Outbreak Reports

An Outbreak of Multidrug-Resistant Tuberculosis in a Secondary School — Hubei Province, 2019

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Summary

What is already known about this topic?

Multidrug-resistant tuberculosis (MDR-TB) is a type of tuberculosis with resistance to common treatments such as isoniazid and rifampicin. MDR-TB is a major global health challenge and needs to be controlled tightly through prevention measures, early diagnosis, and full treatment and management.

What is added by this report?

This outbreak was the first MDR-TB related public health emergency in Hubei Province. In total, five MDR-TB cases and nine clinically diagnosed cases were identified within one class in a secondary school. Students and teachers from other classes were monitored, but no other cases were found.

What are the implications for public health practice?

The implementation of TB prevention and control measures in schools is important to increase knowledge on TB and to raise awareness on protecting personal wellbeing. The Automatic Early Warning Information System alerted the local health department and allowed for a timely response to prevent further disease spread.

On April 6, 2019, Zaoyang-County CDC in Hubei Province received an alert from the Automatic Early Warning Information System for Tuberculosis for a 16-year-old student in a secondary school that had been recently diagnosed with a positive sputum smear for tuberculosis (TB). The Zaoyang-County CDC verified the case, screened all close contacts, and carried out epidemiological investigation immediately (*1*). In total, five multidrug-resistant tuberculosis (MDR-TB) cases and nine clinically diagnosed TB cases were identified and subsequently isolated from school to start a multi-drug regimen. This outbreak was defined as an MDR-TB public health emergency on May 6, and the response was in accordance with the Regulations on Responses to Public Health Emergencies.

Investigation and Results

The outbreak occurred at a public secondary school with 3 grade-levels, over 3,900 students, and over 300 staff members. The index case occurred in a 16-year-old student with positive TB sputum smear tests. An interview with the student revealed that in February 2019 he had an onset of coughing that was treated as a common cold. In late March, the student suffered from significant fatigue, more frequent coughing, and occasional left chest pain. On April 4, the student visited the county hospital for a diagnosis where chest computed tomography (CT) showed his lungs were infected with TB. A positive sputum smear test result confirmed the diagnosis, and the student was subsequently transferred to the Xiangyang Tuberculosis Control Hospital the following day. The student was further tested with GeneXpert testing and anti-TB drug sensitivity test (DST), and the student was shown to have resistance to rifampicin (R), isoniazid (H), and ethambutol (E).

All TB cases in this outbreak were diagnosed according to the National Guidelines of Diagnosis for Pulmonary Tuberculosis (WS 288-2017) (*2*), which require TB cases to be classified as bacteriological confirmed, clinically diagnosed, or presumptive cases and classify patients resistant to R and H to be diagnosed as multidrug-resistant tuberculosis (MDR-TB). According to these guidelines, this patient with MDR-TB was confirmed to be the index case of this outbreak in the secondary school.

According to the National Regulations for Tuberculosis Prevention and Control in Schools (*1*), the Zaoyang-County CDC screened all students' regular classmates as they all had direct contact with the index case of MDR-TB. All close contacts were screened by symptom screening, purified protein derivative (PPD) skin test, chest X-ray, and sputum smear test. Following the results of these tests, some students were further examined with tests including GeneXpert testing and DST.

Out of the student's regular classmates, 30 out of 60 students (50.00%, 30/60) had strongly positive PPD reactions. Chest X-rays showed that 13 out of these 30 students (43.33%, 13/30) had lesions of active TB in lung, which is consistent with imaging manifestations of TB (*3*). In the following days, GeneXpert testing and DST indicated that 4 of these 13 students had confirmed cases of MDR-TB (R, H, and E resistant) and 9 TB cases were clinically diagnosed.

The screening was then expanded to all teachers and students for the index-case patient's grade. Among the remaining 1,144 students in other classes, 22 cases (1.92%, 22/1,144) had strongly positive PPD reaction but had normal chest X-ray results. Screening was ended as no more TB cases were found in the other classes. The rate of strongly positive PPD and incidence of TB in students in the index-case patient's class is significantly higher than other classes (chi-square test, $p<0.05$; Table 1). This indicates that classmates of the index-case patient were more vulnerable due to close contact.

To explore the epidemiological linkage among patients, strains from those five bacteriologically-confirmed MDR-TB students were tested with whole genome sequencing. The results indicated infection by the same *Mycobacterium tuberculosis* (MTB) strain, which means that the index case acted as the source of transmission in this outbreak. Though no further epidemiological investigation was conducted between the index case and the nine clinically-diagnosed TB cases, the patients had close contact as classmates and the index-case patient was also considered as the source of transmission.

The results of an environmental hygiene survey indicated that the secondary school was in good condition. However, most of the doors and windows of classrooms were closed in the winter, which resulted in poor ventilation and encouraged MTB spread in the environment. In accordance with the Regulations on Response to Public Health Emergencies, this outbreak was defined as an MDR-TB public health emergency on May 6 and had been responded to appropriately.

The 14 students with TB were treated with a multi-drug regimen at a hospital for the first two months and then at home for the rest of the treatment course. While preventative treatment effectively lowers the risk of disease progression for contacts of individuals with drug-susceptible tuberculosis, the effectiveness of this strategy is not well understood for contacts of people with MDR-TB (*4–5*). Therefore, students with strongly positive PPD reactions and normal chest X-ray results were strongly encouraged to take chest X-rays and be monitored at regular intervals at 3, 6, and 12 months. The Zaoyang-County CDC provided health education on TB to enhance the awareness of TB control among students, to encourage students with suspected TB symptoms to prioritize visiting clinics, and for TB patients to be compliant to physician-supervised treatment. Presently, no new cases have been reported.

Further epidemiological investigation into the index case by the Zaoyang-County CDC revealed that a distant relative had dinner with the index-case patient towards the end of 2018 and also had MDR-TB. The distant relative's TB drug resistance spectrum was the same as the index case (R, H, and E resistant). However, during the epidemiological investigation of the index case, this distant relative had negative sputum smear test results, and the reporting hospital did not retain the resistant strain during the initial diagnosis. Though a preliminary epidemiological association can be established, gene homology analysis cannot be done to fully confirm MDR-TB.

Discussion

MDR-TB has become a global epidemic due to inadequate TB treatment and a vicious cycle of diagnostic delay and improper treatment (*6*). China ranks 2nd of high burden countries of MDR-TB globally, and TB outbreaks in schools in China are especially problematic. TB treatment has notable morbidity and mortality and is lengthy, expensive, and associated with poor adherence (*4*).

This MDR-TB public health emergency may be the result of several factors. First, the index case was

TABLE 1. Rate of strongly positive PPD and TB incidence among contacts.

Class	No. of students	No. of strongly positive PPD reaction	Rate of strongly positive PPD reaction (%)	χ^2	*p* value	No. of TB patients	Incidence (%)	*p* value*
Index-Case Patient's Class	60	30	50.00	307.35	<0.05	13	21.67	0.000
Other Classes	1,144	22	1.92			0	0.00	

*Using Fisher's Exact Test.

diagnosed extremely late. The patient likely had contact with MDR-TB at the end of 2018 and his symptoms appeared in February 2019, but he did not visit a hospital until April 4 after his condition deteriorated. Delayed diagnosis and treatment increased the probability of transmission in his school, especially among classmates.

Second, infectious disease prevention and control measures in schools were not fully implemented, and early screening failed to identify sick students. Early interventions could include daily screening of symptomatic or absent students by asking their family members, school staff, or fellow students to help identify TB symptoms. In this situation, however, the contacts of these students were not familiar with common symptoms of TB, which include onset of cough and expectoration for more than 2 weeks, so no suspected TB cases were reported or referred to hospital.

Finally, poor ventilation in classrooms in the winter and spring may increase the rate of TB transmission for students studying in these areas. The investigation results indicated that close contact significantly increased the likelihood of TB transmission between the index-case patient and his regular classmates. However, a major limitation in the epidemiological investigation is that the index-case could not be linked to the patient's distant relative due to the fact that hospital discarded the distant-relative's MDR-TB sample.

This investigation showed that local CDCs should increase TB health education efforts in schools, especially during colder seasons which may result in poor ventilation for students. Increased TB knowledge may encourage those with suspected symptoms to seek diagnosis earlier or help close contacts identify possible symptoms.

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