

## Competent enough for *Cryptococcus*: *Cryptococcus gattii* Meningoencephalitis

### Learning Objectives

1. Emphasize *Cryptococcus gattii* as an emerging pathogen causing meningoencephalitis in immunocompetent hosts.
2. Recognize that *C. gattii* is more difficult to treat and clear than *C. neoformans*.

A previously healthy 49-year-old African American male presented with four weeks of fever, headache, back pain, and vomiting unresolved after multiple ER visits and empiric treatment with doxycycline for a tick bite. His headache persisted, and he developed blurry vision. Examination revealed an oriented male with meningismus and bilateral nystagmus upon left lateral gaze. There was no rash, fever, seizures, history of trauma, or travel outside of Alabama in over twenty years. Immunologic work up including HIV antibody, CD4 lymphocyte assay, serum complement and quantitative immunoglobulin levels were negative or normal. Lumbar puncture (LP) revealed opening pressure of 23 mmHg, cerebrospinal fluid (CSF) protein of 129 mg/dl, and CSF glucose of 29 mg/dl. India ink was positive for encapsulated yeast. CSF cryptococcal antigen was positive (1:2048). Amphotericin lipid complex 5 mg/kg/d and flucytosine 100 mg/kg/d were administered. Initial CSF cultures were positive for *Cryptococcus* species and remained positive for fourteen days despite combination therapy. His headache and blurry vision resolved with serial therapeutic LPs. Opening pressures were as high as 46mmHG, and a ventriculoperitoneal shunt was placed on day 14 of hospitalization. MRI revealed cryptococcomas in the cerebrum and spinal cord. Interferon-gamma was initiated on day 20 for refractory infection. The *Cryptococcus* species was identified as *C. gattii*, and he received seventy-five days of amphotericin and was discharged on long-term fluconazole.

Meningoencephalitis is one of the most serious consequences of cryptococcosis, and is a well-known pathogen among immunocompromised patients. Primary infection occurs through the respiratory tract, but it has a propensity for the central nervous system. *Cryptococcus* is a basidiomycetous yeast and is further classified into two species, *C. neoformans* and *C. gattii*, with important differences between the two. *C. neoformans* affects primarily immunocompromised, whereas *C. gattii* affects immunocompetent hosts. A case series from Australia showed that all cases of *C. gattii* were in immunocompetent hosts, and most cases presented insidiously with evolving neurologic symptoms, similar to our patient. Though *C. neoformans* infection has a higher mortality rate, *C. gattii* causes a greater number of cryptococcomas, leading to more neurological sequelae and slower response to treatment. *C. gattii* has been cultured from red gum trees in Australia and was originally seen in places where those trees were endemic. However, since 1999, over 200 immunocompetent cases of *C. gattii* infection have been reported in Vancouver Island, British Columbia, and the northwestern United States; rare cases are now being reported in other areas of the US. *C. gattii* is known to develop resistance to antifungal agents and treatment with Amphotericin and flucytosine is often required for longer than a month. Interferon-gamma was added as adjunct therapy due to its suggested benefit in decreasing time to clearance of resistant *C. neoformans* in immunocompromised patients. *C. gattii* is still rare in most of the US but is emerging in immunocompetent hosts. Education is needed as it can present more indolently than other more common causes of meningoencephalitis and often requires lengthy and more complicated treatment regimens for successful outcomes.