Histoplasmosis

Histoplasmosis is a dimorphic fungal infection caused by *Histoplasma capsulatum*. It is the most common endemic fungal infection in North America and is endemic to the St. Lawrence seaway, including Montreal. While many manifestations of histoplasmosis are self-limiting and do not require treatment, certain manifestations of histoplasmosis may be fatal without prompt antifungal therapy. Pulmonary histoplasmosis should be suspected in patients with mediastinal/ hilar lymphadenopathy, pulmonary nodules or cavitary lung disease.

Incidentally identified pulmonary nodules do not require antifungal therapy. Among immunocompetent patients, mild acute pulmonary histoplasmosis will often self-resolve without antifungal therapy. At the other extreme, severe acute pulmonary disease and disseminated histoplasmosis require prolonged therapy with antifungals, and consultation with **infectious diseases is encouraged for progressive or severe cases of of histoplasmosis.**

Histoplasmosis may **mimic pulmonary sarcoidosis**. It is essential to exclude histoplasmosis prior to starting steroids for suspected sarcoidosis.

Diagnostic considerations:

- CT of the lungs is the initial diagnostic imaging modality (X-ray insufficient).
- Bronchoscopy and BAL for fungal staining, culture and antigen testing.
    - If histoplasmosis suspected: call the laboratory to ensure safe and adequate sample processing.
    - Fungal culture has low sensitivity, and *Histoplasma* may take several weeks to grow in culture
- Histoplasma antigen testing from blood and urine and serology (histoplasma antibody) supports the diagnosis of histoplasmosis (need ID/Micro approval)

Therapeutic considerations:

For cases presenting as asymptomatic mediastinal granulomas, mediastinal fibrosis, or pulmonary nodules, treatment with antifungals is generally NOT indicated.
Treatment may be indicated if upcoming immunosuppression, in conjunction with Infectious Diseases.

PHARMACOLOGIC THERAPY

Mild acute pulmonary, symptoms < 4 weeks	No antifungal therapy (monitor) N.B. Itraconazole may be considered in discussion with ID.
Moderate acute pulmonary symptoms > 4 weeks	**Itraconazole**[2,3,4] loading dose of 200 mg q8h PO for first three days, then 200 mg PO BID then 200 mg once or twice daily for 6 to 12 weeks. Note that in immunocompromised patients (e.g. advanced HIV, stem cell transplant, solid organ transplant,etc.) the duration of therapy will be prolonged and may be indefinite.
Severe acute pulmonary disease (hypoxemia):	**Liposomal amphotericin B**[1] 5 mg/kg IV daily (round to the closest vial of 50mg) for 1-2 weeks *THEN* **Itraconazole**[2,3,4] loading dose of 200 mg PO q8h x 3d then 200 mg PO BID (duration determined in consultation with ID). N.B. If significant/ worsening hypoxemia, consider Methylprednisolone: 0.5 to 1 mg/kg/day IV for first 7 to 14 days, in discussion with ID. Note that in immunocompromised patients (e.g. advanced HIV, stem cell transplant, solid organ transplant,etc.) the duration of therapy will be prolonged and may be indefinite.
Chronic cavitary pulmonary	**Itraconazole**[2,3,4] loading dose of 200 mg PO q8h for first three days, then 200 mg PO once or twice daily for at least 1 year. N.B. Chronic cavitary histoplasmosis may relapse years after finishing therapy. Monitoring with serial imaging every 6-12 months may be indicated.

[1] Ampho B may cause nephrotoxicity; limit concomitant nephrotoxic agents, monitor creatinine and electrolytes.
[2] Itraconazole capsule absorption is increased by high gastric acidity (eg: "cola" drink). Should not be given with antacids, H_2 blockers, or proton pump inhibitors. Discuss itraconazole solution with pharmacist. May cause hepatotoxicity, decreased cardiac function, rash and hypokalemia. Measure transaminases and electrolytes before therapy and intermittently during therapy (eg: 1, 2, and 4 weeks and then every 3 months, if stable). Avoid use in patients with heart failure with reduced ejection fraction. Avoid in pregnancy.
[3] Extensive drug-drug interactions, please consult pharmacist prior to initiating, changing or stopping itraconazole.
[4] Among patients who do not tolerate itraconazole, consider isavuconazole or posaconazole as alternative.

Therapeutic Drug Monitoring: itraconazole

- Measure itraconazole serum concentrations 2 weeks after itraconazole initiation.
- Goal: itraconazole serum concentration > 1mcg/ml (HPLC) or 3 mcg/ml (bioassay).
- Refer to MUHC azole therapeutic drug monitoring guidelines for details.

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