Fingolimod and Cryptococcosis: The Interaction Between Immunomodulation and Infectious Disease

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Introduction

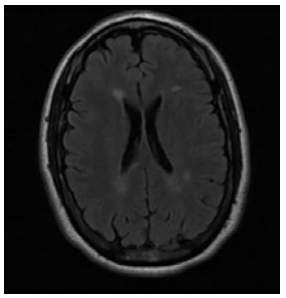
- Fingolimod is a sphingosine-1- phosphate-receptor modulator, promoting receptor internalization, and preventing/impairing egress of peripheral T- and B-cells from secondary lymphoid tissue into blood, reducing access to the central nervous system1
- Pre- and post-marketing surveillance suggests that there may be a greater risk of opportunistic infections, including cryptococcosis, after at least 2 years of fingolimod use.[2]
- Guidelines on balancing efficacious disease-modifying therapies (DMTs) to treat multiple sclerosis (MS), while treating an opportunistic infection associated with DMT have not y

Objectives

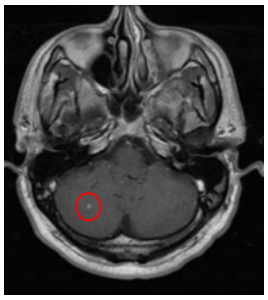
- Describe a case of cryptococcal infection associated with fingolimod use
- Describe the therapeutic considerations that follow
- Provide a potential strategy to balance MS and infectious disease management
- Discuss th y approach and shared decision making with the patient

Clinical History

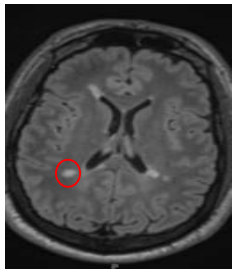
- 45-year-old man with relapsing-remittent MS, found to have enlarging pulmonary lymph nodes
- MS history:
  - Diagnosed at age 28 after presentation with right optic neuritis
  - One year later, bilateral upper extremity paresthesias
  - Started interferon beta 1-a - discontinued after side effects

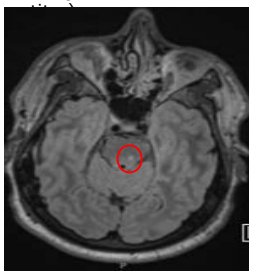


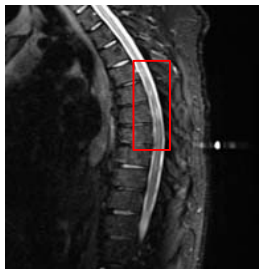
- MRI Brain: 1 month prior to diagnosis of cryptococcosis
- Compliant on fingolimod 3 years
- New T2 FLAIR and enhancing cerebellar lesion
- Lumbar Puncture: normal cell count, protein, glucose, and negative Cryptococcus neoformans or gattii antigen



- CT Chest: Multiple pulmonary nodules
- Repeat Imaging: growth of nodules
- Bronchoalveolar Lavage: rare Cryptococcus neoformans in fungal culture
- Positive cryptococcus antigen in serum (1:80 titer)







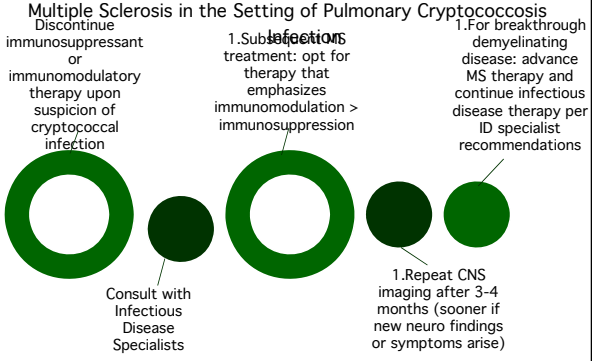
MRI Brain and Thoracic Spine: 3 mo after discontinuing fingolimod and initiating glatiramer acetate, presence of new lesions

Clinical Course

- Discontinued fingolimod
- Consultation with Infectious Disease specialist who initiated oral fluconazole for prolonged therapy of cryptococcosis
- To avoid further immunosuppression with presence of active fungal infection, glatiramer acetate started as next DMT
- Three-month neurological follow-up: Clinical relapses and new MS lesions on brain and spinal cord imaging
- Three month CT Chest: decrease in pulmonary nodules
- MS remained active and cryptococcosis was resolving, prioritization given to optimizing MS therapy
- Infectious Disease specialists made aware, plan to monitor closely, and escalate fungal therapy as needed

Proposed Treatment Model

Multiple Sclerosis in the Setting of Pulmonary Cryptococcosis



References

1. Cohen, J. A., & Chun, J. (2011). Mechanisms of fingolimod's efficacy and adverse effects in multiple sclerosis. *Annals of Neurology*, *69*(5), 759–777.
2. Grebenciucova, E., Reder, A. T., & Bernard, J. T. (2016). Immunologic mechanisms of fingolimod and the role of immunosenescence in the risk of cryptococcal infection: A case report and review of literature. *Multiple Sclerosis and Related Disorders*, *9*, 158–162.