CRP	31.6 ± 48.4 mg/dl	2.2 – 171 mg/dl
WBC	2.97 ± 1.69 x $10^9/_1$	0.67 – 6.04x $10^9/_1$
Neutrophile	1.55 ± 0.93 x $10^9/_1$	0.07 – 3.51x $10^9/_1$
Hb	10.08 ± 1.39 g/dl	7.4 – 12.2 g/dl
PLT	215 ± 112 x $10^9/_1$	100 – 460 x $10^9/_1$

3.4. Treatment and outcomes

Of the 11 patients, 3 patients (27.3%) had pneumonia, 8 patients (72.7%) had bronchitis, 1 patient (9.09%) had diarrhea and two patients (18.2%) had marked increase in aminotransferase level. Only one patient (9.09%) had neutropenia, and ANC recovered slowly due to she got pneumonia and had to use antibiotics combined with antifungal. All of patients used antibiotics, in which there were 2 patients (18.2%) received oral antibiotics. All of patients recovered.

IV. 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 [4], Nakano and Kaplan described clinical features of measles in immunocompromised children[8], [9]. Our first case was the same first case in Ge's research: both cases was undergoing chemotherapy and did not receive measles vaccine since they developed malignancy at the very young age before the age to receive measles vaccine [4]. The rate of vaccinated patients (1-2 doses of measles) was 81.8%, 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 preexisting protective antibodies against vaccine antigens due to long-term impairment of humoral immunity in cancer patients, and other immunocompromised population [1], [11], [12]. Currently, it is recommended that cancer patients could be immunized or reimmunized at appropriate intervals to reduce the risk of vaccine-preventable infection [2], [10]. But live vaccines administrations are usually contraindicated to cancer patients during chemotherapy and are recommanded to be administered to cancer patients 3-6 months after cancer chemotherapy. So, it is difficult to balance the risk and benefit of re-vaccination for patients during

chemotherapy in an outbreak setting, and no existing evidence can be used to guide this practice [2], [10]. 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 transmission of pathogens in susceptible population. This can explain the transmission in our patients, at the beginning, there was one patient with measles, then 10 other patients were exposed with measles. Similarly, Ge showed 20 patients were likely to be exposed to each other [4].

The median age in our patients was 4 years old (range: 1 year to 8 years) which was smaller in Ge's research: the median age was 5.5 years (range: 11 months to 14 years) [4]. The percentage of our patients were possitive for measles-specific IgM antibody in serum were 50%, which was smaller than the percentage in Ge's research: 95.7% patients were possitive for measles-specific IgM antibody [4]. It can be explained the time we did the test too earlier, at the early stage of appearing rash, and we didn't do the second measles-specific IgM test again if the first time test was negative. In some previous literature documented that the measles-specific IgM response maybe either short lived or absent in vaccinated person [6], [7]. However, we could probably diagnose measles based on clinical symptoms and measles endemic. All of our patients had rash, fever, cough and 81.8% had coryza, 63.6% had conjunctivitis and only 18.2% had Koplik's spot. Similarly, Ge showed 43.5% of breakthrough measles in vaccinated immunocompromised children did not present Koplik's spot [4]. All of our patient recovered without any death. Contrast to us, Ge showed 21.7% patient died [4], Nakano reported one patient died [9]. It could be explain that in our research, these pateints did not receive intensive chemotherapy before measles attacked 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 attacked.

V. CONCLUSION

Children with cancer are not only at high risk of developing severe vaccine-preventable infectious disease but may also serve a reservoir for transmission of pathogens in susceptible population. So, getting vaccinated is the best way to prevent measles and improving hospital infection control is very important to protect immunocompromised patients and avoid nosocomial transmission of measles.

REFERENCES

1. Bochennek K, Allwinn R, Langer R, et al. (2014), "Differential loss of humoral immunity against measles, mumps, rubella and varicella-zoster virus in children treated for cancer", Vaccine, 32(27): p. 3357-61.
2. Cesaro S, Giacchino M, Fioredda F, et al. (2014), "Guidelines on vaccinations in paediatric haematology and oncology patients", Biomed Res Int, 2014: p. 707691.
3. Fadic RR and Repetto DG (2019), "Measles: Historical background and current situation", Rev Chil Pediatr, 90(3): p. 253-259.
4. Ge YL, Zhai XW, Zhu YF, et al. (2017), "Measles Outbreak in Pediatric Hematology and Oncology Patients in Shanghai, 2015", Chin Med J (Engl), 130(11): p. 1320-1326.
5. Giannini EG, Testa R, and Savarino V (2005), "Liver enzyme alteration: a guide for clinicians", CMAJ, 172(3): p. 367-79.
6. Hickman CJ, Hyde TB, Sowers SB, et al. (2011), "Laboratory characterization of measles virus infection in previously vaccinated and unvaccinated individuals", J Infect Dis, 204 Suppl 1: p. S549-58.
7. Hyde TB, Nandy R, Hickman CJ, et al. (2009), "Laboratory confirmation of measles in elimination settings: experience from the Republic of the Marshall Islands, 2003", Bull World Health Organ, 87(2): p. 93-8.
8. Kaplan LJ, Daum RS, Smaron M, et al. (1992),

"Severe measles in immunocompromised patients", JAMA, 267(9): p. 1237-41.

9. Nakano T, Shimono Y, Sugiyama K, et al. (1996), "Clinical features of measles in immunocompromised children", Acta Paediatr Jpn, 38(3): p. 212-7.
10. Rubin LG, Levin MJ, Ljungman P, et al. (2014), "2013 IDSA clinical practice guideline for vaccination of the immunocompromised host", Clin Infect Dis, 58(3): p. 309-18.
11. van Tilburg CM, Sanders EA, Rovers MM, et al. (2006), "Loss of antibodies and response to (re-) vaccination in children after treatment for acute lymphocytic leukemia: a systematic review", Leukemia, 20(10): p. 1717-22.
12. Zignol M, Peracchi M, Tridello G, et al. (2004), "Assessment of humoral immunity to poliomyelitis, tetanus, hepatitis B, measles, rubella, and mumps in children after chemotherapy", Cancer, 101(3): p. 635-41.