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An Epidemiological Investigation of a Suspected Meningococcal meningitis Outbreak at a Military Camp

Abstract

On 4 June 2001, the Third Branch Bureau of the Center for Disease Control received a report from a medical center in central Taiwan of a death from meningococcal meningitis. The case was, at the time of death, undergoing training at a military camp. It was reported that the camp had also sent about 20 patients with fever to a military hospital for treatment under isolation. An investigation was soon conducted to ascertain the likelihood of a meningococcal meningitis outbreak in the military camp. The investigation revealed that the death was the only confirmed case of meningococcal meningitis. The 24 suspected cases confined under isolation and 49 more soldiers who had had fever and headache in the previous two weeks were found to be not positive by clinical diagnosis and laboratory testing. To prevent the spread of infection, all officers and soldiers of the camp, staff of the hospitals in contact with the deceased, family members, and other soldiers were given prophylactic medication; disinfection of the environment was carried out and health education provided. No further cases were reported since, thus the incident was considered sporadic.

Introduction

The pathogenic agent of meningococcal meningitis is *Neisseria meningitidis*, a Gram-negative diplococcus. Neisseria *meningitidis* is grouped according to its polysaccharides into 13 serotypes. Serotype A is the main cause of global epidemics. About 50% of sporadic cases are caused by serotype B, and 20% by serotype C. Generally speaking, one epidemic cycle lasts about 8-12 years. In the non-epidemic period, serotype A induces about 1-2% cases. Other pathogenic serotypes of lesser virulence such as W-135, X, Y and Z have been identified recently(1,2).

Though Meningococcal meningitis is now a sporadic communicable disease in Taiwan, there were been several outbreaks in the past, between 1919 and 1926, and again between 1933 and 1946, with about 300 reported cases each year. Since 1946, the number of reported cases has declined to about 20-30 each year. In the last few years, though the number of reported cases has increased, no outbreaks, have been reported. In the seven months between January and July 2001, there were 61 reported cases; 33 of them were confirmed. Of the confirmed cases, seven died. Though the number of suspected cases reported for the year 2001 increased more than that of previous years, and the distribution of serotypes was also different, the possibility of further outbreaks remains to be further investigated(3).

On 4 June 2001, the Third Branch Bureau of the Center for Disease Control received a report from a medical center in central Taiwan of a death from meningococcal meningitis. During the period prior to illness and subsequent death, the case had been undergoing training in a military camp. It was reported that the camp had also sent about 20 soldiers with fever to a military hospital for treatment under isolation. To determine the likelihood of a meniningococcal meningitis outbreak in the camp, an investigation was conducted with the collaboration of the Investigation Center for Complex Diseases, the Surgeon General's Office of the Ministry of National Defense, and the National Institute of Preventive Medicine.

Materials and Method

1.Contents of the Investigation

The soldier in question was enrolled on 14 May. He developed fever on the evening of 31 May, and was referred to two different hospitals. He died on the morning of 1 June at a medical center in central Taiwan. The present investigation covered three specific areas: 1) review of medical records of all officers and soldiers of the camp during the period from 16 May to 4 June 2001 to detect any further transmission of meningococcal meningitis in the camp; 2) investigation of the clinical symptoms of the 24 suspects treated under isolation and laboratory testing of their blood specimens and pharyngeal swabs to confirm the infection; and 3) study of the location of the living quarters of the deceased and the 24 suspects to establish their epidemiological relationship.

2.Investigation of the Environment

Inspections were made of the camp to assess the quality of sanitation of the environment, facilities, and ventilation in the living quarters. A map showing the general location of the camp and a diagram of the living quarters of the deceased and his bed were drawn. Inquiries were also made into the social life and daily activities of the deceased to determine his state of health and his contacts with fellow soldiers before his sudden death. Efforts were also made to identify the index case in order to trace the mode and direction of transmission and thereby to be able to effectively control and prevent further transmission of the disease.

3.Collection of Specimens and Laboratory Testing

A team from the local health station visited the military camp soon after the report on 4 June to collect 49 pharyngeal swabs from soldiers who had had fever and headache in the previous two weeks. Blood specimens and pharyngeal swabs were also collected from the 24 suspected cases undergoing isolation. They were sent to the Third Branch Bureau of the Center for Disease Control for laboratory testing.

Blood and CSF specimens should be collected from suspected meningococcal meningitis cases before antibiotic treatment and transported at room temperature (22-25 ℃)immediately to the laboratory in order to isolate pathogenic agents. Since about 5-15% of the general population carries various types of bacteria in the nasopharynx, and the rate can be higher in the military[(1)], laboratory testing of pharyngeal swabs is of less importance clinically. The amount of blood drawn for testing should be at least 5 cc; the amount of CSF should be, if possible, more than 2 cc. Blood is inoculated directly into a blood agar jar containing 0.025% of SPS, and maintained at 35 ℃ for multiplication in a 5% CO_2 box for 14-17 hours and observed. If the fluid appears turbid or hemolysis of RBCs occurs, the fluid is immediately mixed evenly and placed on chocolate agar culture medium for 48 hours. CSF is inoculated directly onto chocolate agar for culture overnight at 35 in a CO_2 box. The colony of *Neisseria meningiditis* on the chocolate agar is 1 mm by diameter, protruding, smooth bright circular, colorless or grayish. 2-5 suspected colonies are picked up and inoculated on chocolate agar for culture at 35-37 ℃ and 5-10% CO_2 for 18-24 hours for assay[(4-8)].

4.Definition of Case

A case was defined as any officer and soldier of the military camp who was a（1）suspect: laboratory testing positive of CSF antigen; or clinical, appearance of sudden petechial rash with pink macules but with a negative blood culture;（2）confirmed case: with clinical symptoms, and isolation of *N. ningitidis* fr suspected case: laboratory testing positive for CSF.

Results

1.The Deceased

The case was enrolled at the camp on 14 May 2001, and was on home leave from 25-27 May. The father said the case was not feeling well for a week before home leave but did not seek medical treatment. He took some over the counter medicine from a drug store. At 7 p.m. on 31 May, the army had night drill. At 7:40 p.m. on the same day, the case developed fever, and was taken to a hospital for an IV infusion. Later, though the fever decreased, his condition was not stable. At 1:20 a.m. on 1 June, the case was referred to Medical Center A in central Taiwan when he developed chest congestion and hypotension. At 4:30 a.m. on the same day, the case was referred to Medical Center B due to shock. He died at 7:30 a.m. His symptoms were fever, dyspnea, and confusion. *N. mengingitides* (serotype B) was isolated from the blood specimen on 4 June by Medical Center B.

2.Review of Medical Records

A review of the medical records of all officers and soldiers of the military camp for the period between 16 May and 4 June showed that 26 individuals had visited the dispensary for fever during that period. 10 of them were treated with antibiotics. A review of medical records undertaken by members of the investigation center for complex diseases showed that the 26 had upper respiratory tract infection but not symptoms of meningococcal meningitis. They did not meet the definition of a case.

3.Diagnosis of the 24 Suspects under Isolation

After a review of the camp medical records was undertaken, the investigation team, together with members of the investigation center for complex diseases, the Surgeon General's Office of the Ministry of National Defense, and the National Institute of Preventive Medicine, visited the 24 suspected cases at the military hospital. The condition of the 24 suspects was fairly stable. 10 of them were in the same company as the deceased; and eight of them had shared the same living quarters with the deceased. Clinical diagnosis showed that 22 of the suspects did not have fever at the time of hospital admission. The two soldiers who had fever were diagnosed to have viral infection of the upper respiratory tract. All blood specimens of the 24 suspects were reported negative for *N. meningitidis*, though three pharyngeal swabs were reported positive. The three with positive pharyngeal swabs did not share the same living quarters with the deceased. About 5-15% of the general population carry bacteria in the nasopharynx, and the rate of carriage can be higher in the military(1). Of the 49 pharyngeal swabs collected by the local health station from soldiers of the military camp who had had fever and headache in the previous two weeks, five were found to be positive.

4.Living Accomodations of the Deceased and the 24 Suspected cases

The camp of the deceased and other camps are located some distance apart; the nearest one is 500 meters away. All soldiers of the camp shared living quarters in three two-story buildings 30 meters apart. The camp had five companies of 638 soldiers; and the third company to which the deceased belonged had 140 soldiers. The occurrence of a suspected outbreak of meningococcal meningitis in a military camp had already been widely reported by the media, and there were a large number of reporters present when the investigation team arrived. To avoid any unnecessary confrontation, the team did not inspect the living quarters of the deceased, but asked the doctor to draw a diagram indicating the position of beds of the 24 suspects. It can be noted from the diagram that ten suspects being treated under isolation were of the same (third) company as the deceased; eight of them shared the same living quarters with the deceased, though only one was next to him; the remaining seven were 10 meters away. The ten were fever free soon after hospital admission.

5.Preventive Measures

The field investigation revealed that the deceased was the only confirmed case of meningococcal meningitis. Though the 24 suspected cases under isolation and the 49 soldiers who had had fever and headache in the previous two weeks were in the same camp, they were not of the same company. The third company to which the deceased belonged had a higher rate of suspected cases, all 140 soldiers of the company were given prophylactic medication. Prophylactic medication was also given to members of the medical centers, family members and other soldiers in contact with the deceased. The environment was disinfected. All officers and soldiers were given health education on the control of meningococcal meningitis. Since then, no new cases have been reported. Thus this was considered to be an independent incident.

Discussion and Conclusion

Mengingococcal meningitis exists worldwide. It occurs more often in spring and autumn. In 1805, Vieusseaux reported for the first time on meniningococcal meningitis and *Neisseria meningitidis* bacteremia(9) when meningococcal meningitis was causing an epidemic in Geneva. He reported that the outbreak was sudden and violent, and that most patients had symptoms such as distorted facies, feeble pulse, and severe pain. Most patients died 24 hours after onset with pink macules all over the body. They were unconscious and confused before death. The entire process was short and sudden[10]. In 1884, Marchiatava and Chlli detected for the first time the pathogenic agent in meningitis filtrate. In 1887, Weichselbaum obtained a pure culture of the agent from the cerebrospinal fluid of a patient and made a detailed description of it. It was recorded and reported by Jaeger in 1895. Through the efforts of other researchers in later years, *Neisseria meningitidis* was finally confirmed to be the pathogenic agent of meningococcal meningitis[11].

The infection is transmitted primarily either by droplets or through direct contact with asymptomatic carriers. The incubation period is less than four days. Early diagnosis and treatment usually decreases the mortality rate to less than 10% with a fair prognosis. Literature shows that during non-epidemic periods, the asymptomatic carrier rate is about 5-10%. However the rate can be as high as 60-80% in crowded places such as an army base, among pilgrims, in boarding schools, jails, institutions, etc. The rate may increase to higher than 95% during epidemics. The carrier status may last from several months to several years[12]. The present incident of a suspected outbreak occurred in a military camp. Those living in closed or semi closed and crowded communities are often more susceptible to meningitis infection. There have been reports of outbreaks in military training centers and detention centers[13,14]. Several young people have already died of the disease this year. Precautionary measures, therefore, should be taken after clarifying the present incident.

Of the 73 blood specimens and pharyngeal swabs collected for laboratory testing in the present incident, only the blood specimen of the deceased and eight pharyngeal swabs tested positive, indicating that there were still a number of nasopharyngeal carriers in the military camp. One difficulty in the prevention and control of meningococcal meningitis is that groups at risk for meningococcal meningitis cannot be easily categorized by age, ethnicity, sex or even by locality. Some individuals develop serious symptoms after infection, and even die; and some are asymptomatic carriers. One possible reason is that patients with serious symptoms may have some deficiency of the immune system, and once they are in contact with *N. meningitidis*, they quickly develop invasive meningococcal disease(12). When serum bactericidal antibodies are not functioning normally, the risk of developing invasive meningococcal disease increases. A deficiency of the immune system may include: deficiencies in serum bactericidal antibodies, the complement system, and lack of immunoglobulin. Individuals suffering from multiple myeloma, chronic leukemia, renal disease, alcoholism, or having been pancreatectomized, may have reduced amounts or functional defects of immunoglobulin (15). C_3 plays an important role in complement reaction. Its deficiency will increase the risk of infection. Reports show that about 10-20% of invasive meningococcal disease in adults is associated with complement deficiency(16). Migration and travel are other factors associated with infection. There have been, for instance, outbreaks of serotype A infection in pilgrims to Mecca(13,17). Meningococcal meningitis infection is seasonal. In the epidemic areas of Africa, for instance, the infection often begins in the dry season, and declines in the rainy season. In other sporadic areas, infection occurs more often in spring and autumn. The number of cases starts to increase in December, reaches a peak in March and April of the following year, and declines gradually in May. This seasonal trend is similar to that of other viral and bacterial infections of the respiratory tract(13). This factor should be taken into consideration in diagnosis. Many studies have pointed out that smoking and second-hand smoke can damage the mucous membranes of the nasopharynx, and adversely affect the defense mechanisms of the mucous membranes, increasing the risk of infection[13,18]. Individuals with other infections such as viral infections of the respiratory tract and infections with other microorganisms are noted to have a higher risk of invasive meningococcal disease[13]. Though HIV infection though has not been found to be associated with *N. meningiditis* infection in the high epidemic areas of Africa, it is a risk factor in other sporadic areas[12]. Though no immune or complement deficiencies were noted in the deceased, the father said that the deceased was not feeling well a week before home leave. He was not treated by a physician, but took some medicine from a drug store. Whether influenza infection was a factor in the development of the invasive meningococcal disease remains unknown.

In the early stage of *N. meningitidis* infection, patients may develop cold-like symptoms such as sore throat, headache and cough. There will be a sudden onset of fever, chills, intense headache, stiff neck, muscle pain, fatique, vomiting, somnolence or twitching. In the early stage, macules or nettle rashes may appear on the skin. In serious cases, disseminated intravascular coagulation may cause petechiae, purpura, and other hemorrhagic manifestations eventually leading to shock, coma or death. Other likely complications are conjunctivitis, endocarditis, pericarditis, myocarditis, pneumonia, and suppurative arthritis. Early diagnosis and adequate supportive treatment may decrease mortality considerably. However, the mortality rate of fulminant *N. meningitidis* septicemia is still high. The mortality rate before the advent of antibiotic treatment was about 50%. Early diagnosis and appropriate antibiotic treatment can decrease the mortality rate to less than 10%[11,19]. Clinicians should be more vigilant in their diagnosis of patients. Patients with symptoms such as fever, petechiae, changes in consciousness and stiff neck should be suspected of *N. meningitidis* infection. Further laboratory testing should then be conducted in order make an early diagnosis and provide adequate antibiotic treatment, thereby bringing down the mortality rate to the minimum. The deceased in the present incident had fever as the only early symptom. Later, he developed dyspnea and confusion, without however developing any typical symptoms such as petechiae, macules and stiff neck. He was, therefore, not given antibiotic treatment in time. There seems to be an increase in the number of meningococcal meningitis cases this year. The importance of the timely use of antibiotics should be advocated and promoted by local medical associations to their members in order to improve the survival rate of acute meningococcal meningitis infection.

Thus far, penicillin G has been found to be the antibiotic of choice[11,19]. It should be administered for at least seven days or until the fever subsides. If the patient is allergic to penicillin G, chlorophenicol, cefotaxime, or ceftriaxone can be considered. The patient should be given rifampin for two days before discharge from hospital to ensure that Meningococcal colonization of the oropharynx is completely eradicated[19]. Supportive treatment is of the utmost importance to comatose patients. Their blood pressure, pulse rate, arterial blood gases, oxygen saturation, cardiac output, periferal vascular resistance, pulmonary artery wedge pressure, arterial oxygen differential should be carefully followed. Some studies indicated that though short-term use (2-4 days) of dexamethasone did not decrease the mortality rate, it might reduce the risks of sequelae[20]. Prophylactic medication can be given to individuals in close contact with patients.

Close contacts are defined by the World Health Organization as 1) those who live with the patient, 2) persons caring for the patient during the daytime, the nurses for instance, and 3) persons in contact with the nasopharyngeal secretions of the patient, other hospital staff for instance. Recommended antibiotics and dosages for prophylactic treatment are shown in Table 1[13]. When administering prophylactic medication in semi-closed areas such as military camps or nurseries, if the strains in question are sensitive to sulfa drugs, sulfadiazine can be used in all cases to reduce carrier rate and prevent the spread of the infection. Drug resistance to rifampin has been reported[21]. Its use is recommended only for family members and close contacts of the patient. In the present incident, the soldiers lived together, and the illness was reported widely by the media. No drug resistance testing had been performed on the confirmed case. To prevent further cases, prophylactic medication was given to family members, officers and soldiers of the same battalion and company, and medical staff caring for the patient.

Immunization is another preventive measure in addition to prophylactic medication. However, immunization is only recommended for high epidemic areas; it is not recommended as a preventive measure in sporadic areas[13]. Individuals of high-risk groups such as patients having undergone pancreatectomy, persons with complement deficiencies, or persons intending to visit high epidemic areas, may consider immunization. Vaccines against serotypes A, C, Y, and W-135 are now available.

Recommendations

1.Pressure from the media: Intensive coverage by the media of the present incident presented considerable difficulties to the investigation. To avoid reporters, schedules often had to be changed. When the team arrived at the camp, the camp was already flooded with reporters. The presence of reporters caused great inconvenience to the specialists of the investigating team. As large numbers of reporters gathered outside the living quarters of the deceased, it was decided not to investigate the living quarters but to ask the medical officer to draw a diagram. Pressure from the media not only poses an inconvenience for the investigators, but its unverified or unconfirmed reporting can also be a hindrance to proper disease investigation. It is therefore recommended that a press release be made once a day at a fixed time by a designated spokesperson.

2.Privacy of patients: Hospitals often release information about patients without consent of the parties concerned. This not only harms the patients and disturbs their families; it may present the investigation team with unnecessary obstacles in their investigation. Though the Law for the Control of Communicable Diseases has rules that define the role of hospitals in disease prevention and control, the regulations are most probably not familiar to the hospital administration and their staff. More should be done by the health bureaus to instruct hospitals about their responsibilities.

3.Training in the collection and testing of specimens: because Meningococcal meningitis is relatively unknown in Taiwan, it is not familiar to most healthcare workers. Healthcare workers may, therefore, make mistakes in the procedure of specimen collection and transportation. In the handling and specimen collection of rare communicable diseases, healthcare workers should first consult the manual on the collection of specimens to minimize any errors in the procedures of specimen collection.

4.Health education of the public: More should be done to educate the public about Meningococcal infection. Disinfection in a case of meningococcal meningitis means disinfecting only articles and areas contaminated by the nasopharyngeal secretions of the patient and not the entire dwelling. As this was a fatal case, the public was in a state of panic. Further education of the general population about communicable diseases should be carried out.

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Table 1. Recommended Antibiotics and their Dosages for the Prophylactic Treatment of Contacts of Meningococcal meningitis

Antibiotics	Age	Dosage	Route & Duration
Sulfadiazine¶	Children	500mg, every 12 hrs	oral，2 days
	Adults	1000mg, every 12 hrs	oral，2 days
Rifampin*	＜1mth	5mg/Kg, every 12 hrs	oral，2 days
	≧1mth	10mg/Kg, every 12 hrs	oral，2 days
	Adults	600mg, every 12 hrs	oral，2 days
Ciprofloxacin**	Adults	500mg	oral，1 dose
Ceftriaxone	＜15yrs	125mg	Injection, 1 dose
	Adults	250mg	Injection, 1 dose

¶ When sensitive to sulfadiazine (for large-scale prophylactic treatment)

**Anomaly fetuses found in animal tests; not recommended for pregnant women.

***Adverse effects on the development of cartilage found in animal tests; not recommended for children under 18 and pregnant women.