

IRIS in Histoplasmosis

L. Joseph Wheat



Diagnostic Criteria

- New appearance or worsening of clinical or radiologic manifestations consistent with an inflammatory process.
- Symptoms occurring during receipt of appropriate antifungal therapy that cannot be explained by a newly acquired infection.
- Negative results of cultures or stable or reduced biomarkers for the initial fungal pathogen during the diagnostic workup for the inflammatory process.

Treatment Failure in TNF Blocker Patient

Sarcoid on inflix → histo 3 mo later
AmB initiated, inflix discontinued
ARDS 7 d later on AmB → mech vent
CT → increased diffuse infiltrates
Antigen declined, 8.5 → 4.4 u
Lung biopsy → granuloma, yeast
Steroids initiated for “IRIS”
Lung culture negative
5 year later: well, antigen negative



Necrotic Spleen Lesion in AIDS

AIDS recent initiation ART, CD4 37

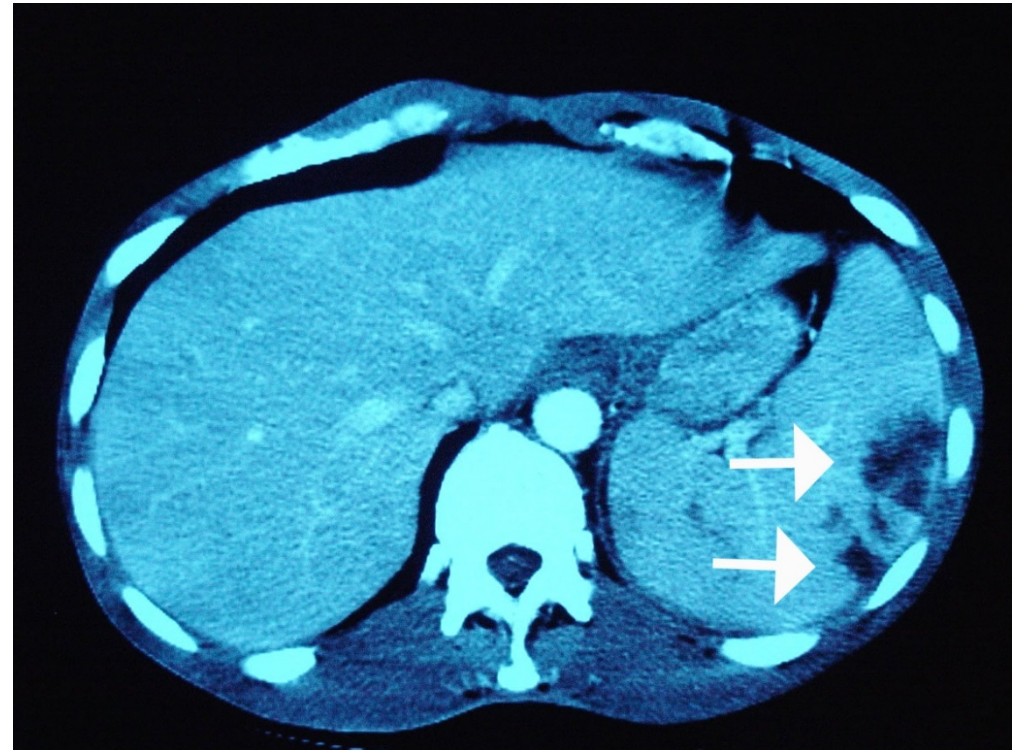
4mo later intractable hiccoughs,
CD4 101

Adenopathy-FNA showed yeast,
cultures grew *H. capsulatum*

Palpable spleen tip

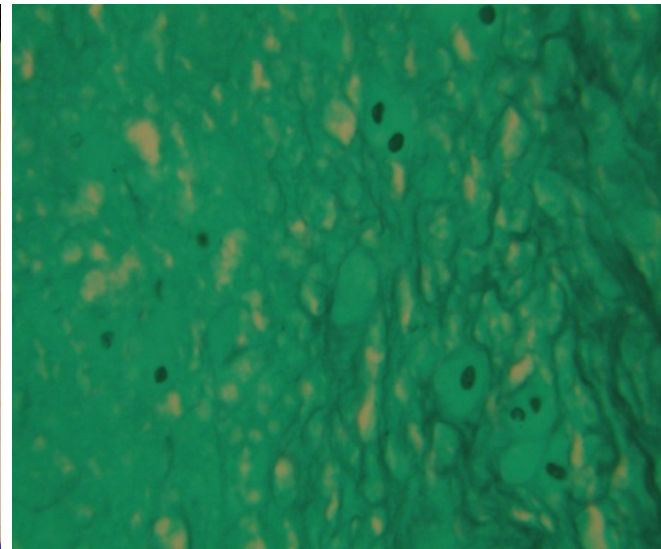
CT hypodense lesions

Recovered with amphotericin B



Suspected Relapse-JRA Case

<u>Baseline</u>	<u>8 mo</u>	<u>12 mo</u>	<u>28 mo</u>
Pneumonia	Well	Adenopathy Hc seen, culture negative	Well
Uag 12.0 ng	7.0 ng	2.2 ng	<0.6 ng
AmB→Itra	Itra >3 µg	Itra→AmB→no response→pred→ resolution	Off therapy



Unpublished Cases

<u>Condition</u>	<u>Manifestation</u>	<u>Antigen</u> -initial -IRIS	<u>Treatment</u>	<u>Outcome</u>
JRA/methotrex	Lymph	-12ng -2ng	Steroids	Recovery
Arthritis/steroid	Soft tissue	-not detected -not detected	Steroids	Recovery
Ulcerative colitis/steroid, azathioprine	Respiratory	-4.4ng -<.6ng	Steroids	Recovery
Transplant	Respiratory	->19ng -2.2ng	Steroids	Recovery



Published Histo IRIS Cases

<u>Parameter</u>	<u>AIDS (n=15)</u>	<u>Other (n=10)*</u>
Lymphadenopathy	33%	10%
Rash	20%	0%
Respiratory	13%	60%
CNS	13%	0%
Other	40%*	3%*
Recover	93%	100%
Footnotes	* spleen, liver, joints, eyes, intestines, bone, hemophagocytic	*spleen, liver, hemophagocytic



Differentiation IRIS & Relapse Histoplasmosis

<u>Parameter</u>	<u>IRIS</u>	<u>Relapse</u>
Pulmonary finding	Yes	Yes
Extrapulmonary finding	Yes	Yes
Months after onset	1-12	6-36
Antifungal therapy	Adherent, itra >1 μ g	Non-adherent, itra < 1 μ g
Fever	Yes or no	Yes or no
Pathology	Yeast seen	Yeast seen
Culture	Negative	Positive
Antigen	Progressive decline	Persist or decline then increase
Response antifungal Rx	No	Yes
Response corticosteroid	Yes	Initially then progressive illness



Management

Differentiate from relapse or new opportunistic infection

Many cases recover without changing treatment

No published studies or controlled trials evaluating treatment

Anti-inflammatory medications (corticosteroids or nonsteroidal agents) may be helpful in patients with more severe or persistent manifestation