C. gattii Emerges in Pacific Northwest, Kills Four

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WASHINGTON — *Cryptococcus gattii*, a meningitis-causing fungus previously confined to tropical and subtropical climates outside of the United States, has caused severe illness in at least 19 individuals—of whom 4 died—in the Pacific Northwest United States since 2006.

The infections were not predominately associated with immunocompromised individuals, unlike past, non-*gattii* cases of *Cryptococcus* infection in North America.

"Twelve of 19 individuals had a delay in diagnosis greater than a week," said Dr. Sarah West at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

The delay was "in part probably because this was not on physicians' radars, and also because this is not something that our labs are routinely testing," she said, speaking of a need for physicians, especially in that area, to be more aware of the infection.

The outbreak was previously reported on Vancouver Island in 1999, when more than 200 cases were identified. Although a *C. gattii* relative—*Cryptococcus neoformans*—is fairly well known in North America, *C. gattii* was "not previously described as causing significant disease in North America," Dr. West said.

The variation is most often seen in Australia, where it is especially associated with eucalyptus trees, and in similarly tropical climates. It is not known why or how the fungus has spread to this new area. Previous studies have speculated that it is related to climate change.

Dr. West and her collaborators first had their interest piqued by a published 2006 case of a man from Puget Sound region of Washington state, who had pulmonary cryptococcoma and who was infected with *C. gattii*. "He had never traveled to Vancouver Island," she said, though the *C. gattii* isolate was genetically identical to the Vancouver strain.

Since then, Dr. West has been querying physicians in Oregon and Washington, checking referrals to local tertiary-care hospitals, and relying on "word of mouth" to put together a retrospective study of 19 culture-confirmed *C. gattii* cases in the region from 2004 to the present. (Most microbiology labs do not routinely differentiate between *C. neoformans* and *C. gattii* in cultures, so the cases were culture confirmed in Dr. West's lab.)

"The bulk of cases were in 2007 and 2008," she said, with patient age ranging from 15 to 87 years (average, 51 years). "At least three had traveled to British Columbia mainland, but none had documented travel to Vancouver Island.,"

"When we compared the *Cryptococcus* data from Oregon with our *C. gattii* cases, we saw some differences in the underlying conditions," she said. Whereas about 78% of the non-*gattii Cryptococcus* cases in Oregon were associated with HIV, cancer, organ transplants, or some other immunosuppressing condition, "just under 40% of the *gattii* cases were associated with these diagnoses, and none of the patients with *gattii* were HIV positive."

Their presenting symptoms were nonspecific, "which also probably led to some delay in diagnosis," added Dr. West, of the Oregon Health and Science University, Portland. As on Vancouver Island, about 75% of cases were associated with pulmonary disease of some kind, including two cases of asymptomatic pulmonary nodules. The remaining 25% were associated with central nervous system disease alone. Overall, about 20% of patients had both CNS disease and pulmonary disease.

"Most of the patients with CNS disease had meningoencephalitis, often associated with severe and symptomatic increase in cranial pressure, and many required semipermanent drain placement," Dr. West said.

All of the patients required prolonged courses of therapy, she said, "longer than is typically given for *Cryptococcus neoformans*."

Poor outcomes were seen even in the 15 patients who survived, including long-term sequelae such as chronic headaches, vision loss, hearing loss, and recurrent, longer hospital stays requiring more intensive care.

An audience member from the Centers for Disease Control and Prevention said that the agency has formed a six-state public health working group for *C. gattii* and has since identified additional cases in Montana and Idaho.

Enzon Pharmaceuticals Inc. supported Dr. West's study. She did not disclose any conflicts of interest related to the study. ■