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Measles in Taiwan, 1990-2008

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Abstract

Measles is a sporadic infectious disease in Taiwan. The measles vaccine was introduced to Taiwan in 1968 and universal vaccination to infants 9 months and 15 months old started in 1978. Over 1,000 confirmed cases were reported in both 1988 and 1989 when measles was first classified as a notifiable disease in 1987. In 1991, Taiwan implemented an eradication project for polio, congenital rubella syndrome, measles and neonatal tetanus, and universal vaccination of MMR vaccine in 15-month-old children in 1992. Since then, less than 50 confirmed measles cases were reported annually. Furthermore, less than 10 confirmed cases were reported in recent 10 years, indicating good control of measles after implementing the eradication project and vaccine policy. The risk factors for measles infection included gender, age, residential environment, immunodeficiency, and vitamin A deficiency. Severe complication may occur in people less than 5 years old or above 20 years old without proper medical treatment, especially patients with immunodeficiency, malnutrition, vitamin A deficiency and no vaccination. Most of the confirmed measles cases were children less than 1 year old and the reason was probably from 3-34% [1]. The number of confirmed due to infection prior to vaccination. Counties with high measles incidence rate were also related with outbreaks or cluster infection. In recent years, several outbreaks or community clusters caused by imported measles cases were found. The measles vaccination rate was over 95% in the recent years and the opportunity of overall outbreak of measles infection was low. However, community infection event may be induced by delayed vaccine inoculation, incomplete inoculation or children younger than the inoculation age. It is important to control the community infection event caused by imported cases in order to eliminate measles infection.

Keyword：measles, vaccination, imported, cluster

Introduction

Measles is a highly transmissible viral disease which usually occurs in spring and summer. Before vaccine was developed, people under 18 years old were the most susceptible population in which 95-98% had history of infection. The average age of infection is about 4 years old. The mortality varies geographically

INSIDE

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measles cases and the associated mortality has dramatically decreased worldwide since the introduction of measles vaccine in 1963. Currently, most confirmed measles cases were found in the developing countries, especially in Africa.

Measles is a vaccine-preventable disease. In 1989 World Health Assembly, the issue of measles elimination was raised. The goal of this issue was to decrease 90% of morbidity and 95% of mortality. Similar issue was also brought up in 1990 World Summit of Children Right. It was recommended that measles vaccination rate should reach 90% or above. In 1996, WHO proposed measles elimination project and set 2005-2010 to be the years of elimination. Four out of six regions of the world (America, Europe, Mediterranean and Western Pacific) have set the elimination year; for the other two regions (Africa and South Eastern Asia), the main goal is to decrease the mortality of this disease [2]. In Taiwan, measles vaccine was introduced in 1968 and universal vaccination to 9-month and 15-month old children started in 1978. The project for elimination of polio, congenital rubella syndrome ,measles and neonatal tetanus started in 1991 and four stages of this project had been accomplished. According to communicable disease statistics, the annual confirmed cases were mostly under 10 in the last 10 years, indicating that measles was well controlled in Taiwan after elimination project was launched.

However, high measles morbidity in nearby countries, coupled with convenient international travel, foreign laborers and brides, and trade relations with China, have caused imported measles cases to Taiwan and induced local epidemic events in recent years. Measles vaccination rate in Taiwan was maintained at 95% or above and the risk of overall epidemic event was low; but local community epidemic events were still noted due to some children having no or uncompleted inoculation program. It is important to control imported cases to prevent local epidemic event.

The Disease

Measles virus (Paramyxoviridae, genus *Morbillivirus*) is a RNA virus and human is the only host and reservoir. Transmission is usually through infectious droplet or nasal/pharyngeal secretion. Incubation period is 7-18 days and the disease is most infectious two days before and after vesicles formed. Around 75-90% of susceptible contacts become measles patients.

After incubation, the patient may show early clinical symptoms such as fever, cough, coryza, and conjunctivitis. These symptoms persist and become most severe until vesicles are formed. Koplik's spots are usually found on oral mucosa 2-3 days before vesicle formation and disappear after vesicles are formed. The vesicles are initially found on cheeks and behind ears, and then extend to extremities and trunk. They may last for 3-7 days. Other symptoms, such as fever, may sustain until 2-3

days after vesicle formation while cough may last for 10 days. It is difficult to diagnose measles because the clinical symptoms and signs are similar to other respiratory infectious diseases. Thus, community infection events are usually caused by the target patients continuing attending schools or other activities without awareness of the infection. These events may also occur in the medical facilities when the infected patients go to the hospital and transmit this disease to other patients in the outpatient service or emergency room [3-4].

People with no measles infection history or no vaccination have higher risk of infection .Ninety of vaccinated individuals have immunity to measles. However, some people may reveal mild or atypical clinical signs and symptoms of measles when they are infected. Children or infant with residual maternal measles antibody may also have subclinical measles symptoms when infected. It is still unknown that these people with atypical clinical signs will transmit virus to other people. Generally, patients with natural infection have life-long immunity [5].

Severe complications may arise, usually found in the age group of less than 5 years old and 20 years old and above, if there is no proper and promptly treatment after infection. Complications are more prevalent in people with immunodeficiency, malnutrition, vitamin A deficiency, and no vaccination. Diarrhea, pneumonia and encephalitis are the most common complications in gastrointestinal, respiratory and neurologic system, respectively. Pneumonia and encephalitis are the most common causes of death for measles. Pneumonia usually develops within two weeks after measles infection. It may be caused by measles virus only, in combination with adenovirus or herpes simplex virus, or secondary bacterial infection. In adults, 49 to 57 percent of patients may complicate pneumonia [5]. Diarrhea is mainly found in patients five years and younger or 30 years and older. Typical measles-related diarrhea usually occurs before vesicle formation. In a research in USA, 8% of measles patients in 1987～2000 had diarrhea. This complication was found in 30-70% of hospitalized patients [6]. Patients with encephalitis often have poor prognosis. In developing countries, measles patients without prompt treatment usually had complication of vision loss and poor prognosis. This situation is most commonly seen in immunocompromised patients, such as human immunodeficiency virus (HIV) infection or leukemia. Encephalitis symptoms, such as changes in consciousness or delirium, may be found within 6 months after measles virus infection and over 80% of these patients may die within a few weeks after these symptoms occurred [7-8].

Risk factors

A. Gender and age: research indicated that the mortality of male patients was higher than female patients. However, a study conducted between 1950 and 1989 indicated that the morbidity of female was slightly higher than male. Recent studies indicate that the complication rate was similar in both male and female patients, but complications may be more severe in pregnant women [9-11]. The age group of 5 years old (and under) and 20 years old (and above) have higher incidence in measles morbidity and complication, and severe complications are usually found in adult patients.
B. Living environment: a study from West

Africa and Europe discovered that higher mortality was found in children infected by household members compared with those from other sources [12-13]. A research in Bangladesh indicated that children living in houses smaller than 18.6 square meters were 2.6 times more likely to contract measles than those living in houses bigger than 37 square meters. However, no such relationship between measles morbidity and size of house was found in USA [14-15].

C. Immunodeficiency: Severe measles complications may be more easily found in children with congenital T lymphocyte insufficiency or undergoing bone marrow transplantation or chemotherapy. Children or infants born to HIV positive mothers who receive no antiviral treatment may have insufficient post-vaccination immune response. Moreover, measles antibodies induced by vaccines decrease more rapidly. In 1989-1991, 50-60% of fatal children patients were HIV positive in New York and New Jersey [16-17].

D. Vitamin A deficiency: higher mortality and complication rate (diarrhea, pneumonia) was noted in children with vitamin A deficiency. In countries with high measles incidence, vitamin A supplementation for 2 days (200,000 IU for children 1 year old and above; 100,000 IU for less than 1 year old) for susceptible children may decrease morbidity by 50%. WHO recommended vitamin A therapy for measles-infected children. Similar recommendation for hospitalized patients less than 2 years old was also given by American Academy of Pediatricians [18-19].

Vaccine efficacy

Before measles vaccine was developed, five million children died due to measles infection annually (based on 2-3% mortality). The medical expenses for measles patient reached 2.2 trillion US dollars in USA and other indirect expenses were 1.6 trillion US dollars [20]. A research conducted in Bangladesh indicated that measles vaccine reduced 36% of mortality and 57% of fatal cases caused by diarrhea, respiratory infection or malnutrition [21]. Measles vaccine was introduced to Taiwan in 1968. Initially, vaccination was voluntary. Universal vaccination was initiated in Taipei City in 1977 with good success. Then, it was expanded to all 9-month-old and 15-month-old children (1 dose of vaccine each) in 1978. This policy was adjusted to apply 1 dose only at 12 months old in January, 1988. But this measure was re-adjusted to the former procedure in May due to significant increase in measles patients. In 1992, MMR vaccine was first administered to all 15-month-old children, and the efficacy reached over 95%. This vaccine was then introduced to elementary school and junior high school students as well as pre-school children in 1992-1994. MMR vaccines were also given to all incoming military recruits from July 1995 to June 1998. Routine vaccination of second dose of MMR was given to first-grade elementary school students starting 2001. Voluntary MMR vaccination to child-bearing-age women started in July of the same year. From December 2001 to March 2004, catch-up MMR vaccination was given to all students 5th grade and under. In January 2006, stand-alone measles vaccine was discontinued and replaced by MMR. Vaccination schedule for first dose of MMR was changed from 12-month-old to 15-month-old children instead of at 15-month-old.

Measles was first classified as a reportable

disease in 1987, and over 1000 confirmed measles cases were reported in both 1988 and 1989. Since then, less than 50 cases per year were reported. The Department of Health initiated the project for elimination of polio, neonatal tetanus, congenital rubella syndrome and measles in 1991. The confirmed measles case number was maintained at 10-20 cases per year in the past 10 years, indicating that measles infection has been well controlled after this project was launched.

Laboratory diagnosis

The definition of reported and confirmed cases of measles is as follows:

A. Reported cases: 3 conditions should be satisfied: 1. Systemic cutaneous vesicles for 3 or more days; 2. Fever (ear or rectal temperature) ≧38℃; 3. One of the following signs: cough, nasal discharge or conjunctivitis (photophobia, ocular discharge or redden eye).

B. Confirmed cases:

1. Laboratory examination confirmed;

2. No laboratory confirmation, but fitting clinical definition and epidemiologically linked to confirmed cases.

Laboratory confirmation: positive result if one of 3 following conditions is satisfied: 1. IgM for measles is positive; 2. Positive result in PCR or viral isolation for measles in throat swab, urine or whole blood samples; 3. Serum IgG antibody becomes positive or increases significantly from acute phase to convalescence phase.

Serum sample should be collected between 3 to 28 days after cutaneous vesicle formation and another serum sample is collected 2 to 4 weeks later. Four times increase in IgG or IgM antibody is the criteria for diagnosis. The existence of IgM antibody indicates recent infection of this disease, but recent vaccination should also be taken into consideration. IgM negative but IgG positive is interpreted as previous infection. If both IgM and IgG are negative, it could be either negative or early stage of infection; thus, second serum sample is necessary for further examination 2 to 4 weeks later.

Urine and nasopharyngeal swab samples for viral isolation should be collected within 7 days after cutaneous vesicle formation. Negative result in viral isolation indicates no virus in the samples, but the timing of sample collection and methods of sample delivery should also be taken into consideration for interpretation. Positive results confirm recent measles infection.

Epidemiologic analysis

Measles is a sporadic infectious disease in Taiwan due to over 95% vaccination rate. Based on the Department of Health records, there were at least 1,000 confirmed measles cases each year between 1985 and 1990 (2,219 cases in 1985, 1,386 cases in 1988, 1,060 cases in 1989). Most of these patients were pre-school age children or primary school students [22]. Similar measles epidemic events were also noted in USA during the same period. Many epidemic events were found in schools and the patients were mostly unvaccinated. The confirmed measles cases decreased significantly to less than 100 since 1990, except in 1992 (over 200 cases). In 1992, universal MMR vaccination was initiated in 15-month-old children. Although the number of confirmed cases was not significantly reduced in recent 10 years, the number of cases was less than 15 cases per year, and most cases were found in infants less than 9 month old who did not receive vaccination.

Records of reported and confirmed case

According to the database of notifiable infectious disease in CDC, Taiwan from 1990 to 2008 , 1225 cases were reported, and 135 cases were confirmed (11%) with no mortality. The confirmed case number was shown in Figure 1.

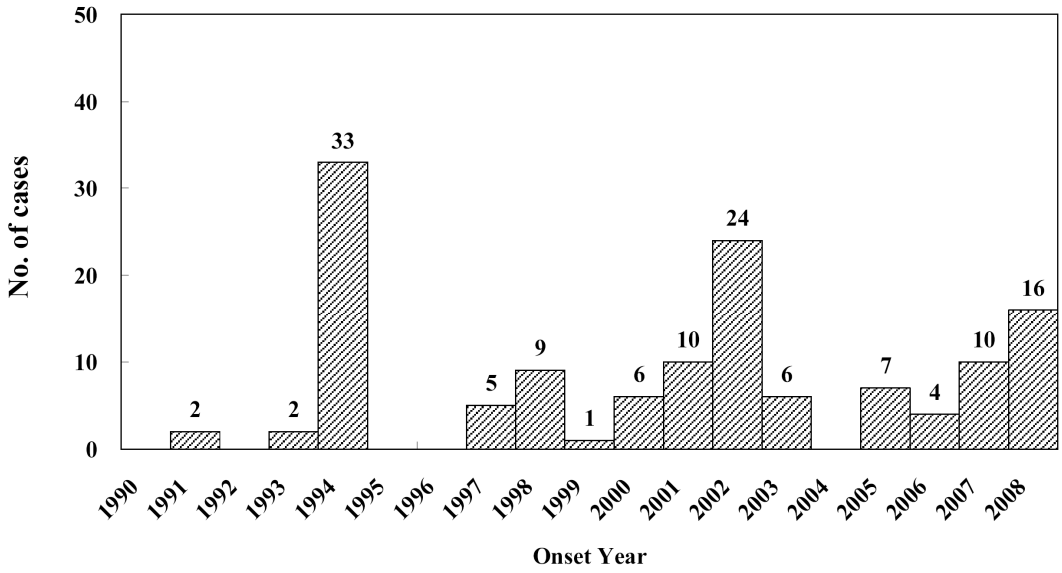

Figure 1. Measles confirmed cases in Taiwain, 1990~2008

Table 1. Number of measles cases in Taiwan, 1990~2008

Onset Year	No. of Reportted Case	No. of Confirmed Case	incidence Rate/100,000 population under 50 yrs old	Outbreaks or Cluster happened
1990	29	0	0.00	
1991	44	2	0.01	
1992	264	0	0.00	
1993	71	2	0.01	
1994	98	33	0.19	Taoyuan County
1995	42	0	0.00	
1996	47	0	0.00	
1997	66	5	0.03	
1998	50	9	0.05	Chiayi County
1999	23	1	0.01	
2000	48	6	0.03	
2001	50	10	0.06	
2002	79	24	0.14	Taichung County
2003	59	6	0.03	
2004	36	0	0.00	
2005	39	7	0.04	
2006	24	4	0.02	
2007	85	10	0.06	
2008	71	16	0.10	
Total	1225	135	0.04	

Note 1: incidence rate/100,000 population under 50yrs old was calucated for confirmed cases.
Note 2: Outbreaks or clusters were calucated if events were mire then 5cases

Cluster community infection events were recorded in 1994 and 2002 in Taoyuen County and Taichung County, which caused significant increase of measles cases. The confirmed measles patients all were under 50 years old and the incidence per 100,000 people under 50 years old each year were shown in Table 1. The average incidence over the past 19 years was 0.04 / 100,000 people.

Analysis of person, time, and location

In 135 confirmed measles patients, 64 were male and 71 were female (0.9:1). Most of these cases were under 15 years old (about 72.6%), in which 53 were less than 2 years old (39.3%) and followed by 31 cases of 5-14 years old children (23%). The incidence of less than 1 year old and one years old was 0.7 and 0.28, respectively, which was the highest in all age groups. There were 17 adult patients (12.6%), aged 25to 29 years old, and the incidence was 0.05 per 100,000 people (Table 2).

In 53 confirmed cases younger than 2 years old, 38 patients were under 1 year old (under vaccine inoculation age) and 13 were imported cases (10 from China, 3 from The Philippines). There were 17 cases in the age group of 25-29 years old, of which 12 were imported cases (China, Thailand, Japan and The Philippines). These information indicate that measles may be imported to Taiwan from other countries easily through travelling or immigration and it is a challenge to prevent following local community infection event. Based on the database in 1990-2008, the highest measles epidemic peak was in March to May, and followed by September (Figure 2).

Table 2. Incidence rate of measles confirmed case by age groups, 1990~2008

Onset Year	0	1	2	3	4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	Total
1990	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1991	0	1	0	0	0	0	0	1	0	0	0	0	0	0	2
1992	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1993	0	2	0	0	0	0	0	0	0	0	0	0	0	0	2
1994	3	2	3	3	2	16	3	0	0	0	0	0	1	0	33
1995	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1996	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1997	1	3	0	0	0	0	1	0	0	0	0	0	0	0	5
1998	5	2	0	0	0	0	0	0	0	0	2	0	0	0	9
1999	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
2000	4	0	0	0	0	0	0	0	1	1	0	0	0	0	6
2001	7	0	0	1	0	0	0	0	0	2	0	0	0	0	10
2002	6	0	0	0	0	5	5	1	0	7	0	0	0	0	24
2003	2	1	0	0	0	0	0	0	0	2	0	1	0	0	6
2004	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2005	1	1	1	0	0	0	1	1	0	0	1	0	1	0	7
2006	2	0	0	0	0	0	0	0	0	1	0	0	1	0	4
2007	2	2	0	0	1	0	0	1	0	2	2	0	0	0	10
2008	5	1	2	0	1	0	0		1	2	2	1	0	1	16
Total	38	15	6	4	4	21	10	4	2	17	7	3	3	1	135
Incidence Rate/100,000 population	0.70	0.28	0.11	0.07	0.07	0.07	0.03	0.01	0.01	0.05	0.02	0.01	0.01	0.00	0.04

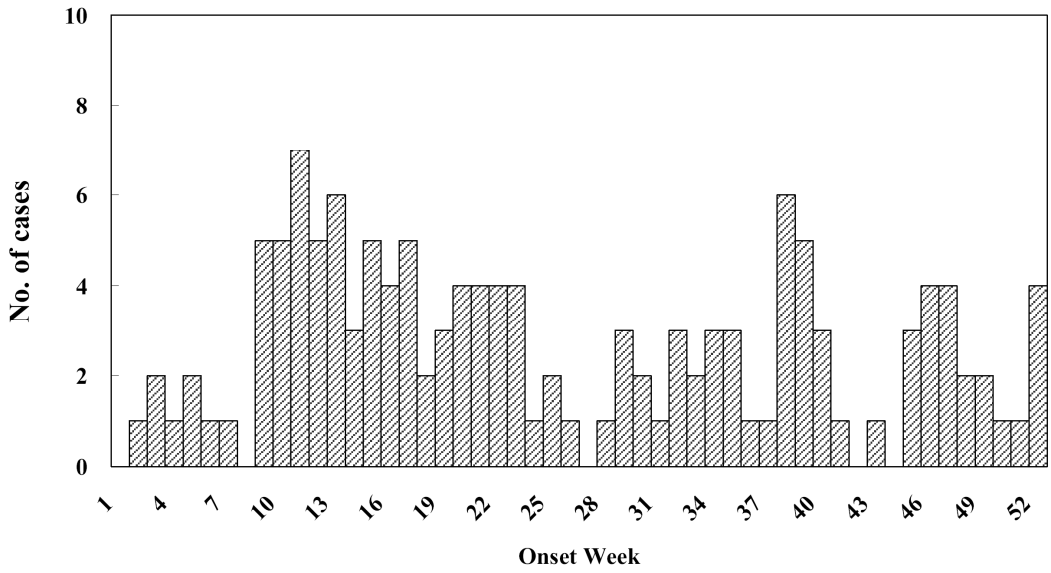

Figure 2. Onset week of measles confirmed cases in Taiwain, 1990~2008

In the same time period, Taoyuen County had the highest number of confirmed measles cases, followed by Taipei County and Taichung County. In the past 19 years, no confirmed case was found in Nanto County, Yunlin County, Penghu County, Kinmen County and Lienjiang County. Jiayi County, Taoyuen County and Taichung County had the highest incidence of measles in Taiwan (Table 3, Figure 3).

A hospital in Jiayi County reported 8 confirmed cases from March to May in 1998. A community outbreak event with 21 confirmed cases reported in 1994 in Taoyuen County. Taichung County had a community outbreak event in 2002 and at least 9 confirmed patients were reported. Scattered confirmed cases were

Table 3. The residence of measles confirmed cases in Taiwan, 1990~2008

County/City	Cumulative Confirmed Cases from 1990~2008	The average annual incidence Rate/100,000 population under 50 yrs
Chiayi County	9	0.13
Taoyuan County	35	0.12
Taichung County	15	0.07
Hualien County	3	0.07
Ilan County	4	0.06
Keelung City	3	0.06
Hsinchu County	4	0.05
Chiayi City	2	0.05
Kaohsiung City	10	0.04
Taipei County	20	0.03
Hsinchu City	2	0.03
Taitung County	1	0.03
Tainan City	3	0.03
Taipei City	9	0.03
Taichung City	4	0.03
Pingtung County	3	0.03
Tainan County	2	0.01
Miaoli County	1	0.01
Kaohsiung County	2	0.01
Changhua County	1	0.01
Nantou County	0	0.00
Yunlin County	0	0.00
Penghu County	0	0.00
Lienchiang County	0	0.00
Kinmen County	0	0.00

Note: two philippines infants hospitalized in Taiwan noresidence

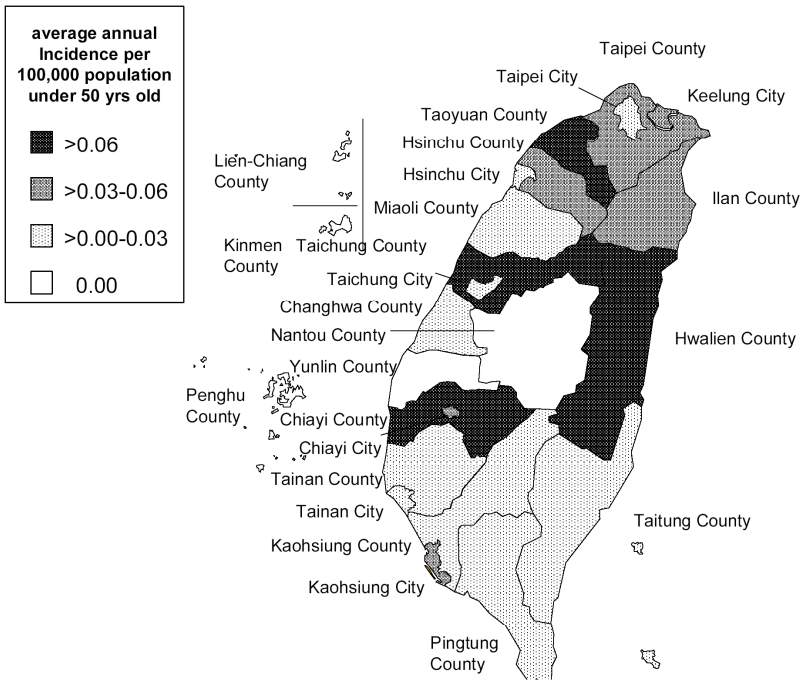

Figure 3. Geographical distribution by average annual incidence of measles confirmed cases in Taiwain, 1990~2008

noted almost every year in Taipei County. In these 135 cases, 39 were imported measles cases,of which 24 were from China, followed by Japan (7 cases, 4 of which in 2007) and The Philippines (5 cases). Especially since 2001, about 3 to 4 cases per year were imported from China.

Clinical symptoms

In the 135 confirmed cases, 64 patients (47.4%) were reported with clinical symptom information. The most prominent clinical symptom was fever (62 cases) and was followed by cutaneous vesicles (61 cases) and cough (27 cases). Only 11 patients presented typical clinical signs as conjunctivitis or Koplik's spots. This indicated that typical measles symptoms, such as cough, conjunctivitis and rhinitis, were not commonly seen in Taiwan. However, many other diseases with cutaneous vesicles, such as enterovirus, mycoplasmosis, roseola, and Kawasaki disease, may need to be included in the differential diagnosis, especially in infants and young children. Taiwan is in the process of measles elimination and the MMR vaccination rate is maintained at above 95%. Except community cluster events and imported cases, measles cases are not commonly found in Taiwan. This situation makes disease diagnosis more difficult for medical professionals. Cluster epidemic event may still be found due to international travel, and accumulation of unvaccinated population.

Vaccination

There were 53 patients younger than 2 years old in the 135 confirmed cases. Thirty out of the 53 cases were not vaccinated due to young age. Twelve cases have reached proper age for vaccination but did not receive measles vaccine. Three cases developed clinical symptoms of measles 10 to 15 days after vaccination. Whether

these cases were vaccine-related needs further investigation. There were eight patients with unknown vaccine history.

Cluster infection

Except sporadic cases, family or school clusters were still noted. Between February to June in 1994, a cluster infection event occurred in a school in Taoyuen County with 21 patients (all children, aged from 2 to 11 years old, 10 male and 11 female). Small family clusters were also found in Taoyuen City, Chungli City and Lujhu City. Similar clusters were reported in Taiping City and Fungyuen City (Taichung County) in September 2002. They included one family and three schools with 9 confirmed patients. Small-scale epidemic events were recorded in Gaoshu Township (Pingtung County) and in North district, Hsinju City in July and September of the same year. Over the years, two to three patients were usually found in small family cluster events, such as Wuchi Township (Taichung County) in May of 1997, Sanshia Township (Taipei County) in November of 2001, Banchiou City (Taipei County) in February of 2005, Chunghe City (Taipei County) in December of 2007, Dalin Township (Jiayi County) in March of 2008, and Chidu District (Keelung City) in August of 2008. The cause of these events was related to delayed or incomplete vaccination, and no vaccination due to young age.

Prevention

Health education :

It is necessary to educate population that children should be vaccinated on schedule. Adults with no vaccination history should avoid contact with oronasal discharge from measles patients. To avoid crowding in living or working space, and to keep indoor air circulation and to maintain good health habit are important to improve immunity against this disease. Vaccination should be completed before leisure or business travel when it is necessary to bring along infants or young children to measles epidemic areas.

Vaccination :

At present, MMR is administered in children age 12 months old and first-grade students in elementary schools. It is estimated that 95% of people vaccinated will generate immunity. However, individuals with the following conditions should not be vaccinated: 1. Fever caused by severe respiratory or other infection; 2. Immonocompromised patients; 3. Patients receiving immunosuppressant or high-dose of prednisolone; 4. Pregnant women. Vaccination should be postponed in certain patients. . Patients receiving intramuscular injection of immunoglobulin or HBIG should postpone vaccination for three months. Patients receiving blood transfusion should postpone vaccination for six months. Patients receiving intravenous plasma, platelet-related product or high-dose immunoglobulin should postpone vaccination for eleven months.

Discussion and recommendation

The measles vaccine was introduced into Taiwan since 1968. The two to three year cycle of measles epidemic disappeared since routine MMR started in 15-month-old children in 1992. The number of measles cases gradually decreased from 1968 to 1992 because of vaccination. However, young and adult people with no or incomplete vaccination were high-risk population for this disease. Due to traveling and commercial relations in recent years, local epidemic events caused by imported cases were

recorded. Cluster infection events may occur in the high-risk population through contacts with imported cases. Since severe complications are usually found in adult patients after measles infection, the issue of whether and how to address catch-up vaccination in this group becomes a problem in countries in the process of measles elimination. Whether protective antibody or life-long immunity can be conferred after vaccination is also an issue. Mild cutaneous vesicles or atypical clinical symptoms were still noted in fully vaccinated patients with natural infection. Infant born to HIV positive mothers have inadequate immune response after measles vaccination, and antibodies induced by vaccine disappeared faster than other children. Although measles vaccination significantly reduces the number of measles cases, it also reduces the number of natural infection. As a result, the issues of whether there is lifelong immunity in infants and young children, and whether booster vaccination is needed in adults need further investigation.

Taiwan has entered the most important stage of measles elimination. Some medical professionals may be inexperienced in this disease and may miss or delay reporting. Thus, local health professionals should collect proper samples for laboratory diagnosis while reporting. It is important to identify chains of measles transmission in order to effectively control and eliminate measles infection.

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Measles Cluster in Tainan Area, Early 2009

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Abstract

Late February to early March, 2009, the public health authorities in Tainan City and Tainan County were informed that suspected measles cases were found in some hospitals. In order to clarify the extent of the disease and the source of infection, Taiwan CDC involved in the investigation and found that this was a measles cluster and the infection origin was a girl less than 1-year old who was infected while visiting Vietnam with her mother and returned to Taiwan. Two series of nosocomial infections in Emergency section was erupted when the girl visited the hospital, including 2 medical staffers and 5 other people. In addition, one of the girl's classmates in the preschool was also infected. The possible causes of the dissemination of this disease were: 1. an un-vaccinated child visited a measles epidemic area; 2. difficulty in early diagnosis and isolation procedure due to rareness of indigenous measles case in Taiwan; 3. measles vaccine was not given to some due age child on

time. Measles cases are decreasing during these years in Taiwan. However, international communication with measles epidemic areas, such as China and countries in South-Eastern Asia, is increasing and so the risk of importing measles cases. The public health authorities should maintain an age appropriate coverage greater than 95% in measles vaccination for children and inform the general public of vaccination examination before visiting epidemic areas. Furthermore, to enhance disease diagnosis and timely report by medical staffs and to reinforce the control procedure for nosocomial infection are very important to achieve the goal of measles elimination project.

Keywords: measles, nosocomial infection, cluster, disease importation

Introduction

Measles is an acute, highly infectious viral disease and human is the only host. This disease is mainly transmitted by air and infectious droplets. Common clinical signs include: fever, cough, conjunctivitis, coryza and skin rash. Infectious period of this disease is 4 days before and after the skin rash occurs. Otitis media, pneumonia or encephalitis may be found in severe patients, deafness, mental retardation or even death may also occur [1, 2].

Measles was once a common and inevitable disease in childhood before the vaccine became available. Over 99% of people had been infected. In undeveloped countries, measles is a major cause of death for children under 5 years old. World Health Assembly (WHA) proposed to decrease the morbidity and mortality of measles by 90% and 95%, respectively in 1989 [3]. World Health Organization (WHO) proposed a measles elimination project in 1996 and established the elimination timeline at 2005 -2010 [4]. The effectiveness of measles vaccine reaches 95% and vaccination is the most effective measure to avoid infection [5]. According to WHO's recommendation, people should receive at least 2 doses of vaccine after 1 year old. Furthermore, the measles vaccination coverage rate should reach 95% to achieve the goal in elimination of measles.

Outbreak of measles affecting thousands of people had occurred every 2 to 3 years in Taiwan before 1970 [6]. Measles vaccine was first introduced to Taiwan in 1968. The Department of Health started giving 1 dose of measles vaccine to 9 months and 15 months old children in 1978. The public health authorities proceeded related measles control program and also implemented a project named "elimination of poliomyelitis, neonatal tetanus, congenital rubella syndrome, and measles" since 1991 based on the recommendation of WHO Western Pacific Regional Office [7]. With years of effort and large scale of measles vaccination to different birth cohorts including students of elementary school and female students of junior high school, endemic measles had been effectively controlled. Recently the number of confirmed measles cases had been fewer than 10 cases per year. The main strategies for eliminating measles in Taiwan are: 1. to strengthen regular measles vaccination coverage rate; 2. to promote monitoring system for measles; and 3. to increase the sample collection rate in suspected patients. Based on these operation and work, the measles vaccination rate has been maintained over 95% and the measles cases are also greatly decreased [8].

On February 25, 2009, a local clinic in Tainan City reported a suspected measles case of

2 years old boy, but his family had no abroad travelling history. Later, another 2 suspected cases were reported in Tainan County including 1 medical resident from Emergency section of A Hospital and a 10-month old boy on March 1 and March 2, respectively. The Fourth Branch of Taiwan CDC and public health authorities of Tainan County initiated an epidemiologic investigation to clarify the infection source and the extent of the disease for further controlling operation.

Background and clinical data of cases

The activity and disease history of suspected measles patients were described as following:

A. Case 1 was a 2 years old child. He lived in Tainan City and went to a preschool in Tainan County. He developed sore throat, cough and running nose on February 16 and was brought to local clinic for treatment. The clinical signs were improved after therapy. However, the clinical signs recurred on February 20. Rash was noted on February 23 and became more severe on February 25. This patient was suspected as measles infection and the local clinic reported this case to public health authorities. The patient and his family did not travel abroad during the past 3 months, and the boy was not vaccinated. Taiwan CDC officials started investigation for the family and the preschool. There were 4 classes with 49 children in the preschool. All children, not including this patient, had received 1st dose of MMR vaccination. All 7 staffers had received measles vaccine or had been infected. This preschool was closed during Chinese New Year vacation and resumed class on February 10. The principle indicated that there was no auditor since school started. All students, staffs, and their family members did not have any sign of measles, and this patient was the only child who did not receive MMR vaccine.

B. Case 2 was a medical doctor who worked in Emergency section in A Hospital. This patient started having sore throat, fever and dry cough on February 25. Clinical signs were not improved and rash occurred on February 28. He received further examination and treatment on March 1. He was suspected and reported as measles patient and was hospitalized in negative pressure isolation ward. This patient kept working in Emergency section on February 25, 27 and 28, and he lived alone. The patient worked in Emergency section during the incubation period. He did not travel abroad and had received 1 dose of measles vaccine in 1981.

C. Case 3 was a 10 months old infant who lived in Tainan County. The patient had fever, dry cough and swollen upper arm on February 13, and visited Emergency section at A Hospital of Case 2. The patient was in observation in this hospital till February 15 and was hospitalized at the same day until February 21 due to cellulitis. This child visited the same hospital 3 times because of coughing and fever since February 24 and rash was noted on February 28. The patient visited B Hospital on March 1. He was suspected and reported as measles infection and was hospitalized in negative pressure ward. Neither abroad travelling history nor measles vaccination was found for this patient. The measles IgM test was positive.

D. On March 2, First Branch, Taiwan CDC, informed that a 32-year-old male (case 4), who was reported as a suspected measles patient, had visited Tainan County during the incubation period. Further investigation found he is a resident of Taipei County and had fever and body sore on February 24. Fever continued on February 25 associated with skin rash. This patient was suspected and reported as a measles case by attending medical center on February 28. The patient visited his mother-in-law in the Emergency room in A Hospital of case 2 on February 14, 15 and 16 during the incubation period. Thus, Tainan County was suspected as the infection locality. This patient had no history of abroad travelling or measles vaccination.

Investigation for possible infection source

The public health authorities noted that cases 3 and 4 had visited the Emergency section of the A Hospital of case 2 during incubation period (February 13-15) and suspected this event as a nosocomial cluster infection, thus, Taiwan CDC officials went to this hospital for further investigation on March 3, 2009.

The Emergency section is divided into 3 main areas including emergency wound care and examination, adult emergency and pediatrics emergency. The average number of patients is 300 to 500 per day. Taiwan CDC staffers made a retrospective investigation on health condition of all medical and other staffs, as well as 1295 emergency patients, in the Emergency section for the period of February 13-15.

A. There were 250 medical and related staffs on duty in the Emergency section during February 13-15, but none had measles suspected symptom. As to the adult patients, 20 had fever associated with respiratory infection. However, none with rash was found.

B. Among 298 pediatrics patients during this period, 3 had suspected measles symptoms (fever, cough and rash) and had no measles vaccination. One patient was a 1 year old girl and was a resident of Tainan County. This patient returned to Taiwan from Vietnam with her mother on February 7. Two other patients were residents of Kaohsiung City and Kaohsiung County, respectively; both patients and family members did not travel abroad during the last 3 months. Blood samples were collected and tested at Kun Yang Laboratory, Taiwan CDC. Measles IgG and IgM were positive for the 1 year old girl of Tainan County (case 5); however, tests were all negative for other 2 patients.

Further investigation found mother of case 5 is a Vietnamese. The girl and her mother visited Vietnam in November, 2008, while the patient was 9 months old and did not receive measles vaccine. They came back to Taiwan on February 7, 2009. The patient started having fever since February 10 and visited the A Hospital due to persistent fever and upper respiratory infection on February 14. The patient was suspected as enterovirus infection and was isolated in an operation room in adult emergency area. There was no independent air condition and the door was opened. The patient was hospitalized on February 15 and skin rash was noted the same day. She was diagnosed as viral rash and was discharged on February 18. The mother indicated that the girl went to a preschool

during February 10 to 12 and the case 1 patient was her classmate, but the preschool staff indicated that there was no auditor student in this preschool.

Developing of the Measles cluster

Medical facilities continually reported 14 suspected measles cases and 4 of these cases were confirmed by laboratory examination. The activity history of these 4 cases was described as following.

A. Case 6 was 11 months old girl who lived in Tainan County. She had fever on February 14 and was sent to pediatrics emergency at A Hospital from 2 am to 5:30 am. She received radiologic examination on 3 am. She had fever again on February 21 and visited a private clinic for medical treatment. The clinical signs were not improved and she was sent to the private clinic again. Roseola was suspected and she was transferred to the A Hospital. Blood examination revealed positive for measles IgM and IgG. This patient did not have history of abroad travelling or measles vaccination.

B. Case 7 was a 37-year-old female, Tainan City resident. She had nasal congestion, cough, conjunctivitis and mild fever, and visited a private clinic on March 4 and 6. Pale petechiation was found in the oral cavity on March 8 and rash was noted on the next day. Rash lesions became severer on March 10 and she visited another private clinic. Measles infection was suspected based on her symptoms. The doctor reported to Bureau of Public Health and transferred her to the A Hospital. This patient was hospitalized in an isolation ward for respiratory infection. Before the symptoms occurred, this patient had visited a relative in the Emergency section in this hospital on 11 pm on February 14 and left on 1 am, February 15. No abroad travelling was noted in this case, however, measles vaccination history was unknown.

C. Case 8 was a 24-year-old male, Tainan County resident. He was a security officer in Emergency section in the A Hospital. His duties included traffic directing, information consulting and public guiding. This patient was on duty in February in Emergency section. He had fever and coughs after receiving MMR vaccination on March 10, and then visited A Hospital on March 13 due to skin rash. The hospital reported him as measles case and he was hospitalized in a negative pressure ward. No abroad travelling was noted and MMR inoculation history was unknown.

D. Case 9 was a Tainan County resident, 24 years old male. He had no abroad travelling history and unknown MMR inoculation. He had sore throat and fever on March 11, and rash was noted on the face on March 13. This patient visited the hospital in the evening on the same day (March 13) and was reported as a suspected measles case. He had accompanied his mother to the Emergency section at A Hospital on February 28. The Bureau of Public Health traced to the family. He was planned to receive MMR but stopped due to disease occurrence.

Analysis of Investigation

During investigation from February 25 to April 10, 2009, there were 21 reported measles

suspected cases in Tainan City and Tainan County. Ten suspected cases were confirmed as measles infection cases by laboratory examination, 9 of which were local cases and 1 was imported case (Vietnam was the infection place). Eight of the 9 local cases were confirmed as a cluster, while the 9th local case was a patient from another cluster. Age distribution of this cluster was between 10 months old to 37 years old (Table 1). The disease occurrence was firstly noted on February 10, and the last measles case was found on March 12. All confirmed patients were hospitalized for medical treatment and were fully recovered without any complication.

Based on the epidemic curve of disease occurrence (Figure 1), there were 3 waves. The first wave was the importation of measles from Vietnam. The second wave was the clustering in the Emergency section in the A hospital, which involved 3 patients, 2 visitors and 1 medical staffs. Also, the imported patient caused measles infection to one classmate in the same preschool. The third wave was a nosocomial infection in the Emergency section caused by the second wave.

Table 1. Cases of measles cluster in Tainan area, by selected patient characteristics, Taiwan, Early 2009

Case no.	Age	Gender	Onset date	Reported date	Measles Ab test		Virus Isolation
					1st sampling	2nd sampling	
case 5	1yrs	F	Feb 10	Mar 4	IgM+, IgG+	Nil	Nil
case 1	2yrs	M	Feb 20	Feb 25	IgM+, IgG—	Nil	Nil
case 2	30yrs	M	Feb 25	Mar 1	IgM—,IgG+	IgM-,IgG+	Throat swab, urine
case 4	32yrs	M	Feb 24	Feb 28	IgM+, IgG—	Nil	Throat swab, urine
case 3	10mos	M	Feb 23	Mar 2	IgM+, IgG—	Nil	Nil
case 6	11mos	F	Feb 27	Mar 4	IgM+, IgG—	IgM+, IgG—	Urine
case 7	37yrs	F	Mar 4	Mar 10	IgM+, IgG—	IgM+, IgG—	Nil
case 8	24yrs	M	Mar 10	Mar 13	IgM—,IgG+	IgM—,IgG+	Nil
case 9	25yrs	M	Mar 12	Mar 14	IgM—, IgG	IgM+, IgG+	Throat swab, urine

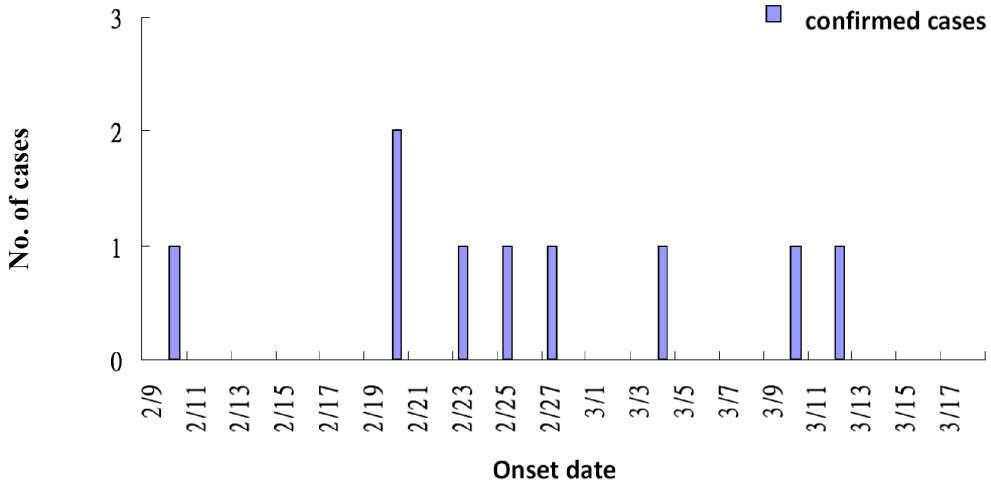

Figure 1. The Cases of measles cluster in Tainan area, by onset date, Taiwan, Early 2009

One visitor and 1 security guard in the Emergency section were affected (Figure 2).

The first measles patient (index case) in this event was an imported case, who visited the relatives with her mother in Vietnam in November, 2008. She was less than 1 year old and thus had not received measles vaccine. She was infected by measles virus and then came back to Taiwan. She attended a preschool for 3 days with the illness and 1 child was infected (case 1) who did not received MMR. Other children in this preschool had received the first dose of MMR and, thus, no disease was found in them.

The Emergency section in the A Hospital is divided into 3 main areas including emergency examination area, adult emergency area and pediatrics emergency area. Each area has therapy rooms and observation rooms. The adult observation rooms are located in 2 places on the first floor and 1 place in the basement. Radiology room is located between adult and pediatrics observation rooms. The adult and pediatrics observation room is separated by an automatic door. The medical staffs of pediatrics emergency may access to adult observation areas or to radiology room through the door. There is a simple equipped surgery room in the adult observation area located across the door of radiology room and is used for wound suturing. The index patient was not diagnosed of measles infection and was placed in the simple equipped surgery room on February 14 and 15 for observation. During the observation period, there was no proper respiratory precautionary measure for this patient and caused measles transmission to 5 people including 1 medical doctor, 2 pediatric patients and 2 visitors. The relative location of the index patient and the patients in

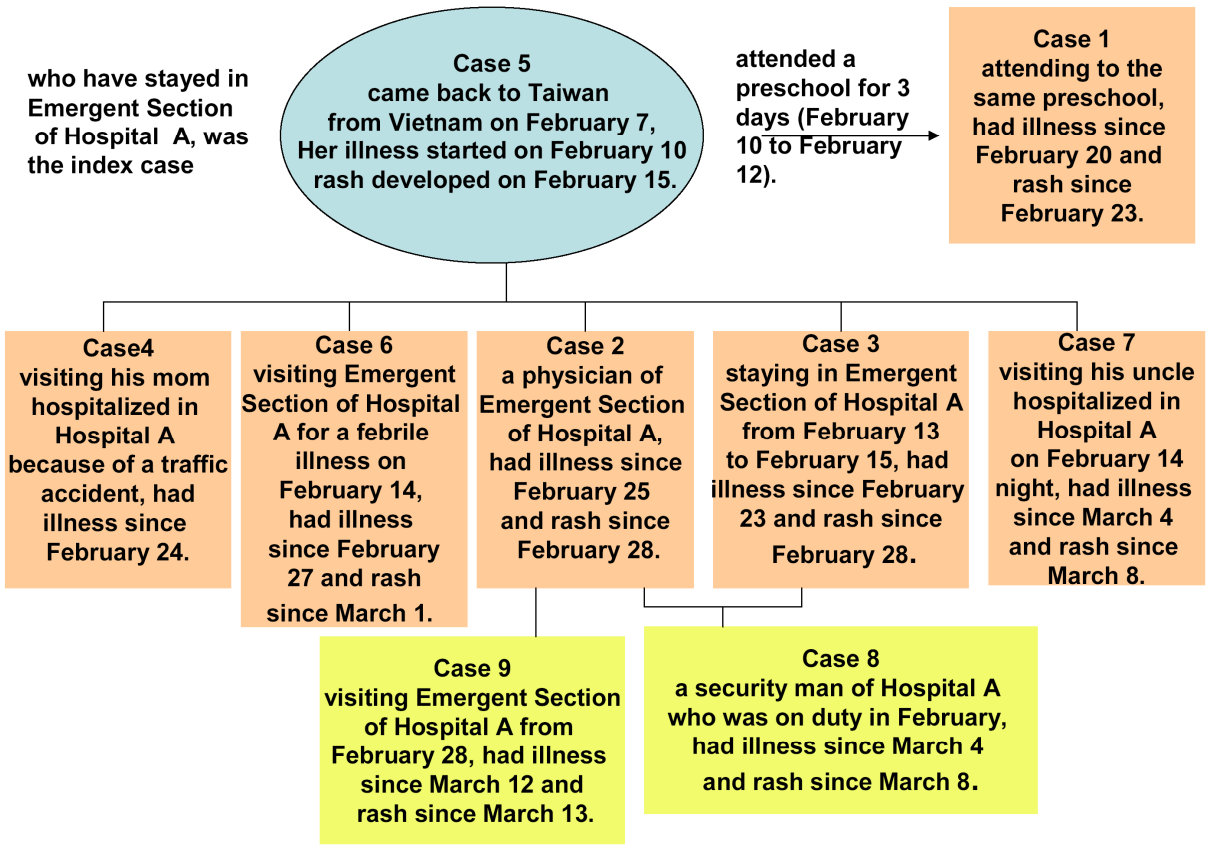

Figure 2. The time sequence of disease occurrence of the confirmed measles in Tainan area

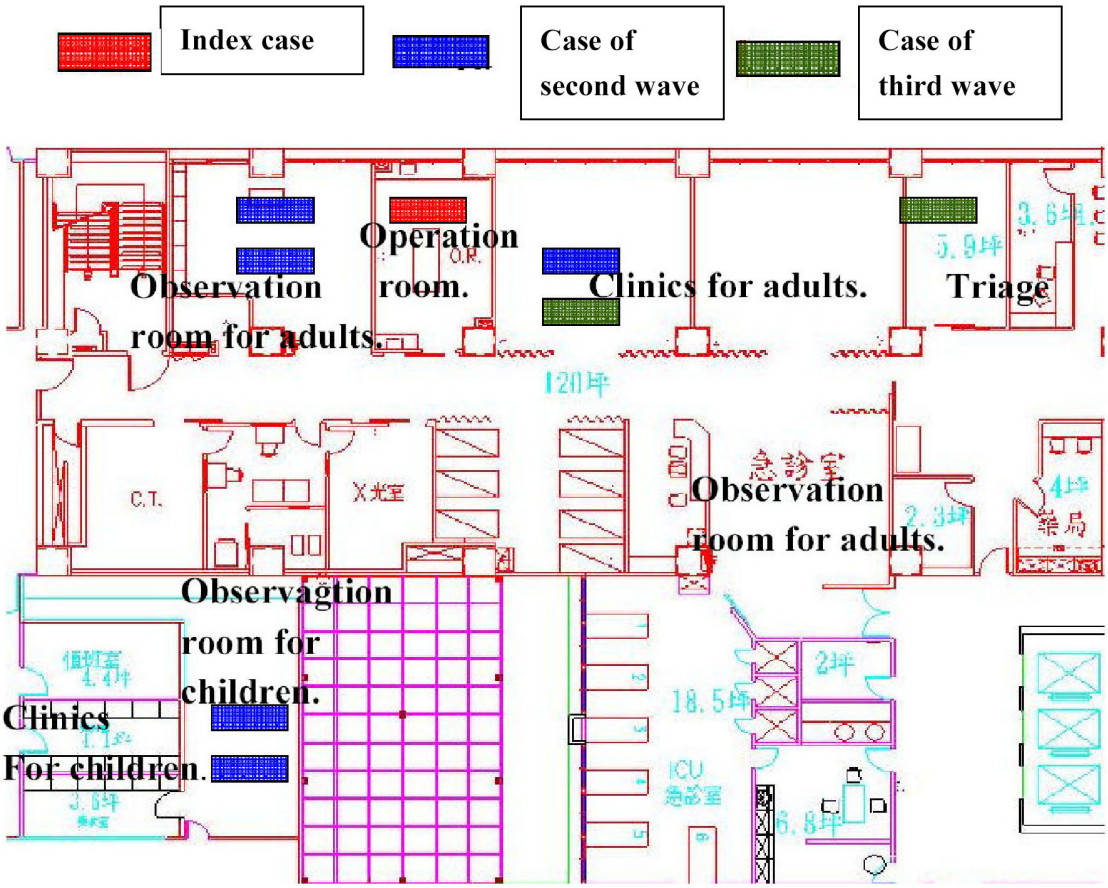

Figure 3. The relative location of the index patient and other confirmed patients in the Emergency section in the hospital

the second and third waves was shown in Figure 3. It was suspected that case 6 was infected during the time when taking radiologic examination next to the index patient. Case 3 was probably infected in the Emergency section or pediatrics ward. Another 2 visitors were exposed under the same air condition area with the index patient, although only for 4 hours, they were infected due to high transmissibility of this disease. Fortunately, the hospitalized patients were less than normal and all pediatrics patients, except case 3, had received MMR. Thus, the disease outbreak in the pediatrics ward was not expanded.

The duty of the security guard (case 8) was traffic directing, information consulting and public guiding. He may be infected by case 2 or case 3 when he was on duty in the Emergency section. Case 9 was probably transmitted by case 2. Case 9 visited the hospital with his mother for emergency service and case 2 was one of attending doctors for his mother.

Disease Control and Prevention

A. Disease control and prevention of the A Hospital

1. The hospital called an emergency meeting for the cluster at end of February and published a warning for measles. Relative measures for disease control and prevention were set up and informed all medical staffs.
2. Initial examination for measles should be performed on all emergency patients.

Suspected patients should wear masks. The hospital listed all patients who visited the Emergency section during the time frame of measles cluster. The hospital also monitored the symptoms of the patients transferred from Emergency section after hospitalization.

3. MMR inoculation was performed on all medical staffs and co-workers with unknown or no history of measles infection and vaccination.
4. All staffs and co-workers were requested for health self-management. If fever occurred, the staffer or co-worker should be listed on the "Daily report for disease control and prevention", and be treated by medical doctor.

B. Disease control and prevention of the public health authorities

1. Tracing, health education, symptom monitoring and immunization for contacts:
   a. The public health authorities had name lists for who were contacted by those measles confirmed patients, such as family members and other patients in the hospital. The authorities also traced the measles inoculation history of those contacts by NIIS data base. Health education and 21-day self health management was required for those people who did not have vaccination history. As for contacts less than 1 year old and exposed to the confirmed patients within 6-day period, these children were transferred to medical facility for evaluation to receive intramuscular immunoglobulin (IMIG) injection. Contacts between 1 to 32 years old without history of measles infection or vaccine inoculation, were given measles-mumps-rubella vaccine (MMR) as soon as possible. Based on the seroepidemiologic investigation, over 90% of the people who were older than 32 years old (born before September, 1976) had measles antibody [9]. Contacts of this age group were recommended for self health management.
   b. Among 101 contacts who were less than 7 years old and without MMR inoculation record, 100 of them were successfully traced. Eighty-one contacts were less than 1 year old, 3 were qualified for IMIG, one refused because the parents concerned about the side effects; 20 contacts were between 1 to 6 years old. 19 of which were traced and received MMR inoculation. Only one contact was not traced due to unavailable information.
   c. As for public health education, contacts should wear masks and avoid taking public transportation to the designated hospital for medical treatment, if suspected measles symptoms were noted. Children of the family without MMR inoculation should be arranged for such vaccination as soon as possible.
2. The Bureau of Public Health in Tainan City and Tainan County published press release and informed medical facilities to enhance disease monitoring and report.

Local health center staffs informed the due age children (> 12 months old) without MMR inoculation record to receive vaccination.

3. In addition to increase regular MMR inoculation rate, Taiwan CDC also established an emergency team to enhance relative disease control and prevention measures. There were 4 main strategies: (i) to enhance monitoring and tracing for contacts; (ii) to prevent nosocomial transmission; (iii) to encourage the due age children for MMR inoculation; (iv) to enhance public health education and quarantine measures for travelers from South East Asia and China. Other priorities including tracing and management of the contacted people, adjusting inoculation age to 12-month-old for MMR vaccination to decrease the possible susceptible, and, preventing and controlling for nosocomial transmission. Taiwan CDC also recommended medical staffs or other high risk professionals without MMR inoculation record should received vaccination, and all medical staffs should implement standard protection measures [10].
4. Advisory Committee on Immunization Practices (ACIP) adjusted the schedule for first dose of MMR at 12 months old on March 25 [10].

Discussion

The origin of this endemic measles cluster was a 1 year old child who went to Vietnam with her Vietnamese mother. Vietnam is still the epidemic area for measles. This child had not received measles vaccination and was infected. The diagnosis of measles for her was delayed and, thus, the disease spread out to her classmate in the preschool and to the medical staffs, other patients and visitors at the Emergency section in the hospital. There were 3 main causes for the spread of this disease: 1. the child under the due age for MMR inoculation visited measles endemic area with the parent; 2. delayed diagnosis for measles due to rareness of native measles case being the main reason for nosocomial infection; 3. the due age children failed to receive MMR inoculation in time being the cause for community infection.

In addition to this cluster, there were several measles clusters occurred from late 2008 and originated in children who were under age for measles vaccination and infected due to visiting measles endemic area with parents. The disease was spread out after they returned to Taiwan and transmitting to the people with insufficient immunity [10-12]. With social, economical and transportation progress, many similar events were reported in developed countries [13-15]. The communication and transportation between Taiwan and other country is increasing, as well as the number of foreign spouse and worker (especially people from Southeastern Asia and China). Many Southeastern Asian countries, such as Vietnam, Thailand, Indonesia and China are epidemic areas for measles. Although the immunity for measles in Taiwan population is high, people still have high risk in measles infection during travelling to these areas if they have insufficient immunity, especially children under age for MMR inoculation or children of due age without vaccine inoculation. The risk of these children is higher than adult people who had been infected by measles or had received measles vaccination. Thus, in order to enhance

measles prevention and to decrease the risk of infection, it is important to make sure to give one dose of measles vaccine for children above 12 months old at least two weeks before travelling, if needed, to these high risk areas.

The index patient had visited medical facility for several times, but the medical staffs may not have enough experience in this disease resulting into delayed medical diagnosis and improper disease prevention measures, which was the main reason for the spread of this disease. According to some reports, increased measles vaccination coverage rate and immunity for measles in public have resulted in decreased community infection. However, high density of infectious pathogens in medical facility may induce increased hospital-acquired infection and the rate of this transmission mode was increasing in measles infection events [14-16]. Cluster infection events were mostly occurred in crowded areas such as pediatrics ward [17]. In the recent four clusters of measles, community transmission accounted only 20% of all cases, while hospital-acquired transmission was 80%. The hospital-acquired transmission mode was mainly patient to patient, patient to companion relatives or visitors, or patient to medical staff. Pediatrics emergency area and pediatrics ward had the highest cases rate (82%) and the patients were mostly under 6 years old [10-12]. In our investigations, the initial clinical symptoms of index cases were not identical and may be diagnosed as upper respiratory infection. Although fever and rash were noted in some patients, they may still be diagnosed as roseola or other viral infections. Measles is a highly transmissible viral disease and is able to infect other people before clinical symptoms occurred. Thus, the medical staffs and other people in the same area were exposed to the infection risk, in this event when the index patient was seen at the hospital. This indicated that medical staffs were inexperienced in measles diagnosis and unable to process further examination and report, which delayed the time for disease prevention and treatment. It is highly recommended to enforce health education of this disease for medical staffs in order to enhance monitoring and to decrease hospital-acquired measles infection event. Medical staffs should inquire thorough history of clinical symptoms, abroad travelling to measles endemic areas (such as China or Southeastern Asia) and contact of suspected measles patients. With accurate diagnosis and isolation measures in time, it is possible to reduce the exposure risk and control the disease.

Medical staffs and workers are frequently exposed to many highly infectious pathogens; they may be infected, or even become reservoirs of measles if they have insufficient immunity or improper protection measures. Many developed countries have listed MMR vaccine in the essential vaccine list for medical staffs or co-workers [18]. In this cluster, measles was spread out in the adult emergency area and many patients were adults. The index patient was initially diagnosed as enterovirus infection. This patient was transferred to an operation room in the adult emergency area because there was no isolation room in pediatrics emergency areas. However, no separate air condition system was equipped in the operation room and the disease was disseminated to the adult emergency areas. Under this situation, some medical staffs, patients and other visitors without sufficient immunity are vulnerable to the infection. This is the first incident of measles transmission from medical staff to a companion visitor in the last

wave. During the measles cluster, the A Hospital adopted emergency measures for measles prevention, including health education for medical staffs, inquiring travelling and clinical symptom history, and MMR immunization for all necessary staffs and workers. It was also advised that all employees including new recruitment without MMR record or without sufficient antibody should receive MMR vaccine. With the reported cases increased, this hospital was able to diagnose the disease and arranged suspected patient for proper isolation, which was helpful for disease control.

Strengthen MMR immunization is the main strategy for measles elimination program by WHO. Taiwan implemented the "Elimination of poliomyelitis, measles, congenital rubella, and Neonatal Tetanus", and changed the regular measles vaccine to MMR vaccine for 15 months old children in 1992. The authorities also included the first grade students in primary school for the second dose of MMR in July, 2001. Several catch-up vaccination campaigns were also supplemented. The coverage rate of 1st and 2nd dose of MMR vaccine was over 95% in years [19]. Endemic measles cases were decreasing during these years; however, measles may still easily be imported from other countries by frequent international communication. According to Taiwan CDC Data, confirmed measles cases was 4 to 24 in each year from 2002 to 2007, except zero case for 2004, and 75% to 100% of these cases were imported. China was the main origin country, followed by Southeastern Asian countries. In 2008, there were 16 confirmed measles cases. Although 7 cases were imported (44%), other 9 cases were cases in local cluster transmitted by 1 imported patient. In Taiwan, the most important challenge for measles prevention is to decrease the risk of importation. It is recommended that a MMR vaccine should be given or measles antibody should be tested before travelling to a high risk area if the traveler has no history of measles infection or inoculation. The traveler should inform the travelling history when visiting hospital after returning to Taiwan. The ACIP (Taiwan) recommended that the age for first dose of MMR should be at 12-month old due to nearly 80% of the patients in recent clusters were children. As for those who cannot keep up with the schedule, it is highly recommended to receive MMR as soon as possible.

Conclusions

Although local measles cases are decreasing during recent years in Taiwan, the risk of measles importation may be high due to frequent communication with measles epidemic countries. In order to achieve the goal of measles elimination, the following issues are essential: 1. maintain MMR inoculation rate at 95% and above; 2. inform public to check immunity for measles before visiting high epidemic areas; 3. enhance diagnostic and reporting mechanism for suspected patients in medical facilities; 4. implement proper nosocomial infection control measures; and 5. intensify disease responding procedures.

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