Asymptomatic coccidioidomycosis in patients with rheumatic diseases: is there value in routine screening?

Jawad Bilal, Dominick Sudano, Shubha Kollampare, Barbara Bode, Susan Hoover, Jeffrey Lisse, and Neil Ampel

Arizona Arthritis Center and Infectious Diseases Section
The University of Arizona College of Medicine

Tucson, AZ

Disclosures

- No Disclosure

QUESTIONS ADDRESSED

- How should we approach the asymptomatic patients with positive coccidioidomycosis serologies on antirheumatic therapy?
- Is there a role of anti-fungal treatment? If yes, what is the optimal duration of therapy?
- Is it helpful to routinely screen patients for coccidioidomycosis who are receiving therapy for rheumatic diseases and living in the coccidioidal endemic region?

BACKGROUND

- The risk of developing coccidioidal infection in the endemic area is estimated to be about 3% per year.
- Patients on immunosuppressive medication are more likely to develop symptomatic and extrathoracic coccidioidomycosis than other hosts.
- In last decade, biologic response modifiers (BRMs), particularly tumor necrosis factor-α inhibitors (TNF-α inhibitors), have become an integral part of most therapeutic strategies and have been used in combination with disease modifying antirheumatic drugs (DMARDS)
- Both of these agents appear to increase the risk of clinically active coccidioidomycosis

WHAT DO WE KNOW?

Clinical Infectious Diseases

IDSA GUIDELINE

2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis

John N. Galgiani,[1] Neil M. Ampel,[2] Janis E. Blair,[3] Antonino Catanzaro,[4] Francesca Geertsma,[5] Susan E. Hoover,[6] Royce H. Johnson,[7] Shimon Kusne,[3] Jeffrey Lisse,[8] Joel D. MacDonald,[9] Shari L. Meyerson,[10] Patricia B. Raksin,[11] John Siever,[12] David A. Stevens,[13] Rebecca Sunenshine,[14,15] and Nicholas Theodore[16]

[1]Valley Fever Center for Excellence, and [2]Division of Infectious Diseases, University of Arizona, Tucson, and [3]Division of Infectious Diseases, Mayo Clinic, Scottsdale, Arizona; [4]Division of Pulmonary and Critical Care, University of California, San Diego, and [5]Department of Pediatrics, Infectious Diseases, Stanford University School of Medicine, California; [6]Division of Sanford Health, Sioux Falls, South Dakota; [7]David Geffen School of Medicine at UCLA, Department of Medicine, Kern Medical Center, Bakersfield, California; [8]Department of Rheumatology, University of Arizona, Tucson; [9]Department of Neurosurgery School of Medicine, University of Utah, Salt Lake City; [10]Division of Thoracic Surgery, Northwestern University, Feinberg School of Medicine, and [11]Division of Neurosurgery, John H. Stroger Jr Hospital of Cook County, Chicago, Illinois; [12]Arizona Pulmonary Specialists, Ltd, Phoenix; [13]Division of Infectious Diseases, Stanford University School of Medicine, California; [14]Career Epidemiology Field Officer Program, Division of State and Local Readiness, Office of Public Health Preparedness and Response, Centers for Disease Control and Prevention; [15]Maricopa County Department of Public Health, and [16]Department of Neurosurgery, Barrow Neurological Institute, Phoenix, Arizona

---

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

WHAT DO WE KNOW?

Arthritis Care & Research
Vol. 64, No. 12, December 2012, pp 1903–1909
DOI 10.1002/acr.21784

ORIGINAL ARTICLE

Management of Coccidioidomycosis in Patients Receiving Biologic Response Modifiers or Disease-Modifying Antirheumatic Drugs

SARA TAROUMIAN,[1] SUSAN L. KNOWLES,[2] JEFFREY R. LISSE,[2] JAMES YANES,[2] NEIL M. AMPEL,[3] AUSTIN VAZ,[4] JOHN N. GALGIANI,[2] AND SUSAN E. HOOVER[2]

Objective. **Coccidioidomycosis (valley fever) is an endemic fungal infection of the American Southwest, an area with a large population of patients with rheumatic diseases. There are currently no guidelines for management of patients who develop coccidioidomycosis while under treatment with biologic response modifiers (BRMs) or disease-modifying antirheumatic drugs (DMARDs). We conducted a retrospective study of how both concurrent diseases were managed and the patient outcomes at 2 centers in Tucson, Arizona.**

Methods. **A retrospective chart review identified patients who developed coccidioidomycosis during treatment with DMARDs or BRMs. Patients were seen at least once in a university-affiliated or Veterans Affairs outpatient rheumatology clinic in Tucson, Arizona, between 2007 and 2009.**

Results. **Forty-four patients were identified. Rheumatologic treatment included a BRM alone (n = 11), a DMARD alone**

WHAT DO WE KNOW?

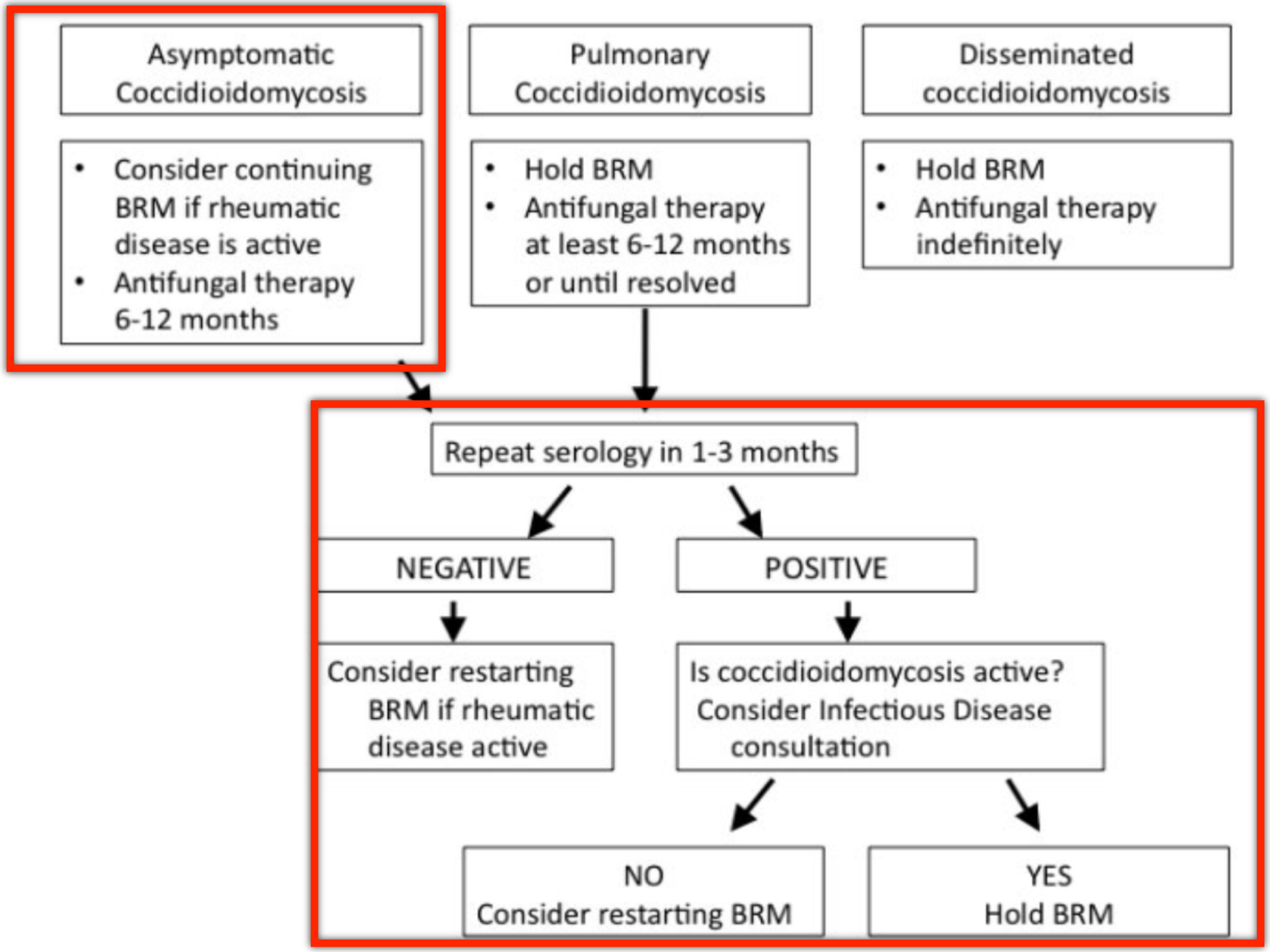

Figure 1. Suggested algorithm for management of patients who develop coccidioidomycosis during treatment with biologic response modifiers (BRMs).

STUDY DESIGN

- A retrospective study at two centers in Tucson, AZ identified patients who developed asymptomatic coccidioidomycosis while on DMARD or BRM therapy.
- Patients were seen at least once between 2007 and 2015
- Management of BRM/DMARD therapy, as well as duration of antifungal therapy is detailed
- Asymptomatic illness was defined as a positive serology found on surveillance labs, not ordered in response to symptoms, and with no concurrent signs or symptoms of active disease

PATIENT CHARACTERISTICS

- 19 patients met the inclusion criteria
  - 16 during routine annual surveillance
  - 3 during pre-BRM therapy screening
- Mean age 56.1 years (range: 26 to 77)
- 4 men, 15 women
- 8 white, 5 hispanic, 4 native American, 2 African-American
- 17 rheumatoid arthritis, 1 psoriatic arthritis, 1 dermatomyositis
- 2 on DMARD alone, 8 on BRM alone, 9 on BRM + DMARD
- 3 were on prednisone

SEROLOGIC RESULTS

- 13 had only a positive EIA serological test.
    - 7 with a positive IgM EIA alone
    - 4 with a positive IgG EIA alone.
    - 2 with both IgM and IgG EIA positive.

- 4 had positive immunodiffusion tests
(1 IDTP, 3 IDCF; 1 both)

- 2 had complement fixation positive.

RESULTS

Among the 19 patients:

- 13 were continued on BRM therapy without interruption
  - 11 were not started on antifungal therapy
  - 6 had antirheumatic therapy interrupted
    - Restarted in 5
    - Restarted within 0.5 – 12 months
- 6 patients received antifungal therapy
  - all received fluconazole
  - duration 9 to 73 months (median 30.5 mos)

OUTCOMES

- 13 (69%) continued the antirheumatic therapy without interruption
- 11 (57%) received no antifungals while DMARDs and/or BRMs were continued without dose adjustment
- **None** had complications related to coccidioidomycosis
- The total duration of follow up was 43 months

CONCLUSIONS

- Continued therapy with DMARDs and/or BRMs appears to be safe in patients with asymptomatic coccidioidomycosis
- Routine use of antifungal therapy may not be warranted
- The role of screening to detect asymptomatic coccidioidomycosis is unclear

Special Thanks

QUESTIONS