Discordance in Mycobacterium tuberculosis Rifampin Susceptibility

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habitat overlaps with that of pteropid bats in southern Vietnam.

Previous studies showed that IgG ELISA results for NiV-positive flying foxes correlated well with NT results (3,4). However, in our study, discrepancies existed between NT results and NiV-N-ELISA and WB results. A reason for these differences could be that NiV-like viruses are circulating among bats in Vietnam, producing antibodies that are cross-reactive by ELISA and WB, but poorly cross-reactive by NT. The cross-reactive antibodies were probably not directed against neutralizing epitopes. To date, no reports have been made of an increased number of febrile encephalitis cases among the residents in Hoa Binh and Dak Lak Provinces where seropositive bats were captured. The circulating viruses may lack the pathogenic potential of Hendra and NiPah viruses.

A survey by questionnaire was conducted among residents of Dak Nong and Dak Lak Provinces, where NiV-N-ELISA–positive C. sphinx bats were captured, to determine the frequency of contact between humans and bats. Risk factors for infection were observed in this study, such as bat hunting and cooking and drinking bat blood. In such situations, persons have direct contact with bat body fluids and feces and might be bitten during bat hunting. Thus, long-term systematic surveillance of bats is needed to determine the ecologic relationship between bats, humans, other animals, and the environment.

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Discordance in Mycobacterium tuberculosis Rifampin Susceptibility

To the Editor: Multidrug-resistant tuberculosis (MDR TB), i.e., TB resistant to at least the 2 most effective first-line antituberculous drugs (isoniazid [INH] and rifampin [RIF]), is increasing globally. World Health Organization estimations of 390,000–510,000 new MDR TB cases and 150,000 related deaths in 2008 highlight the need for timely drug susceptibility testing and improved therapies (1). Although novel rapid drug susceptibility testing tools are increasingly available, their clinical applicability is unsettled. We report a patient with pulmonary TB relapse with discordant genotypic and in vitro phenotypic drug susceptibility testing results associated with a mutation outside the RIF resistance determining region (RRDR) of the rpoB gene.

In August 2009, a 45-year-old homeless woman with AIDS (CD4 T-cell count 3 cells/mm³) and a history of substance abuse sought care for fever, night sweats, weight loss, and cough (online Appendix Table, wwwnc.cdc.gov/EID/article/18/3/11-1357-TA1.htm). Pulmonary TB had been diagnosed in June 2008. At
that time, she received, by directly observed therapy, 6 weeks of INH, RIF, pyrazinamide (PZA), and ethambutol (EMB) through the local health department and was switched to RIF, PZA, and EMB on week 7 after the isolate was determined by liquid culture with BD BACTEC MGIT 960 Mycobacterial Testing System (BD Diagnostics, Sparks, MD, USA) to be INH resistant. During that period, she resided in American Lung Association-supported housing for TB patients and had 97% medication adherence by dose count. Her condition clinically improved, infiltrates completely resolved according to chest radiograph, 12 sputum inductions failed to yield sufficient material for analysis, and she began highly active antiretroviral therapy (HAART). In December 2008, however, because of crack cocaine use and belligerent behavior, she lost housing privileges. Caseworkers could not locate her to complete the 9-month planned directly observed therapy.

The woman was hospitalized in January and again in February 2009 with dyspnea and off medications. In both instances, chest radiographs showed no new changes, sputum specimens were negative for acid-fast bacilli (AFB) by microscopy and culture, and she was treated for presumptive Pneumocystis pneumonia and showed clinical improvement.

In August 2009, she was readmitted with cough and new cavitation on chest radiograph. Chest computed tomographic scan demonstrated right upper lobe infiltrates, bilateral lower lobe cavitation, and hilar and mediastinal lymphadenopathy. Sputum AFB smear was positive (graded 4+), and nucleic acid amplification (Amplified Mycobacterium Direct Test; Gen-Probe, San Diego, CA, USA) was positive for Mycobacterium tuberculosis complex. INH, RIF, PZA, and EMB, along with moxifloxacin (MXF) and amikacin (AMK), were initiated in accordance with 2003 national TB treatment guidelines for possible MDR TB (2). Shortly thereafter, a line probe assay (GenoType MTBDRplus; HAIN Lifescience, Nehren, Germany) performed by Southeastern National TB Center (Gainesville, FL, USA) on the culture of the sputum specimen obtained at admission indicated an inha point mutation but no mutation in the RRDR region of the rpoB gene, which suggested that the isolate was INH resistant but RIF susceptible. AMK was discontinued, and the patient was discharged with RIF, PZA, EMB, and MXF.

One week later, drug susceptibility testing (BD BACTEC MGIT 960 System) results from the state mycobacteriology laboratory demonstrated that the M. tuberculosis isolate was resistant to INH and RIF. The patient was readmitted to resume inyectable aminoglycoside therapy. After 5 weeks, sputum culture became negative, clinical and radiographic improvement was apparent, and HAART was reinitiated. She completed 2 months’ INH/PZA/EMB/MXF/AMK inpatient therapy and was discharged to complete 6 additional months of PZA/EMB/MXF and streptomycin followed by 16 months of PZA/EMB/MFX. With HAART, her plasma HIV RNA viral load became undetectable, but her CD4 count remained low (9 cells/mm³). She died from a motor vehicle accident 10 months after recurrent TB was diagnosed.

In this patient, RIF resistance was not predicted by line probe assay but was identified phenotypically by an automated system (BD BACTEC MGIT 960 System) that continuously monitors for growth and detection of mycobacteria. Through genotyping and DNA sequencing of the 2008 and 2009 M. tuberculosis isolates, the Mycobacteriology Laboratory Branch at the Centers for Disease Control and Prevention (Atlanta, GA, USA) established that the 2009 infection was a relapse, not re-infection, and confirmed the inha mutation in both isolates. Using primers extending beyond the RRDR (the rpoB region surveyed by rapid molecular tests and responsible for >95% of RIF resistance mutations) the laboratory identified a novel rpoB gene mutation at codon 480 (ACC→AAC; Thr→Asn) and another previously described (3→5) mutation at codon 176 (GTC→TTC; Val→Phe) in the 2009 isolate, which has been implicated in RIF resistance. The role of the T480N mutation in RIF resistance is being investigated.

This case demonstrates the limitations of rapid molecular drug susceptibility testing (6). Rapid molecular diagnostics are valuable adjuncts to conventional phenotypic testing because they can quickly confirm clinically suspected MDR TB and have high agreement with other genotypic and phenotypic methods (7–10). However, they should not supplant phenotypic testing, and clinicians should understand their limitations. When rapid molecular tests are negative but suspicion for MDR TB is high, MDR TB treatment should be continued until phenotypic susceptibility results are available. DNA sequencing may be best suited for evaluating suspected drug-resistant M. tuberculosis isolates with discordant results for phenotypic susceptibility and rapid molecular testing.

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LETTERS

High Incidence of Group B Streptococcal Infection in Infants Born to HIV-Infected Mothers

To the Editor: In their cross-sectional study comparing group B streptococcus (GBS) carriage among HIV-infected and HIV-uninfected women in Malawi, Gray et al. found no differences in GBS carriage between both groups but found a higher carriage rate for HIV-infected women with high CD4 cell counts (1). They proposed that a GBS-specific immune defect might exist in HIV-infected pregnant women and suggested that this defect could be blurred by competitive exclusion of GBS as a consequence of changes in microbial flora at lower CD4 counts.

We recently reported an increased incidence of neonatal GBS sepsis in HIV-exposed uninfected (HEU) infants born in Belgium, compared with the general population (2). In our cohort, the risk for GBS infection was 20x higher in HEU infants than in infants born to HIV-uninfected mothers. Moreover, the episodes of GBS sepsis in HEU infants, compared with the general population, were more severe and mostly of late onset. We are currently looking prospectively at GBS carriage in HIV-infected and control uninfected pregnant women to learn whether our observation can be explained by a higher carriage rate in HIV-infected women or by increased susceptibility of HEU infants to this capsulated bacteria. The latter hypothesis would be in line with the higher susceptibility of HEU children to other types of severe infections, as has been described in several studies from sub-Saharan Africa and Latin America (3–5).

The incidence of GBS sepsis in HIV-exposed infants born in Africa is unknown. In addition to the need for further investigation of anti-GBS immunity in HIV-infected pregnant women, we believe that studies comparing the incidence of neonatal GBS sepsis in HEU and HIV-unexposed infants are warranted. If the increased risk for GBS sepsis is confirmed, prophylaxis should be implemented in the population concerned.

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