Fever of unknown origin in a migrant farm worker from Mexico: History, her story and his story

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A 29-year-old migrant farm worker from Mexico presented to a hospital in Ontario with fever of unknown origin.

She had arrived in Canada six weeks previously to work at an orchard. Her past medical history included two caesarean sections, postpartum hemorrhage requiring transfusion, and cholecystectomy. She was not on any medications.

She began experiencing daily rigors one week after her arrival, often accompanied by drenching sweats, and she lost approximately 5 kg of weight. She had intermittent midthoracic back pain, but no other localizing symptoms.

Painful vaginal sores and dysuria developed one week later. She presented to the emergency room, where she was diagnosed with genital herpes simplex and secondary bacterial infection. She was prescribed a one-week course of cephalexin and one dose of azithromycin, but she continued to have rigors.

One week later, she developed intermittent epigastric pain with no nausea, vomiting or diarrhea. She returned to the emergency room with a fever of 39.5°C, and was admitted for presumed pelvic inflammatory disease. She was treated with various broad-spectrum antibiotics and acyclovir but remained persistently febrile. All cultures were negative and her pelvic ultrasound was unremarkable.

She was transferred to a tertiary care hospital one week later for consultation with an infectious disease specialist. Further

questioning revealed that she was from a city in Mexico where she lived in close proximity to chickens. She denied having recent insect bites, sick contacts, intravenous drug use and tattoos. She had two previous male sexual contacts, including her husband, who she said had died at 27 years of age from lung cancer.

On examination, she was hemodynamically stable and slightly tachypneic, with a temperature of 38.4°C and an oxygen saturation of 96% on room air. Her head and neck examinations revealed two small umbilicated papules on the right upper eyelid and white lesions on the tongue and buccal mucosa. There was no lymphadenopathy. Her cardiovascular, respiratory, abdominal and neurological examinations were unremarkable.

Blood tests on admission were significant for the following: hemoglobin of 90 g/L with a mean corpuscular volume of 75.8 fL, white blood cell count of $3.1 \times 10^9/\text{L}$ ($2.9 \times 10^9/\text{L}$ neutrophils and $0.2 \times 10^9/\text{L}$ lymphocytes), aspartate aminotransferase level of 132 U/L, alanine aminotransferase level of 28 U/L, alkaline phosphatase level of 386 U/L, bilirubin level of 6 $\mu\text{mol}/\text{L}$ and lactate dehydrogenase level of 1283 U/L. Her chest x-ray showed a diffuse reticulonodular pattern.

Diagnostic tests were performed.

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Received and accepted for publication August 27, 2007

DIAGNOSIS

Given that the patient's husband was unlikely to have died of lung cancer at such a young age, and combined with the other findings, the index of suspicion was high for HIV. HIV serology was confirmed to be positive, and the patient's absolute CD4 count was $0.03 \times 10^9/L$ with a CD4 percentage of 8%. *Pneumocystis carinii* (*Pneumocystis jiroveci*) pneumonia was thought to be the most likely cause of her fever in light of her chest x-ray, so she was started on oral trimethoprim-sulfamethoxazole.

She remained febrile after three days of treatment, and bronchoscopy was carried out to confirm the diagnosis. Bronchoalveolar lavage was reported to be negative for Gram stain, *P. carinii*, fungi and acid-fast bacilli. Trimethoprim-sulfamethoxazole was discontinued.

The patient remained febrile, and bronchoalveolar lavage cultures were reported to be negative; four days later, she underwent open lung biopsy. Histological examination of the sample revealed the presence of yeast forms consistent with *Histoplasma capsulatum*, which was later confirmed on culture. She was started on amphotericin B, 1 mg/kg/day, as a continuous intravenous infusion over 24 h, and defervesced within five days. She was discharged one week later because her fellow workers were returning to Mexico. She was prescribed 200 mg of itraconazole, orally, three times a day, with her family doctor to initiate antiretroviral therapy when the acute illness had resolved.

DISCUSSION

The health of migrant workers is becoming an important issue in Canada as the agricultural industry expands while fewer Canadian residents choose to work as farm labourers. The demand is largely filled by seasonal workers, often from Central America and the Caribbean islands. In 2004, there were 10,777 migrant workers in Canada from Mexico and 8110 from the Caribbean (1).

Fever is a common presenting symptom when migrant workers encounter the Canadian health care system. This may present a diagnostic challenge, because they can have infectious diseases from their native countries, unique occupational exposures and are at a higher risk of being infected with HIV than the general population.

The differential diagnosis of fever in this population includes tropical diseases. Studies of both migrants and travellers returning from tropical areas and presenting with fever have found that malaria is the most common diagnosis, followed by gastroenteritis and respiratory tract infections (2). However, one large prospective observational study (3) showed that compared with travellers, migrants with fever are more likely to have tuberculosis, chronic hepatitis and parasitic infections.

In addition to tropical infectious diseases, farm workers may be exposed to unique pathogens by virtue of their occupation. They often work with and live in close proximity to animals, which puts them at increased risk for a variety of zoonotic infections, including anthrax, animal influenza viruses and Q fever (4). They may also acquire fungal infections from working with soil, such as coccidiomycosis and histoplasmosis.

HIV infection is another important consideration; the prevalence among migrant farm workers in the United States is estimated to be 10 times the national average (5). Various risk factors likely contribute to the increased prevalence. In addition, seasonal workers often come from HIV-endemic countries, where the prevalence rates are higher than in North America (6,7). HIV status will alter the differential diagnosis of fever. One study (8) found that over 90% of fevers of unknown origin in HIV-positive patients had infectious etiologies, compared with approximately one-third of cases in immunocompetent patients. Of note, the vast majority of cases in this series did have an identifiable etiology, indicating that fever in this population should not be attributed to constitutional effects of the HIV virus. A full diagnostic workup is required, with a focus on opportunistic infections and other infections that may present insidiously in immunodeficient patients.

Migrant worker health is a potentially challenging field, complicated by tropical infections, occupational exposures and HIV. However, it will become increasingly important to be aware of these issues as this population continues to grow in Canada.

REFERENCES

1. Brem M. Migrant workers in Canada: A review of the Canadian Seasonal Agricultural Workers Program. <http://www.nsi-ins.ca/english/pdf/MigrantWorkers_Eng_Web.pdf> (Version current at August 31, 2007).
2. Parola P, Soula G, Gazin P, Foucault C, Delmont J, Brouqui P. Fever in travelers returning from tropical areas: Prospective observational study of 613 cases hospitalised in Marseilles, France, 1999-2003. *Travel Med Infect Dis* 2006;4:61-70.
3. O'Brien DP, Leder K, Matchett E, Brown GV, Torresi J. Illness in returned travelers and immigrants/refugees: The 6-year experience of two Australian infectious disease units. *J Travel Med* 2006;13:145-52.
4. Snashall D. ABC of work related disorders. Occupational infections. *BMJ* 1996;313:551-4.
5. Fitzgerald K, Chakraborty J, Shah T, Khuder S, Duggan J. HIV/AIDS knowledge among female migrant farm workers in the Midwest. *J Immigr Health* 2003;5:29-36.
6. Cohen J. HIV/AIDS: Latin America & Caribbean. Mexico: Land of extremes: Prevention and care range from bold to bleak. *Science* 2006;313:477-9.
7. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2004 report on the global HIV/AIDS epidemic: 4th global report. <http://www.unaids.org/bangkok2004/GAR2004_pdf/UNAIDSGlobalReport2004_en.pdf> (Version current at August 31, 2007).
8. Miller RF, Hingorami AD, Foley NM. Pyrexia of undetermined origin in patients with human immunodeficiency virus infection and AIDS. *Int J STD AIDS* 1996;7:170-5.