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Cluster of *Angiostrongylus cantonensis* Infection in Tainan County, 2009

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Abstract

Angiostrongylus cantonensis is a common parasitic worm in rats' lungs. It is also an endemic disease that occurs throughout the Southeast Asia and Pacific basin, and is a common pathogen of eosinophilic meningitis. On March 18, 2009, Taiwan CDC was informed by National Cheng Kung University Hospital that 3 Thai workers were suspected to have been infected by *Angiostrongylus cantonensis*. An investigation was soon conducted to figure out the extent, the infection source, and the transmission route of the cluster. It was found that in late February 2009, several Thai workers went out together on a holiday. Five of them caught golden apple snails in a fish pond under a bridge in Zen-De Township, Tainan County, and ate them raw with chili and vinegar. From March 5 to 19, 5 cases started to have symptoms of headache, myalgia, general malaise, stiff neck, and vomiting. Four of them sequentially went to the same hospital and hence a suspected cluster of *Angiostrongylus cantonensis* infection was reported. A cluster event of *Angiostrongylus cantonensis*-caused eopsinophilic meningitis due to eating raw golden apple snails was subsequently proved through testing related samples. Taiwan CDC has since issued letters to related agencies to request strengthening of hygiene education for Thai foreign workers.

Key words: *Angiostrongylus cantonensis*, eosinophilic meningitis, golden apple snail.

Introduction

In 1933, when Chen was investigating the parasites of rats in the suburbs of Guangdong, China, he found out that there was an unknown parasite in 10.7% of rats' lungs. He than named it

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Pulmonema cantonensis [1]. In 1935, Matsumoto discovered that the rats in Hua-lien in the east coast of Taiwan were also infected by the same parasite, and he named it *Haemostrongylus ratti* [2]. Ubelaker indicated that *Pulmonema cantonensis* and *Haemostrongylus ratti* are the same genus as *Angiostrongylus*, which was named by Kamenskii in 1905[3].

In 1945, Nomura and Lin reported the first case of infection with this parasite in Taiwan in a 15-year-old boy who died due to suspected meningitis [4]. Worms later proven to be immature *Angiostrongylus cantonensis* were found within his cerebral spinal fluid. In 1959, Professor Hsieh Hsien-chen, a parasitologist at the Kaohsiung Medical College, described the discovery of Nomura, Lin [4], and Rosen [6], in 1935, 1945, and 1962 respectively in an article titled “Outline of Parasitic Zoonoses in Taiwan” [5], which was published in “Taiwan science”. It was when *Angiostrongylus cantonensis* infection started to gain attention around the world.

By 1978, 259 cases had been discovered since 1945, the year that Nomura and Lin reported the first case in Taiwan. The majority of cases presented with eosinophilic meningitis or meningoencephalitis. The geographical distribution of this disease was mainly in the southern and eastern parts of Taiwan, and there were no cases reported form the outlying islands. Most of the cases occurred in summer, and 80% were children. There was no difference in sex of the patients [7]. Somehow in Thailand, 70% cases were adults between 30-39 years in age. This difference might have been due to different chances of exposure to the intermediate host [8].

Angiostrongylus cantonensis is a common parasitic worm of rats’ lungs. It is also an endemic disease which occurs throughout the southeastern Asia and Pacific basin, and it is one of most common pathogens which cause eosinophilic meningitis [9]. Numerous researches and studies on *Angiostrongylus cantonensis* were done in Taiwan. The intermediate host of *Angiostrongylus cantonensis* was giant African land snails (*Achatina fulica*) and golden apple snails (*Ampullarium canaliculatus*) [10, 11]. Rats are the definite host of *Angiostrongylus cantonensis*, while slugs and snails are the intermediate hosts. As a result, human only get infected when eating contaminated food or the raw intermediate hosts or reservoir hosts, such as crabs and frogs [7, 10, 11].

Regarding the parasite’s life cycle, it starts with adult worms that live within the pulmonary artery of rats. Every female worm lays about 1500 eggs each day. First stage larvae are born in rats’ lungs and migrate to their trachea before being swallowed into the stomach and intestines.

Finally, the larvae will be defecated with stool and opportunistically penetrate into snails, which were their intermediate host. After peeling twice in 2 weeks, they become third-stage larvae, which are contagious. Human and rats will be infected after eating the snails or the vegetable that contain third-stage larvae. In rats, the larvae will become adult worms when they were transmitted to rats' brain by the blood flow in 4 weeks. At last, the worms will move to the pulmonary artery, where they will lay eggs in 2 weeks. Then, the first-stage larvae again migrate to trachea then are swallowed into stomach and intestines. When humans get infected, symptoms started to be noted when larvae have been transported to the central nervous system [6].

On March 18, 2009, CDC was informed by National Cheng Kung University Hospital that 3 Thai workers were suspected to be infected by *Angiostrongylus cantonensis*. An investigation was soon conducted to figure out the extent, the infection source and transmitted route.

Materials and methods

1. Cases of investigation: the 5 Thai workers that ate raw golden apple snails.
2. Duration of investigation: from March 18, 2009, the date on which the cases were reported, to April 18, the date when the monitoring was ended.
3. Medical record review: reviewing the 5 cases' medical records after their symptom onset to understand the clinical course, treatment and recovery.
4. Sample collection and test: Cerebral spinal fluid (CSF) and serum were collected and tested soon after the cases were reported. If the result of the first set of samples was negative, a second set of samples was collected and tested. Antibody against *Angiostrongylus cantonensis* usually elevates after 2 weeks. Hence, the second set (2 weeks after symptoms onset) was tested when the first set (within 2 week after symptoms onset) showed negative result. In addition, CSF would be examined for the presentation of the worm. Besides, professor Yen Chuan-Min's parasitology lab at Kaohsiung Medical University was assigned to perform the antibody test. *Angiostrongylus cantonensis* antigen purified via monoclonal antibody was used as ELSA to detect the presentation of serum IgM, IgG and IgA [12].

Investigation report

On Feb. 28, 2009, several Thai workers went out together on holiday. Five of them caught golden apple snails in a fish pond under a bridge in Zen-De Township, Tainan County, and ate them raw with chili and vinegar.

On March 5, the first case (case 1) started to have symptoms of headache and generalized myalgia. Since March 7, the employer had taken case 1 to a local clinic at Zen-de Township 3 times with the concern of a common cold. However, with persistent symptoms, the employer soon contacted the supplying labor agency for further management. On March 12, case 2 began to have symptoms of vomiting, headache and general malaise, and was taken together with case 1, who still had persistent symptoms, to the city hospital. The doctor there noted the history of eating raw snails. Hence, further evaluation at National Cheng Kung University Hospital was suggested to the labor agency should there be no improvement in the

coming days. On March 18, case 3 appeared to have symptoms of headache, pain over left shoulder and right leg. The agency soon took 3 cases to National Cheng Kung University Hospital, where *Angiostrongylus cantonensis* infection was suspected and reported. Besides, case 1, 2 and 3 were in the same agency, while the other 2 cases were in different ones.

Case 4 started to have symptoms of headache and stiff neck on March 12. *Angiostrongylus cantonensis* infection was suspected when he went to city hospital on March 16. Though with the suspicion of *Angiostrongylus cantonensis* infection, general anti-inflammation agent was given instead of antiheminthic drug. Since the symptoms were improved on March 24, case 4 was sent back to Thailand as his wish on the same day.

On April 2, case 5 was reported by National Cheng Kung University to have suspected *Angiostrongylus cantonensis* infection. Upon further investigation, the patient had headache on March 19, the same day he fell down off a bike. Hence, head trauma was initially considered, and case 5 was sent to an orthopedics clinic in Zen –De town ship. On March 27, case 5 went to the city hospital due to a persisting headache. Later, the labor agency became aware of the hospitalization of case 5's friends at the National Cheng Kung University Hospital due to similar symptoms and consequently sent case 5 to the university hospital on April 1. With milder symptoms, case 5 was treated at the outpatient department. The epidemic curve of this cluster was shown in Figure 1.

Results

All 5 cases were male Thai workers, aged between 20 to 28 years, and had been in Taiwan for more than 6 months Without travel abroad; they were all endemic infection cases. All 5 cases had eaten raw golden apple snails. And their dates of symptoms onset were between March 5and March 19. Hence, their incubation periods were probably 6 to 20 days. Except case 5, all the other 4 cases experienced headache, myalgia with additional symptoms of fatigue, neck pain or stiffness, or diarrhea and vomiting (see table 1)

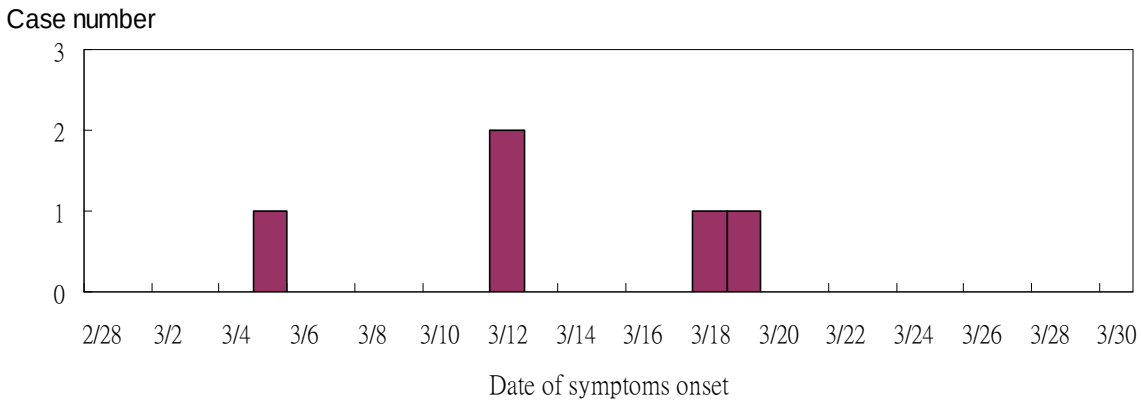

Figure 1. Number of *Angiostrongylus cantonensis* infection cases, by date of onset－ Tainan County, 2009

Table 1. Clinical symptoms and treatment of *Angiostrongylus cantonensis* infection cases－Tainan County, 2009

Case no.	age	sex	date of symptoms onset	symptoms	hospitalized	treatment
1	23	male	2009/3/5	Headache, myalgia, fatigue, neck pain, diarrhea, not able to rotate eye	yes	Mebendazole
2	28	male	2009/3/12	Headache, myalgia, fatigue, stiff neck, vomit, back pain, arthrialgia	yes	Mebendazole steroid
3	23	male	2009/3/18	Headache, myalgia, fatigue, stiff neck, left shoulder and back pain,	yes	Mebendazole steroid
4	23	male	2009/3/12	Headache, myalgia, stiff neck	yes	Non-antihelmithic
5	23	male	2009/3/19	Headache, myalgia, fatigue	no	steroid

Table2. Laboratory results of *Angiostrongylus cantonensis* infection cases－Tainan County, 2009

	Blood					CSF				
Case no.	WBC (k/ul)	Eosinphil (%)	CRP	Acute phase antibody	Convalescent phase antibody	Appearance	WBC	Eosinphil (%)	Antibody	Worm body
1	11.3	15	<7 mg/L	＋	＋	clear	79 /ul	2	＋	－
2	11.9	26.1	<7 mg/L	－	＋	clear	540 /ul	27	－	－
3	11.9	21.1	<7 mg/L	－	－	clear	571 /ul	66	－	－
4	11.6	12	N.D	N.D	N.D	clear	210 /ul	－	N.D	－
5	N.D	N.D	N.D	＋	N.D	clear	N.D	N.D	N.D	－

N.D: not done (the test was not performed)

The lab data of blood and CSF of 5 cases were described in table 2. Leukocytosis was noted in cases 1-4. Eosinophils accounted for12-26.1% of WBC, which was far above the normal value. There was no blood lab data collected from case 5. According to the results of ELISA (enzyme-linked immunosorbent assay) for blood, cases 1, 2 and 5 showed positive results, while ELISA was not performed on case 4. As for the results of cerebrospinal fluid ELISA, only case 1 turned out positive; ELISA was not performed on cases 4 and 5. However, there was no pathogen found in the CSF of these 5 cases, whose CSF all appeared clear. The bacterial isolation, virus culture of blood and CSF showed negative results for all 5 cases.

Discussion

From 1935, when Matsumo reported the first case, until now, 7 of the 15 rat species captured all around Taiwan have been found to be infected by *Angiostrongylus cantonensis*. They are *Rattus coxinga*, *R. losea*, *R. norvegicus*, *R.rattus*, *R. rattus mindanensis*, *Bandicota indica nemorivaga*, and *R. rattus rufescens*. The infected ratio of *Bandicota indica nemorivaga* is 50%, which is highest among all the other species [7].

Research from China also indicates that the infected ratio of *Angiostrongylus cantonensis* among its intermediate host are: 13.4% for giant African land snails, 6.8% for golden apple snails, 6.5% for slugs, 0.3% for other terrestrial snails,

and 0.05% for other freshwater snails [12]. But giant African land snail is the main intermediated host in southern Taiwan, and its infected ratio in nature is as high as 65% [8], whereas 14-31% of golden apple snails are infected by third-stage larvae [13]. Common intermediate hosts in Taiwan are shown in figure 2.

Giant African land snail was imported to Taiwan as a dietary substitute in order to increase the people's protein intake in 1932 while golden apple snail was imported illegally in 1979. Both of them were discarded into creeks and farms and caused damage to local ecology. The natural infected-ratio of the giant African land snails collected in Pin-dung Agricultural Improvement Station was 61.2%; 56% of the worms were distributed in the lungs, 21% in kidneys, and 14% in gastro-intestinal tracts [14].

Cases of *Angiostrongylus cantonensis* -induced meningitis were occasionally reported in Taiwan. Contact history and eating snails were the main causes among children. For example, in the town of Mei Non in Kaohsiung County, there were four cases, all under the age of 6 years, who reported having played with golden apple snails and subsequently grilled and consumed them two weeks before their symptom onset in late August, 1985 [8].

However, in recent years, *Angiostrongylus cantonensis* infection has been seen among adults. In June 1985, 9 members of a family in Tau-Yan had been infected due to eating raw giant African land snails. Symptoms started after1-3 weeks; 4 of them died, including 1 case that had become one-eye blind due to central ophthalmic vein occlusion. All the other family members had recovered. In 2001, there were also reported cases of 5 Taiwanese (ages from 30-57) getting infected due to drinking contaminated vegetable juice [15]. Some of the adults infected have been Thai workers, and the major transmission route among this population is eating undercooked snails. For example, clusters of *Angiostrongylus cantonensis* infection due to eating undercooked snails happened in both 1998 and 1999 (a total of 17 Thai workers were infected) [17].

Hung and Chen [9] classified the clinical symptoms of *Angiostrongylus cantonensis* infection into 5 groups: meningitis, meningoencephalitis, ocular lesion, rediculomyelitis, and cranial nerve involvement. In general, live worms seldom cause disease or cause slight inflammation response only, while dead worms or debris may induce infiltration of eosinophils and macrophage. There are numerous kinds of drugs available to treat *Angiostrongylus cantonensis*, such as


Giant African land snail


golden apple snail


slug

Figure 2. Common intermediate hosts of *Angiostrongylus cantonensis* in Taiwan

(Pictures from wikepedia:http://zh.wikipedia.org)

thiabendazole [18], albendazole [19], mebendazole [20], levamisole [21], and ivermectin [22]. Steroid may also be used for treatment. However, some scholars believed that more serious brain injury may be caused by the death of parasites with antihelminthic drug therapy.

All 5 cases in this cluster event had the same symptoms of headache and myalgia; 4 of them had fatigue. Additionally, stiff neck, back pain, general malaise, and vomiting were also noted. Case 1 even mentioned that he couldn't rotate his eyes. None of them had fever, and only cases 1-3 were diagnosed to have eosinophilic meningitis, while case 4 was diagnosed to have aseptic meningitis. According to the laboratory data from the hospital, Eosinophil ranged from 12-26.1% in the cases' serum and 2-66% in their CSF. Though all 5 cases' CSF appeared clear and absent of worm bodies, this might be due to the patients' position when performing lumbar puncture, which should have been performed with an upright position to let the worms flow down with gravity. Cases 1-3 were treated with Mebedazole, and case 4 was treated symptomatically. Steroid was given in cases 2, 3 and 5. Hence, although with negative antibody tests, cases 3 and 4 were still considered *Angiostrongylus cantonensis* infected cases according to their exposure history and clinical symptoms. For cases 1-3, there had been no complications 6 months after their hospital discharge. Case 4 had become healthy when discharged and went back to Thailand on March 24. Case 5, who presented with mild symptoms, were treated at the outpatient department, and no complication had been noted by the labor agency.

Conclusion

Due to the improvement of environment and hygiene in Taiwan, only few people eat raw snails now. But, in recent years, there are still some Thai workers infected because of eating raw golden apple snails. Hence, putting more emphasis on educating people and foreign workers to be cautious of the danger of eating raw snails and golden apple snails is a must. Besides, since vegetables may be contaminated by the parasite and become an infectious source, eating uncooked vegetables should be taken with caution or be avoided. After this cluster happened, CDC also issued letters to related agencies to strengthen the hygiene education of foreign workers. Only via reducing the chance of eating the intermediate hosts could infection be avoided.

Acknowledgement

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Importation Related Nosocomial Measles Cluster in Taipei Area, 2009

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Abstract

During the latter half of February, 2009, the Centers for Disease Control, Taiwan, received report of six suspected cases of measles which were confirmed by laboratory examination later. Epidemiologic investigation of the six cases was conducted to trace the possible source of infection. It was found that the original source of infection came from an imported case of measles that transmitted infection to the index case, who subsequently infected five other patients. The venue of transmission involved two hospitals in the northern and southern area of Taiwan. Due to the increased risk of measles transmission from imported infectious cases, it is important for public health authorities to improve the knowledge regarding measles in the general population and to reduce the number of individuals who are susceptible to measles infection. In addition, hospitals should strengthen their hospital-acquired infection control measures, and clinicians need to raise their level of awareness toward the differential diagnosis of measles for better control of measles infection in Taiwan.

Key words: measles, MMR vaccine, imported case, hospital-acquired infection, cluster infection event

Introduction

Since late February, 2009, First Branch Office, Centers for Disease Control (Taiwan CDC) has continually received 6 suspected measles cases notified from hospital A in Taipei area and then confirmed. Age distribution of these cases was from 9 months to 29 months old; the average age was 14 months; and there were 3 cases younger than 12 months. These 6 people all were hospitalized or had been in hospital A. The infection source of the first case (index case) was a measles patient hospitalized with index case in the same ward in hospital B in southern Taiwan, and contact exposure locations of the following morbidities were emergency room or wards of hospital A. As the result, an importation-related measles nosocomial infection cluster occurred.

Index case

The index case of the measles cluster is a 5-year-old boy living in Taipei area, whose mother is a new immigrant from China. The boy has received a measles vaccine at 9 months old in China, but he did not inoculate with Measles, Mumps & Rubella (MMR) vaccines. While visiting relatives during Chinese New Year, he had been in hospital B in southern Taiwan for 4 days because of illness, and an 11 months old girl who hasn’t inoculated MMR

was in the same ward with him. Since she returned to Taiwan from China in the middle of January, with symptoms of fever, cough, and rhinorrhea, she had been in hospital twice. Doctor notified her as suspected measles on February11th, 2009. The test results from CDC laboratory revealed IgM positive and IgG negative, she was confirmed as a measles case. To trace the infection source, we estimate the incubation period to be 7-18 days (normally 14 days) before onset of rash. It was determined that the girl may have been infected in China, and it's very possible that measles was transmitted to the index case during hospitalization. After the index case came back home in northern Taiwan, he developed fever on February 4th, and because his condition didn't improve, he went to the emergency and hospitalized in hospital A on February 8th, and developed rash on February 9th, the period of communicability was from February 5th to February 13th.

Cluster investigation

Five confirmed cases after index case were reported (Table 1). According to contact history and morbidity history, Case 1 started to have rash on February 18th, possibly infected during January 31st to February 11th and had contact with index case in emergency and X ray room of hospital A during this period. Case 2 started to have rash on February 21st, possibly infected during February 4th to February 14th. Case 2 was in the same ward with index case 1 from February 9th to February 12th. Case 3 began to have rash on February 22nd, possibly infected from February 5th to February 15th. Case 3 was also in the same pediatric ward from February 8th to February 10th. Case 4 began to have rash on February 22nd, possibly infected from February 5th to February 15th. Case 4 was in the same pediatric ward from February 8th to February 15th because of rotavirus infection. Case 5 began to have rash on February 24th, possibly infected from February 7th to February 17th. Because case 5's younger sister was in pediatric intense care unit of the hospital from February 5th to February 12th, case 5 and her mother have been in and out of the hospital several times, and they usually ate in the hospital and stayed over night there. Exposure and contact history of the cluster was shown as Figure 1. The 5 confirmed cases didn't have abroad travel history recently, and the families stated cases have never contacted with any suspected measles case before. According to laboratory analysis, measles virus genotypes of the 5 confirmed cases and the index case were all H1 type. Both epidemiologic investigation and laboratory data proved that all 5 cases and the index case belonged to the same cluster event.

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

Case no.	Age	Onset Date	Speculated Infected Period	Rash Appearing Date	Hospitalization Period	Immunization records
Index	5 yrs	Feb 4	Jan 22 - Feb 2	Feb 9	Feb 8 - Feb 11	a measles vaccine at 9 months old
Case 1	10 mos	Feb 17	Jan 31 - Feb 11	Feb 18	No hospitalized	No
Case 2	9 mos	Feb 18	Feb 4 - Feb 14	Feb 21	Feb 9 - Feb 12	No
Case 3	17 mos	Feb 22	Feb 5 - Feb 15	Feb 22	Feb 8 - Feb 10	No
Case 4	8 mos	Feb 15	Feb 5 - Feb 15	Feb 22	Feb 8 - Feb 15	No
Case 5	29 mos	Feb 19	Feb 7 - Feb 17	Feb 24	No hospitalized	No

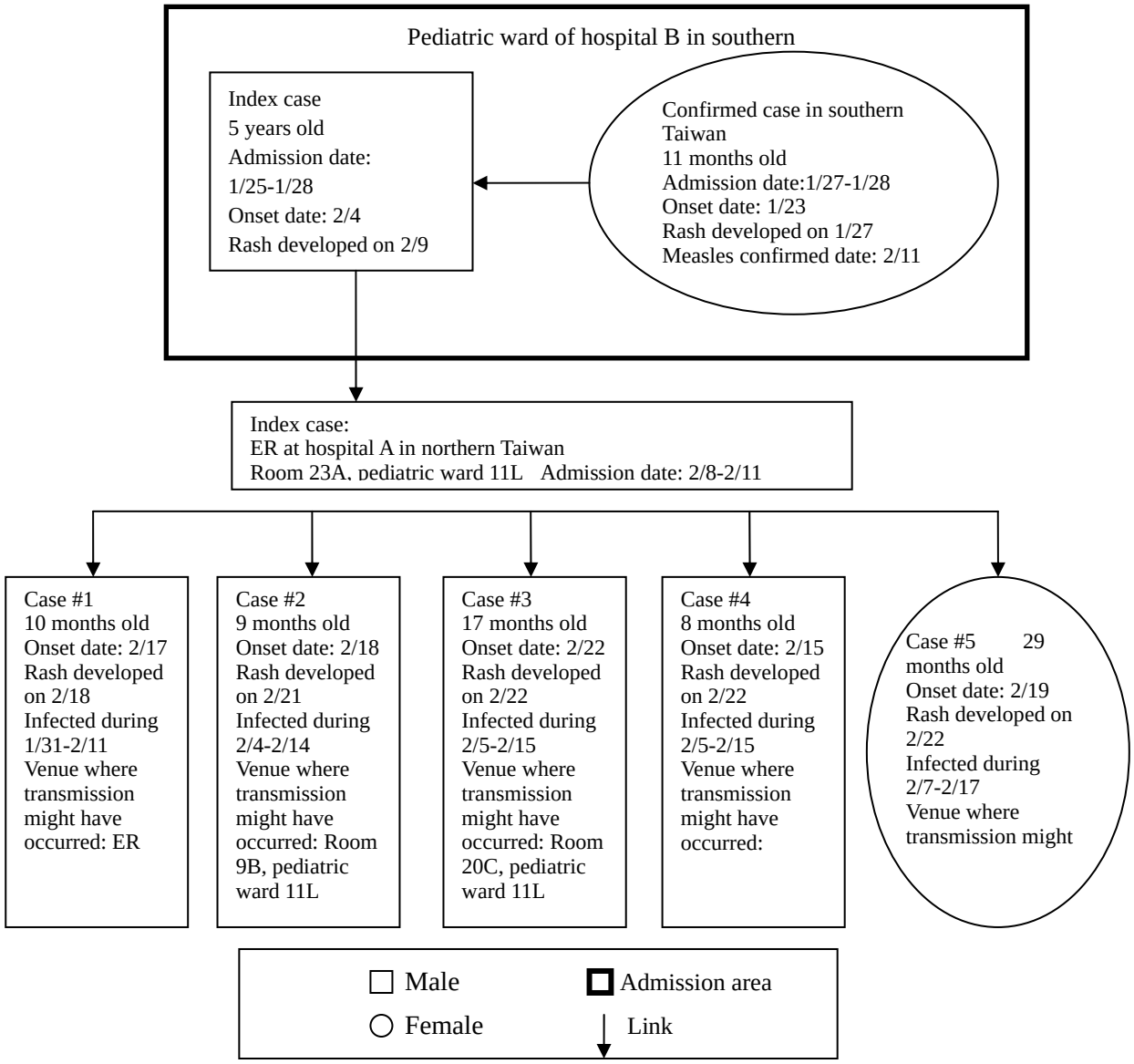

Figure 1. Epidemiologic link of the measles cluster cases in Taipei area, Taiwan, early 2009

Control and preventive measures

Based on the fact that the 5 confirmed cases distributed in Xin-Zhuang City, Shu-Lin City, and Lin-Kou Region, the Public Health Bureau of Taipei County investigated the measles vaccination status among the 3 towns, and results showed that coverage rates of MMR among children at the due age were all beyond 85%. In order to enforce the MMR supplementary vaccination, through "National immunization information system", children under age 7 who do not have vaccination record were screened. Then health stations continued to follow-up and proceeded to provide intramuscular immune globulin (IMIG) or MMR vaccine.

Public Health Bureau of Taipei County proceeded implementing the supplementary vaccination among 7,200 children of the due age (age 1-4), who haven't had MMR vaccine

through Chunghwa Telecom voicemails. Also, the message was sent to all hospitals and clinics in Xin-Zhuang City, Shu-Lin City, and Lin-Kou Region to enforce notification. At the same time, the announcement was sent by a press release to doctors regarding the measles differential diagnosis, and to remind the public on the measles-related symptoms. Besides, letters were sent to Taipei County Medical Association and public health centers in villages and towns to enforce notification and MMR supplementary vaccination.

The last case of this cluster was on February 24th, there was no additional case after 28 days (2 times of measles incubation period) reported, and the epidemic alert was lifted on March 24th.

Discussion and suggestions

Although measles immunization coverage is higher than 95%, there were still some small clusters. In order to protect people's health, routine education of parents, medical personnel, and travelers regarding immunization and prevention is still necessary. From the experience of this cluster, here are some advices on preventing the succeeding measles cluster:

A. Measles is very contagious and causes high morbidity. Through "National immunization information system" screen, enforcing the MMR supplementary vaccination to due age children who do not have vaccination record is recommended to control the epidemic quickly and effectively.

B. Investigate the immunization coverage among floating population and implement supplementary immunization if needed.

C. Due to high immunization coverage and unusual domestic measles cases, the insufficient experience on measles diagnosis among young doctors procrastinated reporting and prevention time, therefore, leads to the occurrence of this measles nosocomial outbreak. Training on measles differential diagnosis of first-line doctors should be enforced to avoid missing epidemic prevention time.

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