National HIV Curriculum

Disseminated *Mycobacterium Avium Complex* (MAC): Prophylaxis and Treatment

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Last Updated: August 5, 2024

Disclosures

Dr. Kalapila has no financial conflicts of interest or disclosures.

Disseminated Mycobacterium Avium Complex (MAC) Treatment: Outline

- Background
- Prevention
- Clinical Manifestations & Diagnosis
- Treatment
- Medication side effects
- Summary

Background

Background – Disseminated MAC

- MAC is a ubiquitous group of non-tuberculous mycobacteria
- Exposure occurs via inhalation or ingestion
- Disease occurs when CD4 <50 cells/mm^3
- Disseminated MAC typically presents as a multi-organ infection
- Rates of disease have decreased with wider use of ART

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Prevention

Prevention of Disseminated MAC infection

- Primary prophylaxis is not recommended when ART is initiated
- Primary prophylaxis is indicated when
  - CD4 <50 cells/mm^3 *and*:
  - Patient is not on fully suppressive ART
- Before starting prophylaxis, exclude active infection by:
  - Clinical evaluation *and*:
  - Blood culture
- Primary prophylaxis can be discontinued with fully suppressive ART

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Primary Prophylaxis Regimens for Disseminated MAC infection

Preferred Regimen	Alternative Regimen
Azithromycin 1200mg po weekly ***or***	Rifabutin 300mg po daily
Clarithromycin 500mg po BID ***or***	
Azithromycin 600mg po twice weekly	
Note: Active tuberculosis should be ruled out prior to drug initiation with rifabutin	

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Clinical Manifestations & Diagnosis

Clinical Manifestations of disseminated MAC infection

- Fatigue, fever, weight loss, abdominal pain, diarrhea
- Physical exam findings include hepatosplenomegaly and/or lymphadenopathy
- Abnormal labs include cytopenias, elevated LDH and Alkaline Phosphatase
- CT findings include hepatosplenomegaly, mesenteric lymphadenopathy, thickened small bowel wall

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Diagnosis of MAC infection

- Isolating organism from sterile body site
- 2 sets of mycobacterial blood cultures has a sensitivity >90%
- Diagnosis can also be made using lymph node or bone marrow biopsy

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Treatment

Treatment of disseminated MAC infection

Preferred Therapy **Should include ≥2 drugs initially**	**Alternative Therapy** **Includes addition of a 3rd or 4th drug**
Azithromycin + Ethambutol ***or***	Rifabutin ***and/or***
Clarithromycin + Ethambutol	Aminoglycoside (Amikacin or Streptomycin) ***and/or***
	Fluoroquinolone (Levofloxacin or Moxifloxacin)
Note: Macrolide susceptibility testing is recommended	**Note:** Consider adding 3rd/4th drug with high risk of mortality, advanced immunosuppression, high mycobacterial loads, and/or absence of effective ART

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Initiation of ART with New Diagnosis of Disseminated MAC Infection

- Start ART as soon as possible
- Be mindful of drug interactions with anti-mycobacterial medications

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Monitoring Response to Disseminated MAC Treatment

- Symptomatic improvement
- Repeat anti-mycobacterial blood cultures after 4-8 weeks if no symptom improvement

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Disseminated MAC and Immune Reconstitution Inflammatory Syndrome (IRIS)

- Unmasking IRIS can occur following ART initiation
- Initial improvement following by worsening of MAC disease symptoms
- Moderate MAC IRIS can be managed with NSAIDs
- More severe symptoms may need prolonged corticosteroid taper
- Continue ART
- Prognosis is good

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Discontinuing Disseminated MAC Treatment

- Completion of ≥12 months of treatment

and

- No signs and symptoms of MAC disease

and

- CD4 >100 cells/mm^3 for ≥6 months on ART

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Restarting Disseminated MAC Therapy

- If CD4 decreases to <100 cells/mm^3

and

- Fully suppressive ART is not feasible

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Medication Side Effects

Potential Side Effects of Medications use for treatment or prevention of disseminated MAC infection

Medication	Potential Side Effects
Macrolides	GI Disturbance (Clarithromycin > Azithromycin), QTc prolongation
Ethambutol	Optic neuritis (dose- and duration- dependent)
Rifabutin	Drug interactions, hepatotoxicity, staining of bodily secretions
Fluoroquinolones	Diarrhea, QTc prolongation, tendinopathy
Aminoglycosides	Renal toxicity, neurotoxicity, ototoxicity

Summary

Disseminated MAC Treatment: Editor's Summary

- Causes disseminated, multi-organ infection in PWH with a CD4 <50 cells/mm^3
- Primary prophylaxis is not routine indicated if fully suppressive ART is initiated
- Diagnosis made based on isolating organism from sterile site, usually blood
- Preferred treatment consists of Azithromycin (or Clarithromycin) + Ethambutol
- Treatment is for ≥12 months, until CD4 >100 cells/mm^3 on suppressive ART
- ART can be initiated ASAP

Source: HHS. Opportunistic Infections Guidelines. Disseminated MAC infection. February 2019.

Acknowledgments

The production of this **National HIV Curriculum** Mini-Lecture was supported by Grant U1OHA32104 from the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS). Its contents are solely the responsibility of University of Washington IDEA Program and do not necessarily represent the official views of HRSA or HHS.

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