ISSN 1021-366X

An Epidemiological Investigation of Group A β-Hemolytic Streptococcus Infections and a Scarlet Fever Outbreak in a Private Kindergarten in Peitou District of Taipei City

Abstract

An epidemiological investigation of a scarlet fever outbreak and infections of group A β-hemolytic streptococcus at a private kindergarten in Peitou District of Taipei City on 27 November 2000 was conducted. The purpose was to understand the scale of infections of scarlet fever in the kindergarten and its routes of transmission for adequate disease control measures. The investigation took the forms of physician diagnosis, collection of throat swabs from suspects, follow-up of sources of infection, and establishment of surveillance and reporting system, instead of the conventional disease control measures of general screening and prophylactic medication. Control measures were group health education, encouraging individuals with symptoms for medical care, and disinfection of the environment. Of the 566 children, 39 teachers and employees, two scarlet fever cases and eight GABHS carriers (symptoms not meeting definition of scarlet fever) were detected by physician diagnosis and screening for symptoms. The attack rate of scarlet fever for the

kindergarten as a whole was 0.3% (2/605). Results of the investigation suggested that the location of the classroom of the cases, crowdedness of classrooms, long-time stay in kindergarten, and close personal contact were major routes of transmission. Follow-up of the sources of infection found that the index case had been infected with scarlet fever three times in six months. As no GABHS serotyping was made, it was not possible to decide whether the infections were by GABHS of the same serotype, or because of drug resistance, or other factors. More investigations are required.

Introduction

Group A β-hemolytic streptococcus (GABHS) can cause, generally, three different kinds of symptoms and diseases[1-4]. They include local infections such as streptococcal sore throat, and possibly pharyngitis, tonsillitis, and streptococcal skin infections (impetigo or pyoderma); invasive infections such as scarlet fever, puerperal fever, septicemia, otitis media, peritonsillitis, wound infections, and toxic shock-like syndrome, if GABHS enters the tissues; and secondary infections such as rheumatic fever and acute glomerulonephritis as a result of the unfavorable reactions caused by reactions of the immunity system of the host. From the viewpoint of public health, outbreaks of any of the diseases mentioned above, scarlet fever (which is classified as a Group B of Category III notifiable disease[5]) in particular, are serious and require investigation. According to Taiwan Provincial Records, large-scale outbreaks of scarlet fever occurred in 1934 and 1935, affecting 418 and 227 patients respectively. Ever since, the number of reported cases of scarlet fever had stayed around several tens a year[4]. Since 1984, the yearly number of

confirmed cases of scarlet fever had remained around 200[6]. By October 2000, the number of both the reported and confirmed cases of scarlet fever had increased suddenly to 451 and 811 respectively[6,7]. Though there had been clustering of scarlet fever during this period, few epidemiological investigations had been conducted[8-10].

Scarlet fever occurs in children of 3-8 years, more so in kindergarten children of 4-6[11]. On 27 November 2000, a child of a private kindergarten in Peitou District of Taipei City took sick leave for high fever, rash, and strawberry tongue. He was then taken to the Hsinkuang General Hospital for medical care. When it was diagnosed as scarlet fever, the case was immediately reported to the Department of Health, Taipei City Government. The Control of Communicable Disease Section of the Department of Health of Taipei City Government informed the Peitou District Health Center on 6 December. The Health Center visited the kindergarten on 11 December for investigation and examination of contacts. Specimens were then collected from 26 children. From them, 8 were detected GABHS positive. The Division of Surveillance and Investigation of the Center for Disease Control, DOH, for the relatively large number of GABHS infections and to prevent the spread of scarlet fever, sent a group of the FETP trainees for epidemiological investigation. This report presents the process of investigation and its findings for the investigations and control of scarlet fever.

Materials and Method

The investigation took the forms of physician diagnosis, collection of specimens from suspects, surveillance and reporting. They are summarized as follows.

The Environment and Activities of Children

The kindergarten is located in Peitou District of Taipei City in a space of about 8,000 m^2. The kindergarten contains 11 senior and junior classes respectively. The location of their classrooms is shown in Figure 1. Senior classes are located on the two ends of the first floor of the same building. Junior classes are on the first and second floors of another building. Each classroom accommodates 25-30 children. In general, areas in and out the classrooms are relatively spacious, and ventilation is good. Classrooms are divided into areas for classroom activities and special activities. Children learn, eat, and nap in their own classrooms. Though classrooms are spacious, the special activity area occupies a section of the classroom, children work, and play mostly in the classroom activity area. They sit close to each other during class hours, on eating and napping. Upon outdoor activities or after class, children of different classes can play together outdoors. At the time of the incident in December, air conditioning was not in use. Windows were open to allow the flow of fresh air.

Subjects for Study

The kindergarten has 566 children, 288 (159 males and 129 females) in the senior classes and 278 (175 males and 103 females) in the junior classes, and 39 teachers and employees.

Definition of Case

A GABHS carrier was defined as one who had throat swab specimen tested GABHS positive. By regulations on the reporting diseases[12], if the case developed further one of the three symptoms, strawberry tongue, rash, or desquamation of skin, he/she was defined as a typical confirmed case of scarlet fever. If no GABHS was isolated from throat swabs, and the case showed no symptoms of scarlet fever, he/she was defined as “normal”. A confirmed

scarlet fever case may have symptoms such as acute fever, sore throat, swollen throat or tonsillitis. They are, however, not necessary requirements for a confirmed scarlet fever case.

Diagnosis by Physicians and Screening for Symptoms

The index case is in the senior 10th class. The Health Department of Health of Taipei City Government asked a pediatrician of the Municipal Yangming Hospital to conduct screening of symptoms for all children of the senior classes on 16 December, and for children of the junior classes and all teachers and employees on 20 December. Throat swabs were collected from anyone with typical scarlet fever symptoms such as strawberry tongue, rash, desquamation of skin on hands and feet, and suspected symptoms such as swollen throat, sore throat, acute fever, and mucosal rash. Collection of specimens by classes is shown in Table 1. The Peitou District Health Center visited families of all confirmed scarlet fever cases and GABHS positive cases for follow-up. They were encouraged for medical care. Throat swabs were also collected from their family members. Swabs collected were placed in the Cary-Blair transport medium and sent to the Division of Laboratory Research and Development of the Center for Disease Control within 24 hours for laboratory testing.

Follow-up of Sources of Infection

For tracing the sources of infection, the index case was interviewed of his medical history and conditions of family members. Medical records of the index case were also reviewed to understand his medical care and treatment. His fellow classmates were interviewed of any GABHS symptoms in the past three months.

Laboratory Testing[13]

The throat swabs collected were inoculated on a blood plate of 5-10% sheep

blood, divided in four sections and punctured several times for better hemolysis. The plate was placed under 35-37 ℃, and cultured for 18-24 hours in air with 5% CO_2. If colonies of 0.5-1.5 mm in diameter, mucoid, glossy, cream colored, and of clear hemolytic zone were noted, it was that the red blood cells in the rings were destroyed, and this was the β-hemolysis. They were suspected colonies if gram-positive. Two to five suspected colonies were then picked up and inoculated on the blood plate, and cultured under 35-37 ℃ in air with 5-10% CO_2 for 18-24 hours for bacitracin susceptibility assessment and catalase testing.

In the bacitracin susceptibility assessment, suspected single colonies on the blood medium were cultured again. Then, a test strip containing 0.04 units of bacitacin (Difco Laboratories, Detroit, MI, USA) were put on the first section, cultured under 35-37 ℃ in air with 5-10% CO_2 for 18-24 hours. The appearance of inhibition rings indicates Group A streptococci. The accuracy of the bacitracin susceptibility assessment is poor, re-assessment was made by pyrrolidonylaminopeptidase (PYR) in the following procedure. Bacterial fluid of turbidity larger than McFarland No. 2 was prepared in 0.25 mL saline water, added one tablet of L-pyrrolidonyl-β-naphthylamide, and cultured under 35-37 ℃ for 4 hours. Three drops of aminopeptidase reagent were added. If colonies carried aminopeptidase, they would dissolve the substance to release β-naphthylamide. If they reacted with aminopeptidase reagent, the fluid would be in red color, and it could be decided to be Group A streptococcus positive. In the catalase testing, one drop of 3% H_2O_2 was placed on the plate, and fresh colonies were added in the fluid. If there were bubbles, they should be Group A streptococcus positive.

Disc diffusion test was used for the antibiotic sensitivity test of GABHS in the following way. Four to five GABHS-like colonies were picked up with sterile needle, inoculated in 4-5 mL tryptic soy broth (TSB) tube, and cultured under 35 ℃ in culture box with 5% CO_2. Allow the culture to reach a turbidity close to McFarland No. 0.5 $BaSo_4$ standard solution (equivalent to a bacterial quantity of $1.5x10^8$ CFU/mL). Dip a cotton swab in the fluid, pressed it gently against the tube to remove excess fluid. The swab was then inoculated on the Mueller-Hinton agar containing 5% sheep blood. Smear the swab on the culture plate on three directions (turn 60 degree each time) to allow bacteria to distribute evenly. Selected antibiotics were then placed on the culture plate, left under 35 ℃ in culture box containing 5% CO_2 overnight for 16-18 hours. Antibiotics used included Cefotaxime (CTX), Erythromycin (E), Ofloxacin (OFX), Oxacillin (OX), Penicillin-G (PG), Chloramphenical (C), Sulfamethoxazole Trimethprin (SXT), Rifampin (RA) and Clarithromycin (CLR). Measure the diameters of the inhibition rings. NCCLS standards were used to assess the susceptibility and drug resistance or intermediate of antibiotics.

Group Health Education

To gain the confidence and cooperation of the kindergarten and parents, talks on the basics of scarlet fever, its epidemiology, and the investigation to be made and control measures taken, was given to the teachers and employees. Children were asked to take home leaflets on scarlet fever. Parents of confirmed scarlet fever and GABHS cases were asked to come to the kindergarten for individual health education. They were also urged to take their children for medical care. These measures allowed teachers and parents to understand the infection of scarlet fever and GABHS in the kindergarten and the control measures that the kindergarten had taken to avoid unnecessary

panic.

Disinfection of Environment

To avoid damage of disinfectants on children, β-Iodine of lower volatility supplied by the Peitou District Health Center was used. On the weekend, 17 December, the kindergarten as a whole, including chairs and desks, was totally cleaned and all windows open to allow fresh air ventilation. The kindergarten was suggested to periodically wash the curtains and screenings of the air conditioners.

Results

With the exception of 10 children not screened for sick leave, 595 of the 605 children, teachers and employees of the kindergarten had been screened for suspected scarlet fever symptoms, at a screening rate of 98.3%. Throat swabs were collected from classmates (contacts) of the index case and children with suspected symptoms, 42 in total, at a collection rate of 7.1% (42/595). Altogether, a total of two scarlet fever cases were confirmed, one from the 10 GABHS positive cases, and one was the index case. The 10 children on sick leave were followed up by telephone to know that they did not have any symptoms of scarlet fever nor fever, sore throat, or tonsillitis. The attack rate thus was 0.3% (2/605). Families of confirmed scarlet fever cases and GABHS positives were also screened to find five GABHS cases. None of them had any of the above-mentioned symptoms.

The index case was treated and reported as scarlet fever by the Hsinkuang General Hospital on 17 June 2000. The clinical symptoms were fever, vomiting, rash, and strawberry tongue. Drug resistance test showed that the case was sensitive to the antibiotics Cephalexin Monohydrate (Keflex) used by the Hospital. After 10 days treatment of Keflex, the symptoms disappeared.

The case developed again fever, rash, and strawberry tongue on 27 November, and was reported as scarlet fever by the Hsinkuang Hospital. He was also treated with Cephlexin Monohydrate and cured, though the drug sensitivity test showed resistance to Co-trimoxazol (Bactrim). Re-examination of the case on 16 December by the Division of Laboratory Research and Development of the Center for Disease Control still found GABHS positive. The case was referred on 20 December to the Municipal Yangming Hospital for care. The Hospital, for the strawberry tongue, gave the case Amoxicillin for two days, and conducted testing of urine, blood and throat swab. Testing of urine and blood was normal, and throat swab showed negative to GABHS. Amoxicillin was given for seven more days.

Findings of the antibiotic sensitivity test conducted by the Division of Laboratory Research and Development of the Center for Disease Control are shown in Table 2. GABHS strains were found to be resistant to Cefotaxime, Sulfamethoxazole Trimetinprin, Rifampin and Clarithromycin; sensitive to Erythromycin, Lfloxacin and Oxacillin; and intermediate to Penicillin-G and Chloramphenicol.

Discussion and Conclusion

Literature[14] indicates that in general, about 20% of school age children are GABHS carriers. That the GABHS positive rate in this kindergarten was a low 1.8% (10/605). It was probably due to the fact that the investigation was not a general screening of all children, laboratory testing was performed only on children with suspected symptoms initially screened by a physician. The positive rate thus was low. Two of the 10 GABHS positive cases were confirmed scarlet fever for their typical symptoms of high fever, rash, strawberry tongue, and rash on circumoral pallor. The rest eight without

typical scarlet fever symptoms were GABHS carriers for their general symptoms of swollen throat, sore throat, tonsillitis, or enlarged lymph glands. Differences in symptoms were probably brought about by the immunity, nutrition[15], and physical conditions of the cases, and the amount or serotypes of bacteria. The two confirmed cases were given antibiotic treatment for ten days. Parents of the GABHS cases were suggested to take their children for medical care. Some reports were that the communicability and chances of developing complications of GABHS positive cases were not significant[14]. Some physicians were of the opinion that GABHS was a commonly found germ in humans, asymptomatic carriers required no treatment. Some physicians, however, insisted on antibiotic treatment to avoid complications. Further studies are needed in this regard.

GABHS that induces scarlet fever exists commonly in the respiratory tracts and skins of humans. It is transmitted primarily by droplets, and sometimes by direct or close contact with patients or carriers[1,3]. Each class of the kindergarten accommodated some 30 children; the room was fairly spacious. However, as all teaching activities were carried out in classrooms, and a large part of the classroom was fully decorated on certain theme, the space available for children's activities was limited and crowded to increase chances of personal contacts. Weiss et al.[16] suggested that chances of developing the same GABHS type as the index case increased after contact of more than 24 hours a week with the index case. Of the 26 (not including the index case) of the class of the index case, 8 were identified GABHS, and one each from the two neighboring classes. Date of onset was known for the index case only, the rest cases were identified through screening, not knowing their dates of onset of symptoms. By geographic relations and long-time close contact of children,

the incident was considered to be induced by personal contacts.

Before the Second World War, scarlet fever was regarded as a serious communicable disease of high fatality. Since the birth of antibiotics, scarlet fever has been effectively controlled, and even eradicated in some developed countries[17]. For its high communicability and possibility of developing serious complications, scarlet fever is still listed as a Group A Category III communicable disease for control[5]. In the case of scarlet fever outbreaks, local health authorities usually conduct general screening and prophylactic medication. This process requires a large amount of manpower and facilities, and may also cause public panic. In the present investigation, in addition to the disease control workers of the local health center, epidemiologists and pediatricians had also participated. The pediatrician first made a general screening of symptoms for all children. Specimens were then collected from children with suspected scarlet fever symptoms. Parents were told to take the children for medical care if GABHS was identified in their throat swabs. Results of antibiotic testing were provided to the Hsinkuang General Hospital and hospitals treating GABHS positive cases for their reference in the use of antibiotics. A surveillance and reporting system for suspected scarlet fever symptoms was then established in the kindergarten to report suspected cases each day. The system was maintained till a week after the appearance of the last case (about two incubation periods of scarlet fever). The scarlet fever outbreak was officially declared over when the two confirmed cases and eight GABHS carriers were tested negative after re-examination. Group health education on scarlet fever and its epidemiology for teachers and employees of the kindergarten was considered essential to help them understand the situation and to prepare them for the inquiries of parents to gain their cooperation.

The index case in this incident was diagnosed scarlet fever by the Hsinkuang General Hospital and the Municipal Yangming Hospital respectively on 17 June, 27 November, and 20 December. Clinical symptoms disappeared after the initial two treatments, and the case was announced cured. In the two treatments, however, no re-examination for GABHS and its typing were made, it was difficult to decide whether the second and third infections were new infections or continued infections from the first one. It could have been a new infection. Kaplan[18] reported that three children in a family were infected at different times in four years by the same or different types of Group A *streptococcus*. If infection was continued from the past, drug resistance of GABHS strains would be a serious problem. Drug resistance could be due to cases not taking drugs regularly or cases infected by primary drug resistant strains. By interviewing the mother of the case, it was confirmed that the case took medicines regularly. He was probably infected by primary drug resistant strains. In the first two treatments, the Hsinkuang General Hospital had conducted drug resistance test of the cultured strains and found that they were sensitive to Cephalexin Monohydrate. However, human immunity system is more complex than the laboratory environment, antibiotics found effective in laboratory testing may not necessarily be effective on human body. Gerber[19] is of the opinion that failures in the treatment of GABHS infections can be clinical and bacteriological. The first and second treatments at the Hsinkuang General Hospital were clinically successful. However, for the lack of re-examination, it was difficult to decide whether they were bacteriologically so.

Laboratory testing by the Division of Laboratory Research and Development of the Center for Disease Control is only to decide whether cases are GABHS positive, no serotyping is made. It was therefore not possible to

decide the three infections of scarlet fever of the case in one year were repeated infections caused by different strains or whether they were the same infection of one strain because of drug resistance. Serotyping is most important. It helps to understand the epidemiological changes of diseases caused by GABHS; to detect the clustering or outbreaks of GABHS infections; to differentiate causes of exposure or clinical characteristics; or to offer recommendations on treatment or disease control[17]. In general, GABHS can be typed by its M or T protein[20,21]. Clinical manifestations of infections by different serotypes are different. For instance, T4, T11 and T12 are associated with scarlet fever[22-24]; the virulence factors of M-1, M-3 and M-16 will, in addition to inducing scarlet fever, induce rheumatic fever and acute glomerulonephritis[25].

The drug resistance test conducted by the Division of Laboratory Research and Development used the kinds of antibiotics recommended by the US National Committee for Clinical Laboratory Standards. These antibiotics are not quite the same as the ones used by medical care institutions in Taiwan or reimbursed by the National Health Insurance. Findings of the drug resistance test will have little help to medical care institutions in the selection of antibiotics. We suggest that the Division of Laboratory Research and Development needs to know the antibiotics used by medical care institutions in Taiwan or reimbursed by the National Health Insurance and uses them to conduct any corresponding drug resistance tests. Findings thus obtained will be more useful to medical care institutions in the use of drugs.

Prepared by: Jiang DD[1], Huang CC[2, 3], Chen YY[4], Lin LR[5]

1. Division of Surveillance and Investigation, CDC, DOH
2. FETP, Division of Surveillance and Investigation, CDC, DOH

3. Bureau of Chronic Disease Control, Kaohsiung County

4. Division of Laboratory Research and Development, CDC, DOH

5. The Chronic Disease Control Station of Kaohsiung County Government

Please direct correspondence to Dr. Jiang DD.

Acknowledgment

Thanks are due to the Health Department of Taipei City Government, Peitou District Health Center, the Municipal Yangming Hospital, and the kindergarten for their assistance in the investigation.

References

1. Stevens DL. Invasive group A streptococcal infections: the past, present and future. Pediatr Infect Dis J 1994; 13: 561-566.
2. Control of Communicable Disease Manual, 16th ed. American Public Health Association, 2000; 470-476.
3. Bannister BA, Begg NT, and Gillespie SH. Infectious Diseases. Oxford, Balckwell Science Ltd., 1996; 114-116
4. Center for Disease Control, DOH. Communicable Disease Control Manual. February 2001, Scarlet Fever-1 – Scarlet Fever-8.
5. Center for Disease Control, DOH. Laws and Regulations on Communicable Disease Control. February 2001; 1-11.
6. Center for Disease Control, DOH. Information System on Cases of Communicable Diseases.
7. Center for Disease Control, DOH. Report of Cases of Category III Notifiable Diseases. Epidemiology Bulletin 2000; 16(11): 571.
8. Hsueh PR, Teng LJ, Lee PI, et al. Outbreak of scarlet fever at a hospital day care center: analysis of strain relatedness with phenotypic and genotypic characteristics. J Hosp Infect 1997; 36(3): 191-200.
9. Lu HC, Chao TY, Chiu CS, et al. An epidemiological study of a scarlet fever outbreak in a kindergarten in Taichung City. Epidemiology Bulletin July 1998; 14(7): 227-236.
10. Chiang TH, Lien HL, Tu CC, et al. An investigation of a scarlet fever outbreak in a nursery in Taichung City. Epidemiology Bulletin 2001; 17(6): 287-295.

11. Huang YC. Scarlet fever. J of Nosocomial Infect Contr 1996; 6(5): 262-265.
12. Center for Disease Control, DOH. Definitions for the Reporting of Notifiable Diseases. 2000; 9.
13. Center for Disease Control, DOH. Standard Operational Procedures for Laboratory Testing for Disease Control. 2001; 1-52 – 1-54.
14. Michael A. Treatment failures and carriers: perception or problems? Pediatr Infect Dis J 1994; 13: 576-579.
15. Duncan CJ, Duncan SR, and Scott S. The dynamics of scarlet fever epidemics in England and Wales in the 19th century. Epidemio Infect 1996; 117: 493-499.
16. Weiss K, Laverdiere M, Lovgren M, et al. Group A *streptococus* carriage among close contacts of patients with invasive infections. Am J Epid 1999; 149 (9): 863-868.
17. Efstratiou A. Group A streptococci in the 1990s. J Antimicrob Chemother 2000; 45 Suppl: 3-12.
18. Kaplan EL. Public health implications of group A streptococcal infections in the 1990s. Pediatr Infect Dis J 1994; 13 (6): 580-583.
19. Gerber MA. Treatment failures and carriers: perception or problem? Pediatr Infect Dis J 1994; 13 (6): 576-579.
20. Lancefield RC. Current knowledge of type-specific M antigen of group streptococci. J Immunol 1962; 89: 307-313.
21. Griffith F. The serological classification of *Streptococcus* pyogenes. J Hygiene 1934; 34: 542-584.
22. Ohga S, Okada K, Mitsui K, et al. Outbreaks of group A Beta-hemolytic streptococcal pharyngitis in children: correlation of serotype T4 with scarlet fever. Scand J Infect Dis 1992; 24: 599-605.
23. Pan TM, Lin SS, Yu YL, et al. Serotype distribution and antimicrobial susceptibility of group A streptococci (*streptococcus* pyogenes) isolated in Taiwan. Zhonghua Min Guo Wei Sheng We Ji Mian Yi Xue Za Zhi 1996; 29 (3): 153-161 (in Chinese).
24. Espinosa de lost Monteros LE, Bustos IM, Flores LV, et al. Outbreak of scarlet fever caused by an erythromycin-resistant *streptococcus* pyogenes emm22 genotype strain in a day care center. Pediatr Infect Dis J 2001; 20 (8): 807-809.
25. Markowitz M. Changing epidemiology of group A streptococcal infections. Pediatr Infect Dis J 1994; 13: 557-560.

Table 1. Collection of Specimens and Laboratory Testing for Children with Suspected Scarlet Fever Symptoms

Class		No.	Specimens Collected	Clinical Symptoms	GABHS (+)	No. of Confirmed Cases
December 16	Sr-1	26	0		0	
	Sr-2	25	0		0	
	Sr-3	27	0		0	
	Sr-4	26	0		0	
	Sr-5	27	0		0	
	Sr-6	29	2	Sore throat	0	
	Sr-7	25	2	Sore throat、strawberry tongue、rash	1	1
	Sr-8	26	5	Fever、swollen throat、sore throat	1	
	Sr-9	25	0		0	
	Sr-10*	27	26	Fever、rash around mouth、strawberry tongue	8	1 (index case)
	Sr-11	25	2	Swollen throat、sore throat	0	
December 20	Jr-1	25	1	Swollen throat	0	
	Jr-2	25	1	Enlarged lymph glands	0	
	Jr-3	25	1	Suspected strawberry tongue	0	
	Jr-4	26	0		0	
	Jr-5	26	0		0	
	Jr-6	26	0		0	
	Jr-7	25	0		0	
	Jr-8	25	0		0	
	Jr-9	24	0		0	
	Jr-10	25	0		0	
	Jr-11	26	1	Swollen throat、sore throat	0	
Make-up testing for Children on sick leave		24	1	Tonsillitis、swollen throat	0	
Teachers and employees		39	0		0	
Total		605	42		10	2

*testing for contacts

Table 2. The Results of Antibiotic Sensitivity Test for GABHS（+）Children

Cases	CTX		E		OFX		OX		PG		C		SXT		RA		CLR	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
1*	22-23	R	20-21	S	20-21	S	18-19		23-24	I	21-22	S	0	R	17-18	I	15-16	R
2	24-25	R	19-20	I	17-18	S	20-21	S	24-25	I	18-20	I	0	R	15-16	R	15-16	R
3	22-23	R	21-23	S	18-19	S	18-20		25-26	I	18-20	I	0	R	21-22	S	19-20	I
4	22-23	R	20-21	S	16-17	S	19-20		27-28	S	20-21	S	0	R	20-21	S	17-18	I

*Index case

Antibiotics：CTX：Cefotaxime；E：Erythromycin；OFX：Ofloxacin；OX ：Oxacillin；PG：Penicillin-G；C：Chloramphenicol；SXT：Sulfamethoxazole Trimethprin；RA ：Rifampin；CLR：Clarithromycin。

Antibiotic sensitivity：R：Resistance; I：Intermediate；S：Sensitive。

1：Inhibition ring by nm;2：Sensitivity