Coccidioidomycosis (Valley Fever) What Is It and How Is It Different From Tuberculosis

Tuberculosis and Cocci Webinar
December 5, 2019

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Disclosures

Drs. Galgiani
Has no conflicts of interest to disclose
What Is Valley Fever?

- Caused by soil fungi
  - *Coccidioides immitis*
  - *Coccidioides posadasii*
- Other names:
  - Coccidioidomycosis
  - “COCCI”
- Inhalation of one spore causes infection
- Spectrum of disease
  - Sub-Clinical: 60%
  - Self-Limited: 30%
  - Complicated: 10%
- After infection, most persons develop lifelong immunity to a second infection
Valley Fever Endemic Regions
The Valley Fever Corridor: 2/3 of all U.S. disease occurs here
Valley Fever in Non-endemic States

Figure 1. Reporting state and frequency of travel to coccidioidomycosis-endemic areas (Arizona, California, Nevada, New Mexico, Texas, Utah, Washington, Mexico, and Central or South America) in the 4 months before symptom onset or first positive coccidioidomycosis test among coccidioidomycosis patients reported from 14 low-endemic and nonendemic US states, 2016.

Benedict et al. EID, 2018
Valley Fever in the U.S.

- Total Infections: 150,000-
- Seek Medical Attention: 15,000-
- Diagnosed/Reported: 1,500-
- Disseminated Infection: 150-
- Deaths: 15-

75% Stopped working,
50% lost > 2 weeks
50% Illness >4 months
40% Hospitalized (Az)
Cost=$700M (CA, 2017)
Total US Impact: >$1 B/year
Common “Mild” Self-Limited Valley Fever

Signs and Symptoms, < 1 months from exposure:
- Cough, chest pain, fever, weight loss
- Fatigue
- Bone and joint pains (a.k.a. Desert Rheumatism)
- Skin rashes (painful or intense itching)

Course of illness:
- Weeks to months
- 25% of college students are sick for > 4 months
- 50% of workers lose > 2 weeks
Current Clinical Practice for Valley Fever in Arizona

Arizona CAP
- ~ 25% - 30% due to Coccidioides
  BUT
- < 15% are tested for Coccidioides

~ 1,000 new AZ medical licenses/year
- 12% received MD in AZ
- 40% no AZ GME

80% didn’t know:
- VF is reportable
- Vaccine does not exist

40% of clinicians are not confident to treat VF
Only 247 out of 1,812 unique patients (13.6%) who were newly diagnosed as Cocci in primary care clinics (orange bar)

Dots indicate percent of patients receiving anti-bacterial drugs.
Delay of Valley Fever Diagnosis

BUMC-P
45% of Diagnoses Delayed > 1 month

Ginn et al. EID, 2019
Delay of Valley Fever Diagnosis

BUMC-T
43% of Diagnoses Delayed > 1 month

Donovan et al. EID, 2019

Figure 1.

Days of Delay until Diagnosis

Percentage Diagnosed

Acute Pulm
Chron Pulm
Asymptomatic
Dissemin
What Do Weeks of Delayed Diagnosis Mean?

- Unnecessary anti-bacterial drug use
- Protracted patient anxiety and fear
- Over-utilization CT scans and bronchoscopies, even thoracotomies

**Hypothesis:** Earlier diagnosis would improve outcomes and reduce cost
Valley Fever
(Coccidioidomycosis)

A Training Manual for
Primary Care Professionals

Available online:
VFCE.ARIZONA.EDU
Primary Care of Coccidioidomycosis

- **Consider** the diagnosis
- **Order** the right tests
- **Check** for risk factors
- **Check** for complications
- **Initiate** management
Consider the diagnosis

Respiratory: Previous visit, needs X-ray or antibacterial Rx?
Musc/Skel: More than one week, associated with fever or fatigue.
Rashes: *E. nodosum* or *E. multiforme*

Clinician reviews chief complaint(s) and medical history, examines patient, and documents findings (HPI, ROS, PE)

Syndrome: respiratory? musculoskel? rashes?

Endemic Exposure? residence or recent travel

Go to: Order the right tests

Valley Fever Process Completed
Have you diagnosed a patient with Valley Fever in the last 12 months?

A. Yes
B. No
Have you tested for Valley Fever in the last 12 months?

A. Yes
B. No
Number of Clinicians for Each Test Count
BMG and BUMG, total, 2018

Total Clinicians: 223
# ≤ 2 tests ordered: 119
% ≤ 2 tests ordered: 53%
Table 5. Consider testing for coccidioidomycosis if endemic history and any of the following:

- Respiratory symptoms plus one of:
  - More than 1 office visit
  - Chest X-ray ordered
  - Antibiotic prescribed
- Two of the following for a week or more:
  - Fever, Fatigue, Arthralgia
- Unexplained peripheral blood eosinophilia
- Skin lesions of:
  - *Erythema nodosum* or *Erythema multiforme*
Order the right tests

EIA screen for coccidioidal antibodies with reflex to immunodiffusion and quantitative CF.

Illness resolved in 3 weeks

No

Test Negative

Test Positive

Go to: 3 & 4 Check for risks and complications

Yes

Valley Fever Process Completed

2

Order the right tests

Order EIA screen for coccidioidal antibodies
Order the Right Tests:
EIA screen for Coccidioidal Antibodies

Enzyme Immunoassay (EIA) test

– A positive test is very specific and usually is diagnostic.

– A negative test never rules out Valley Fever. Repeated testing improves diagnostic sensitivity.
Check for Risk Factors

Immunosuppression (HIV, organ recipient, Rheum/GI/Derm response modifier Rx, renal failure)
Diabetes, major cardiac or pulmonary comorbidities, pregnancy

Risk factors present?

No

Go to: Management, Uncomplicated infect.

Yes

Complicated VF: Refer to Specialist (ID or Pulmonary)
Risk Factors

Pulmonary Complications
- Diabetes mellitus
- Cardio-pulmonary or other co-morbidities (Evidence: “common sense”).

Disseminated Infection
- Major and critical
  - Cell immunodeficiency
  - Pregnancy
- Minor and small effect
  - Males > Females
  - Racial background
  - Adults > Children
Check for complications evident by physical exam or imaging

Focal ulceration or skin/soft tissue inflammation.
Asymmetric skeletal pain, joint effusions.
Progressive or unusual headache.

Risk factors present?

Complications present?

Go to: Management, Uncomplicated infect.

Complicated VF: Refer to Specialist (ID or Pulmonary)
Detecting Focal Lesions in Coccidioidomycosis

• Review of Systems: Pain or discomfort
  – Headache
  – Back pain
  – Joint pain or loss of function

• Physical Examination:
  – Skin lesions
  – Subcutaneous fluctuation
  – Joint effusions
Disseminated Coccidioidomycosis
Disseminated Coccidioidomycosis
Disseminated Coccidioidomycosis
Disseminated Coccidioidomycosis
Check for Complications

• Most complications are focal
• A review of systems and physical examination will usually detect or exclude the possibility of complications.
• New focal findings warrant either evaluation or referral for Infectious Diseases or Pulmonary consultation.
Primary Care of Coccidioidomycosis

Consider the diagnosis

Order Cocci Serologies

Check for Risk Factors

Check for complications

Initiate management

Repeat evaluations

Order Cocci Serologies

Check for Risk Factors

Check for complications

Initiate management

Specialty Referral

Retest
Management
Low Risk, Simple Early Infection

• Follow-up office visits
• Serial body weights
• Check for new symptoms or signs
• Repeat coccidioidal antibody testing
• Repeat Chest PA and Lateral X-rays
• Most patients do not need therapy
2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis
“It should be emphasized that no randomized trials exist to assess whether antifungal treatment either shortens the illness of early uncomplicated coccidioidal infections or prevents later complications.”
Median days to ≥50% decline in total clinical score

P = 0.899

Ampel et al. CID 2009
Outcome of Subjects
(> 1 month follow-up)

• 50 not treated
  – Median follow-up: 3.1 years
  – All without complications

• 51 treated
  – Median follow-up: 2.9 years
  – 38 off-therapy and without complications
  – 5 remained on treatment
  – 8 had relapses
    • 5 with pulmonary disease
    • 3 with extrapulmonary dissemination
    • Relapses occurred up to 2 years after stopping treatment

Ampel et al. CID 2009
Valley Fever Can Look Like TB

- Illness is often subacute or chronic pulmonary syndrome.
  - Nights sweats, weight loss, hemoptysis and fatigue are common symptoms.
  - Treatment for bacterial pneumonia has failed is a common history.
  - Chest X-rays may show fibrocavitary lung lesions.
TB or Cocci?
TB or Cocci?
TB or Cocci?
The Binational Project improving the Diagnosis and Surveillance of Coccidioidomycosis in the Border Region of “Four Corners” Arizona-Sonora and New Mexico-Chihuahua

Dra Nubia Hernandez, Orion McCotter, Katherine Perez-Locket, Mariana Casal, Cristhian Tapia, Robert Guerrero, Dr. Gumaro Barrios, Dr Francisco Navarro Galvez, Olvera Alba Sergio, QC Rosario Aguayo, Frida Adams, Marta Alicia Bueno, Cesar Vera, Gloria Carrete, Ken Komatsu

Secretaría de Salud Pública de Sonora
Secretaría de Salud Pública de Chihuahua
Arizona Department of Health Services
New Mexico Department of Health Services
Algorithm for detection, notification and sample for Coccidioidomycosis cases.

Possible Tuberculosis case

Notification due to epidemiological study and identification of case in TB platform

Sample send to PH laboratory with copy of TB epidemiology study

Serum sample 100% cases, 100% deaths

PH laboratory: testing IgG/IgM for Coccidioidomycosis

Reactive (+) For one or both Ig’s

Undetermined result Process again

InDRE/PH lab: immunodiffusion confirmatory test and report InDRE results

Non reactive (-) For one or both Ig’s

Report positive (+) result with the specific reactivity

Report negative (-) result to both Ig’s

FINAL classification of the case by the Notification Unit. Consider clinical, epidemiological and laboratory criterias.
Sonora Preliminary Results

Total samples 2012-2013

<table>
<thead>
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<th>samples tested</th>
<th>159</th>
<th>17%</th>
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<tr>
<td>Negatives</td>
<td>132</td>
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Positive samples 2012-2013

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<tr>
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<th>IgM</th>
<th>IgG</th>
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<tr>
<td>IgM</td>
<td></td>
<td>5</td>
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Ask your doctor to test you for Tuberculosis or Valley Fever TODAY!

¡Solicite a su médico hacerle exámenes de Tuberculosis o Fiebre del Valle AHORA!
New Banner Clinical Practice for Ambulatory Management of Valley Fever

Thank-You

For more information:
http://vfce.arizona.edu/toolkit
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Valley Fever in Non-endemic States

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