A new strain of a tropical fungal interloper has been discovered in the United States...but no matter how it arose, this party crasher looks like “it’s going to stick around…”

INTRODUCTION

Cryptococcus gattii is an encapsulated, pathogenic yeast, closely related to Cryptococcus neoformans.1 Until 1999, it had been thought limited to tropical and subtropical climates; but in that year it emerged on Vancouver Island, resulting in one of the highest incidences of C. gattii infection reported anywhere in the world.1-3 Human illnesses caused by C. gattii were subsequently confirmed on the British Columbia mainland, in Washington State, and, since 2004, in Oregon.

THE PATHOGEN

Cryptococcus gattii is most easily distinguished from C. neoformans by the blue color it produces when plated on differential CGB® agar.4 The natural reservoir of C. gattii seems to be soil and plant debris; the fungus has been associated with numerous tree species including eucalyptus, fir, Garry oak, etc.5-8 When inhaled, it may infect humans and a variety of mammals such as dogs, cats, goats, elk, ferrets, etc.9 Multilocus sequence typing subcategorizes the organism into four genotypes: VGI, VGII, VGIII, and VGIV. Further genetic analysis divides the VGII genotype into three subtypes: VGIIa, VGIIb, and VGIIc.5-9 Although VGII is the genotype most commonly found recently in the Pacific Northwest and in British Columbia, it is uncommon in other C. gattii-endemic parts of the world, where VGII is isolated most frequently.10 Interestingly, VGIIc has been isolated only from humans, animals in Washington and Oregon and so far only from Oregon soil.

EPIDEMIOLOGY

In the wake of the Vancouver Island outbreak, in November 2004 the Oregon Public Health Division began to solicit cryptococcal isolates from Oregon clinical laboratories for testing at the Oregon State Public Health Laboratory (OSPHL). C. gattii infections were soon confirmed among Oregonians, including some who had never traveled to British Columbia.11 Of 91 Cryptococcus isolates processed by the OSPHL sixty cases (66%) of C. gattii infection were reported in Oregon between November 2004 and October 2011; most cases were identified after September 2008 when we began to solicit cases more actively (Figure 1). Thirty-three (55%) of the cases were female. The median age was 57 years (range, 10 months – 96 years; Figure 2).

HUMAN ILLNESS

Cryptococcus gattii appears to differ from its sibling species C. neoformans, both in its clinical manifestations and in its ecologic niche. C. gattii may be more likely to cause cryptococcoses and less susceptible to antifungal drugs.12,13 In addition, whereas the primary risk factor for C. neoformans cryptococcosis is severe immunosuppression (e.g., from HIV infection), both immunocompromised and previously healthy individuals seem to be at risk for C. gattii infection.12-14 Cryptococcus gattii causes life-threatening infection of the pulmonary and central nervous systems in all hosts. Through November 2010, 46 of the Oregon cases have been reviewed thoroughly. Of these, 21 (46%) were primarily pulmonary, 12 (26%) primarily CNS, 9 (20%) CNS and pulmonary, 1 (2%) bloodstream alone and 3 (6%) were other (nail bed infection, thrush, urinary tract infection).

Of those, 34 (74%) had an underlying chronic medical condition. Twenty-four (52%) patients had an immunosuppressing condition, including nine with solid organ transplants and 11 with a variety of autoimmune diseases. This is a bit at odds with the pictures of C. gattii infection as reported from British Columbia, where only 41 (39%) of 124 confirmed cases during 1999–2007 were immunocompromised; and Victoria, Australia, where 0 of 20 cases identified during 1980–1990 were immunocompromised.15-17 Perhaps cases in immunocompetent patients in Oregon were missed, given that reporting was voluntary. N.B.: as of August 19, 2011, cryptococcal infection is now reportable in Oregon; and laboratories will be required to forward the isolates to OSPHL for speciation.1

EPIZOOTIOLOGY

Oregon veterinarians and veterinary laboratories have reported C. gattii cases since 2008. Through October 2011, the Oregon State University’s Veterinary Diagnostics Laboratory (VDL) has identified 40 cases: 15 cats, 9 dogs, 5 alpaca, 5 goats, two elk, a ferret, a horse, a dolphin and a sheep (Figure 3, verso). Of the C. gattii isolated at VDL, 10 were isolated from lungs, 10 from nasal cavities, 9 from skin abscesses, 7 from the brain or CSF, 2 from kidneys, and one each from an oral lesion and a rectal sample. Of the 40 isolates, 39 were serotyped: 23 were VGIia, 6 VGIIb, 9 VGIIc and 2 VGIII.
Because human beings are wont to travel, and the incubation period for C. gattii infection is long (median, 6–7 months; range of 2–13 months), it’s difficult to know where a given human case acquired his or her infection. Figure 3 shows where the non-human cases resided — probably indicating more reliably where the fungus abides.

Figure 3. Geographic location of animal C. gattii cases, Oregon, 2008–2011

ECOLOGY

To zero in on environmental niches, we collected samples from around the residence of a 9-month-old dog (with no travel history!) from which C. gattii VGIIa was cultured. The soil and tree bark samples of a Pseudotsuga menziesii var. menziesii collected a year apart yielded C. gattii VGL, VGIIa, VGIIb and VGIIc. We hope to collect more environmental samples around the homes of animal cases without travel history, the better to define the ecology of this fungal pathogen in Oregon.

CONCLUSION

Cryptococcus gattii appears to be established in Oregon, and case counts may be rising. Both immunosuppressed and previously healthy persons appear to be at risk. More information is needed about the effectiveness of azole antifungal agents in treating C. gattii, so that we can purge you from our print mailing list, thereby saving trees, taxpayer dollars, postal worker injuries, etc.

REFERENCES