Case 1 (TV13-74)

TV Colby MD
Mesothelioma ??

Why is this not a mesothelioma ??
Differential Diagnosis:
Mesothelioma
Metastatic Carcinoma
Lung, thyroid, other
Case 1 History

61F
History of cardiomyopathy
Increasing dyspnea
Exudative right pleural
Pleural biopsies taken

Does this help in the D/D ??
You want immunos don’t you ??

Differential Diagnosis:
Mesothelioma
Metastatic Carcinoma
Lung, thyroid, pap serous
**Immunohistochemistry:**
Positive: WT1, ER, AE1/AE3, MOC31
Negative: CK5/6, calretinin, PR, TTF-1, TG
Case 1 Diagnosis

**Diagnosis**: Serous papillary tumor of the pleura, borderline vs carcinoma (favor the former but we have no published criteria)

**Metastasis from the peritoneum or genital tract to be excluded**

**Follow-up**: Both ovaries found to have clinically occult papillary serous carcinoma

Case courtesy Dr. J Devitt, Cincinnatti
Serous tumors of the Pleura

Review of the Literature

Whoops!! ....Not much found
So I went for expert opinion: Andrew Churg agreed with diagnosis...
...And reviewed my files:

5 additional cases of pap. serous carcinoma presenting as pleural effusion
All women; 48-63 yrs
Abdominal disease known/found in 2, no f/u in 2, 1 with no abd. disease at 18 mos.
Case 1 Discussion Points

1. Serous tumors of the pleural space

A unique case of serous psammocarcinoma of the ovary presenting with pleural effusion ... implants in the pleural cavity....

(Tiro AV, Talukdar R, Lewis MG. Gynecol Oncol. 2009;113:402-4)

2. Diagnosis of mesothelioma
Diagnosis of Mesothelioma

The diagnosis of mesothelioma is microscopic!! It is made by the pathologist.

The clinical, radiologic, and gross surgical findings may be very suspicious for mesothelioma but the diagnosis is made by the pathologist microscopically.
Diagnosis of Mesothelioma

Location affects Dx/Dx: pleural vs peritoneal
Sex affects Dx/Dx

Asbestos/erionite exposure is irrelevant for diagnosis but not for cause
Histologic Approach to Diagnosis of Mesothelioma

Suspected Mesothelial Proliferation

- Epithelioid
  - Benign
  - Malignant

- Spindled
  - Malignant
  - Benign
Suspected Mesothelial Proliferation

ISSUE #1

Epithelioid

Benign

Malignant

Reactive mesothelial cells  VERSUS  Mesothelioma cells
Mesothelioma vs Reactive Mesothelial Cells

Primarily a cytologic/histologic determination

None of these is 100% accurate in the individual case.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Reactive Mesothelium, No. (% Positive)</th>
<th>Mesothelioma, No. (% Positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmin</td>
<td>32/45 (71)</td>
<td>33/45 (73)</td>
</tr>
<tr>
<td>EMA</td>
<td>22/45 (49)</td>
<td>27/45 (60)</td>
</tr>
<tr>
<td>CD10</td>
<td>37/45 (82)</td>
<td>37/45 (82)</td>
</tr>
<tr>
<td>CD31</td>
<td>33/45 (73)</td>
<td>33/45 (73)</td>
</tr>
<tr>
<td>CD44</td>
<td>24/45 (53)</td>
<td>27/45 (60)</td>
</tr>
<tr>
<td>CD146</td>
<td>24/45 (53)</td>
<td>30/45 (67)</td>
</tr>
<tr>
<td>CD147</td>
<td>28/45 (62)</td>
<td>30/45 (67)</td>
</tr>
<tr>
<td>GLUT-1</td>
<td>32/45 (71)</td>
<td>33/45 (73)</td>
</tr>
<tr>
<td>IMP3</td>
<td>28/45 (62)</td>
<td>30/45 (67)</td>
</tr>
</tbody>
</table>

CD146, CD147, GLUT-1, IMP3 positivity recently touted as markers for mesothelioma

Malignant Mesothelioma

Invasion is the key finding in confirming a diagnosis of mesothelioma

Invasion difficult to assess

CK: Clearly invasive
Mesothelioma vs Reactive Mesothelial Cells
Can one diagnose mesothelioma without demonstrating invasion?

Yes!!
Cytologists do it all the time
In the presence of a bulky pleural mass
Compelling cytologic features in histologic sections
Suspected mesothelial proliferation

Epithelioid

Benign

Malignant

Mesothelioma  VERSUS  Metastatic Carcinoma and other mimics of mesothelioma

ISSUE #2
MESOTHELIOMA VERSUS METASTATIC (ADENO)CARCINOMA

This is most common histologic problem encountered by the surgical pathologist.

Immunohistochemistry is extremely important in this situation.
Pleural Metastasis of Lung Adenocarcinoma

Clues to carcinoma: Paucity of cells, high grade cytology
Lung Adenocarcinoma invading the Pleura

Why several antibody stains?
POSITIVE MESOTHELIOMA MARKERS IN LUNG ADENOCARCINOMAS

(Miettinen and Sarlomo-Rikala, AJSP 2003;27:150-158)

Calretinin: ~13%
Thrombomodulin: ~14%
Keratin 5: ~12%
Mesothelin: >50%
Mesothelioma vs Metastatic Carcinoma

Recommendation

At least 2 markers favoring mesothelioma

At least 2 markers favoring carcinoma

In practice most experts do at least 6 markers, including a pankeratin to assess positivity, pattern, and immunogenicity
### IMMUNOHISTOCHEMISTRY: MESOTHELIOMA VS. CARCINOMA

<table>
<thead>
<tr>
<th>Positive Markers</th>
<th>Negative Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calretinin</td>
<td>pCEA</td>
</tr>
<tr>
<td>WT-1</td>
<td>Ber-EP4</td>
</tr>
<tr>
<td>CK 5/6</td>
<td>B72.3</td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>CD15</td>
</tr>
<tr>
<td>Mesothelin</td>
<td>BG8</td>
</tr>
<tr>
<td>D2-40</td>
<td>MOC31</td>
</tr>
<tr>
<td>HBME-1</td>
<td>TTF-1</td>
</tr>
<tr>
<td></td>
<td>ER/PR*</td>
</tr>
<tr>
<td></td>
<td>PSA, CDX2*</td>
</tr>
</tbody>
</table>

* Site, sex, type of ca in D/D are factors
MESOTHELIOMA

CK 5/6

Calretinin

Invasion is highlighted
WT1 of no value in the peritoneum in a woman where ovarian type serous carcinoma is a consideration
Inconclusive Immunostains?
Inconclusive panels of stains?

Prioritize the immunostains (eg. MOC31 in meso vs TTF in meso)

When the immunostains don’t fit or are inconclusive I revert to gross/radiologic findings input and routine H+E’s.

Some cases are insoluble:

Eg. “Malignant tumor, carcinoma favored over mesothelioma”
Suspected Mesothelial Proliferation

ISSUE #3

Spindled

Malignant

Desmoplastic mesothelioma VERSUS Fibrous pleuritis

Benign
Desmoplastic Mesothelioma

Not quite right for reactive fibrosis

And to repeat....Pancytokeratin is usually the only marker needed in this setting; most others are a waste of resources

Pancytokeratin is usually the only marker needed in this setting
Gross and radiologic features are not always helpful!

And surgeons can be fooled!

The diagnosis of mesothelioma is made microscopically.

Desmoplastic Mesothelioma

Empyema
Desmoplastic Mesothelioma

Invasion of Chest Wall Fat
Desmoplastic Mesothelioma
Invasion of the Lung
Desmoplastic Mesothelioma
Invasion of the Lung

Lung invasion is subtle and easily missed

Alveolar spaces
Desmoplastic Mesothelioma

Bland infarct-like necrosis
Desmoplastic Mesothelioma

Sarcomatoid Focus

Disorganized CK
REACTIVE FIBROUS PLEURITIS

Uniform thickness, zonation and vertically oriented vessels
DESMOPLASTIC MESOTHELIOMA

Disorganized, abrupt changes in cellularity
Suspected Mesothelial Proliferation

ISSUE #4

Spindled

Malignant

Sarcomatoid mesothelioma  VERSUS  Sarcomas and Other spindle cell tumors

Benign
OTHER PLEURAL (SARCOMATOID) TUMORS

Epithelioid hemangioendothelioma
High-grade angiosarcoma
Leiomyosarcoma
Clear cell sarcoma
Synovial sarcoma
Liposarcoma
Myxoid chondrosarcoma
Desmoplastic small round cell tumor

All are rare
Molecular Aspects of Mesothelioma*

9p21 (the locus harboring CDKN2A) homozygous deletions (p16) in mesothelioma:

? Diagnostic usefulness
? Prognostic significance

*Chiosea et.al. in Mod Pathol 2008; 21: 742
*Husain et.al. in Arch Pathol Lab Med 2012 Epub
*Betta et.al. in Arch Pathol Lab Med 2012; 136: 253
*Jean et.al. in Arch Pathol Lab Med 2012; 136: 277)
9p21 deletion (p16) and mesothelioma histology

Epithelioid, Biphasic, Sarcomatoid

Slide courtesy S. Dacic MD
p16 DELETION IN PLEURAL MESOTHELIOMAS CORRELATES WITH LONG TERM SURVIVAL

Mesothelioma
Patterns of Presentation

1. Diffuse serosal process - most common
2. Localized mass: eg. chest wall, lung, mediastinum, abdomen, liver, et.al.
3. Lymphadenopathy
   D/D benign mesothelial cells in LNs
4. Diffuse lung disease
WHAT TYPE OF BIOPSY??

Bigger the better

Cytology may be adequate
   Especially in epithelioid mesothelioma
   Experienced cytopathologist

Cytology rarely of value in desmoplastic mesothelioma

Needle biopsies adequate if invasion seen

Large VATS biopsies usually needed for desmoplastic mesothelioma
SUMMARY: MESOTHELIOMA

The Dx/Dx varies with problem: spindle cell proliferations vs epithelioid proliferations.

Immunohistochemistry must be tailored to the situation.

Most mesotheliomas can be recognized on H+E; immunohistochemistry is confirmatory.

Demonstration of invasion is the key feature in confirming malignancy.
THANK-YOU FOR YOUR ATTENTION!
Case 2 (TV13-216)

TV Colby
Case 2

Surgical lung biopsy for interstitial lung disease
Patchy fibrosis
With fibroblast foci

UIP right...... ??
You should be asking: Why is this **not** UIP

Let’s look at the history and the rest of the case...
And then there is the history: (Case 2, TV13-216)

- 45 yr. old physician
- 3 month history of: cough, dyspnea, and fatigue
  ILD on CXR; No CT at that time
- BAL with 19% lymphs
  TBBx- Bronchial mucosa only
Surgical lung biopsy performed: “Drs -- and Colby feel that this represents “diffuse interstitial pneumonitis with moderate fibrosis, so-called ‘usual type”’ = UIP
Very diffuse process with germinal centers and increased inflammatory cells
Increase interstitial inflammatory cells

Plasma cells
Fibrosis... but it is not subpleural and paraseptal and we see no honeycombing
Fibroblast foci are not specific for UIP
Organizing pneumonia vs fibroblast foci; is not patchy in this field
Case 2 (TV13-216): Follow-up

Placed on steroids, 60 mg. per day
1 year later stable on 30 mg prednisone per day with PFTs “about 65% of normal”
Alive and stable 22 yrs after biopsy; no details on functional or radiologic findings
Retrospective diagnosis: Fibrotic NSIP, ? In association with CTD.
Histopathological Variability in UIP and NSIP

Cumulative proportion surviving

Years

Concordant UIP

Discordant UIP

NSIP

Flaherty et al: AJRCCM, 2001
UIP for Comparison

UIP

Case 2
UIP for Comparison

UIP

Case 2
UIP for Comparison

Not very different in these fields
Case 2 Lessons and Discussion

Too many red flags for a diagnosis UIP/IPF

Role of the pathologist in Interstitial Lung Disease (ILD): be part of the multidisciplinary discussion (MDD)

Role of the pathologist in UIP diagnosis
Is UIP what you see?
If it is UIP, then is it IPF?

Familiarity with lung biopsy techniques:
TBBx, TB cryobiopsy, SLBx

Pathologist’s role in clinical trials for IPF
CASE

69M with increasing dyspnea
Lifelong nonsmoker
Bilateral lower lobe infiltrates with honeycombing in the RLL; VATS biopsy performed……

What is your diagnosis ??
Fibroblast foci
Dense, patchy scarring
UIP Right ?
MORE TO THE CASE...

Pt had had birds for years
Dx: Chr. Hypersensitivity pneumonitis

Foci of organizing pneumonia and granulomas
2011 DIAGNOSTIC ALGORITHM FOR IPF

Suspected IPF

Identifiable cause for ILD? (CTD, drugs, exposures, ...)

YES

NO

* Chest HRCT

UIP

HRCT c/w UIP
HRCT Inconsistent/w UIP

Surgical lung biopsy

SLBx: -UIP
-Possible UIP / Probable UIP
-Non classifiable fibrosis

* MDD

IPF

Not UIP

IPF / Not IPF

Not UIP

Not IPF

Am J Respir Crit Care Med 2011; 183: 788-824

Slide courtesy Luca Richeldi
The accuracy of the diagnosis of IPF increases with multidisciplinary discussion (MDD) between pulmonologists, radiologists, and pathologists experienced in the diagnosis of interstitial lung disease.

Multidisciplinary discussion (MDD) = clinical-radiologic-pathologic correlation

Multidisciplinary team (MDT) is a term also being used.
Pathologist and ILD

It all starts with UIP, the morphologic pattern found in idiopathic pulmonary fibrosis (IPF).

UIP is the most common pattern
UIP carries the worst prognosis
Our issue: Is it UIP in IPF ??

UIP pattern also seen in: CTD, Chronic HP, drug reactions, misc. other settings
UIP and the Pathologist

Major decision points:

UIP versus Other ILD
UIP/IPF versus Other cause of UIP

If Other ILD: subclassify
USUAL INTERSTITIAL PNEUMONIA (UIP) & IDIOPATHIC PULMONARY FIBROSIS (IPF)

Idiopathic UIP = IPF
Clinical: Progressive restrictive disease
Radiologic: Progressive bilateral infiltrates with peripheral basal honeycomb change on HRCT
Prognosis: Poor (median survival < 3 yrs)

As illustrated, not all cases of UIP occur in the setting of IPF
Usual Interstitial Pneumonia (UIP):
The most common/important pattern

- Dense scar, honeycombing
- Fibroblast foci
Treatment Trials for IPF have necessitated algorithms for patient accrual
<table>
<thead>
<tr>
<th>Definite UIP</th>
<th>Possible UIP</th>
<th>Inconsistent with UIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>(all four features)</td>
<td>(all three features)</td>
<td>(any of the seven features)</td>
</tr>
<tr>
<td>Subpleural, basal predominance</td>
<td>Subpleural, basal predominance</td>
<td>Upper or mid lung predominance</td>
</tr>
<tr>
<td>Reticular abnormality</td>
<td>Reticular abnormality</td>
<td>Peribronchovascular predominance</td>
</tr>
<tr>
<td>Honeycombing with or without traction bronchiectasis</td>
<td>Absence of features listed as inconsistent with UIP pattern</td>
<td>Extensive ground glass abnormality (extent &gt; reticular abnormality)</td>
</tr>
<tr>
<td>Absence of features listed as inconsistent with UIP pattern (see third column)</td>
<td>(see third column)</td>
<td>Profuse micronodules (bilateral, predominantly upper lobes)</td>
</tr>
</tbody>
</table>

Levels of confidence are included and these have been sort of validated

Slide courtesy Luca Richeldi

*Am J Respir Crit Care Med 2011; 183: 788-824*
HISTOPATHOLOGICAL CRITERIA FOR UIP PATTERN

<table>
<thead>
<tr>
<th>Definite UIP</th>
<th>Probable UIP</th>
<th>Possible UIP</th>
<th>Not UIP</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>(all four criteria)</em></td>
<td><em>(all three criteria)</em></td>
<td><em>(any of the six criteria)</em></td>
<td></td>
</tr>
</tbody>
</table>

- Evidence of marked fibrosis/architectural distortion, +/- honeycombing in a predominantly subpleural/paraseptal distribution
- Presence of **patchy involvement** of lung parenchyma by fibrosis
- Presence of **fibroblast foci**
- Absence of features against a diagnosis of UIP suggesting an alternate diagnosis (see fourth column)

OR

- Evidence of marked fibrosis/architectural distortion, +/- honeycombing in a subpleural/paraseptal distribution
- Absence of either patchy involvement or fibroblastic foci, but not both
- Absence of features against a diagnosis of UIP suggesting an alternate diagnosis (see fourth column)

- Patchy or diffuse involvement of lung parenchyma by fibrosis, with or without interstitial inflammation
- Absence of other criteria for UIP (see UIP pattern column)
- Absence of features against a diagnosis of UIP suggesting an alternate diagnosis (see fourth column)

- Hyaline membranes
- Organizing pneumonia
- Granulomas
- Marked interstitial inflammatory cell infiltrate away from honeycombing
- Predominant airway centered changes
- Other features suggestive of an alternate diagnosis

“Levels of confidence” again included

Slide courtesy Luca Richeldi

Am J Respir Crit Care Med 2011; 183: 788-824
1. Clear evidence of **chronic scarring and architectural destruction**
2. Evidence of active fibrosis as **fibroblast foci**
3. Typically patchy, subpleural or paraseptal
4. Absence of features suggesting an alternative diagnoses
Combining HRCT and Pathology interpretations to determine if IPF is present

<table>
<thead>
<tr>
<th>HRCT Diagnosis</th>
<th>Pathology</th>
<th>IPF Present?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite UIP</td>
<td>Definite UIP</td>
<td>Yes</td>
</tr>
<tr>
<td>Definite UIP</td>
<td>Probable UIP</td>
<td>Yes</td>
</tr>
<tr>
<td>Definite UIP</td>
<td>Possible UIP</td>
<td>Yes</td>
</tr>
<tr>
<td>Definite UIP</td>
<td>Not UIP</td>
<td>No</td>
</tr>
<tr>
<td>Consistent with UIP</td>
<td>Definite UIP</td>
<td>Yes</td>
</tr>
<tr>
<td>Consistent with UIP</td>
<td>Probable UIP</td>
<td>Yes</td>
</tr>
<tr>
<td>Consistent with UIP</td>
<td>Possible UIP</td>
<td>No</td>
</tr>
<tr>
<td>Consistent with UIP</td>
<td>Not UIP</td>
<td>No</td>
</tr>
<tr>
<td>Suggests alternative Dx</td>
<td>Any Path</td>
<td>No</td>
</tr>
</tbody>
</table>

From NIH IPFnet
The concept is a useful in clinical trials. Radiologists have a similar approach. Framework for patient management.
The criteria were pulled out of thin air and are not validated.

NOT something for routine path reports (unless part of the comment/discussion)
Pathologic issues

Many biopsies are “possible” UIP
DAD and OP may be focal changes in UIP
    - Usually not an issue unless widespread (? AE)
Granulomas: definition, number present?
Airway-centering: how widespread?
Inflammation: how much is too much?
Here are some examples:
Airway centered changes

When do we decide these are significant??
Peribronchiolar Metaplasia (PBM)

Dx: Chronic HP

PBM is common incidental finding

Occurs in UIP..(59%*)...

...But also Chronic HP and airway disease

The features of “Not UIP” are arbitrary, subjective and have not been validated.

*AJSP 2005; 29: 948
Increased inflammation and germinal centers as clues for connective tissue disease
Sometimes UIP in the CTD’s is identical to IPF
Often there are clues that a CTD is present

Increased inflammation

Fibr. focus
Pathologic and Radiologic Differences Between Idiopathic and CTD-Related UIP

(Song JW et.al. Chest 2009; 136: 23)

<table>
<thead>
<tr>
<th>Category</th>
<th>CVD-UIP Patients</th>
<th>IPF/UIP Patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroblastic foci</td>
<td>1.56 ± 0.74</td>
<td>2.01 ± 0.81</td>
<td>0.007</td>
</tr>
<tr>
<td>Germinal centers</td>
<td>1.04 ± 1.07</td>
<td>0.33 ± 0.61</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total inflammation</td>
<td>2.10 ± 0.69</td>
<td>1.74 ± 0.66</td>
<td>0.010</td>
</tr>
<tr>
<td>HC (size)*</td>
<td>1.71 ± 1.09</td>
<td>2.20 ± 1.09</td>
<td>0.034</td>
</tr>
<tr>
<td>Plasma cells</td>
<td>1.72 ± 0.68</td>
<td>1.43 ± 0.71</td>
<td>0.044</td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td>0.33 ± 0.53</td>
<td>0.38 ± 0.60</td>
<td>NS</td>
</tr>
<tr>
<td>Intraalveolar macrophages</td>
<td>0.76 ± 0.54</td>
<td>0.85 ± 0.45</td>
<td>NS</td>
</tr>
<tr>
<td>Pleural fibrosis, % of affected cases</td>
<td>4 (10.5)</td>
<td>7 (11.5)</td>
<td>NS</td>
</tr>
</tbody>
</table>
The current dogma: Surgical/VATS lung biopsies required to recognize patterns; esp. UIP, NSIP

Transbronchial occasionally useful with clinical- radiologic correlation

Transbronchial cryobiopsies may change the entire paradigm!

-Architectural features as seen on SLBx can be appreciated
Transbronchial cryobiopsy in IPF

Images courtesy Alberto Cavazza MD

- Honeycombing
- Patchy fibrosis
- Fibroblast foci
## 2002 ATS/ERS Classification of Idiopathic Interstitial Pneumonias*

<table>
<thead>
<tr>
<th>Clinicopathologic Diagnosis</th>
<th>Pathologic Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic pulmonary fibrosis (IPF)</td>
<td>UIP</td>
</tr>
<tr>
<td>Desquamative interstitial pneumonia (DIP)</td>
<td>DIP</td>
</tr>
<tr>
<td>Respiratory bronchiolitis interstitial lung disease (RBILD)</td>
<td>RB</td>
</tr>
<tr>
<td>Cryptogenic organizing pneumonia (COP)</td>
<td>OP (BOOP)</td>
</tr>
<tr>
<td>Acute interstitial pneumonia (AIP)</td>
<td>DAD</td>
</tr>
<tr>
<td>Nonspecific interstitial pneumonia (NSIP)</td>
<td>NSIP</td>
</tr>
<tr>
<td>Lymphocytic interstitial pneumonia (LIP)</td>
<td>LIP</td>
</tr>
</tbody>
</table>

*ATS/ERS International Consensus Panel; Am J Respir Crit Care Med 2002; 165:277
The IIPs have been recategorized:

- Major IIP’s
- Rare IIP’s
- Unclassified IIP’s

A new condition added (PPFE)
Revised (2013) ATS/ERS IIP Classification
(Clin-rad-path/CRP Diagnosis)

**Major Idiopathic Interstitial Pneumonias**
- Idiopathic pulmonary fibrosis (IPF)
- Idiopathic nonspecific interstitial pneumonia (NSIP)
- Respiratory bronchiolitis interstitial lung disease (RBILD)
- Desquamative interstitial pneumonia (DIP)
- Cryptogenic organizing pneumonia (COP)
- Acute interstitial pneumonia (AIP)

**Rare Idiopathic Interstitial Pneumonias**
- Idiopathic lymphocytic interstitial pneumonia (LIP)
- Idiopathic pleuropulmonary fibroelastosis (PPFE)

**Unclassifiable idiopathic interstitial pneumonias**

Slide courtesy WD Travis MD
Case 2

Role of the pathologist in Interstitial Lung Disease (ILD): be part of the multidisciplinary discussion (MDD)

Role of the pathologist in UIP diagnosis
Is UIP what you see?
If it is UIP, then is it IPF?

Familiarity with lung biopsy techniques:
  TBBx, TB cryobiopsy, SLBx

Pathologist’s role in clinical trials for IPF
Case 3 (TV11-287)

TV Colby
Case 3: Some History

This one is a little closer to home

Well known retired Professor of Pathology

But none of these found on Google…
Case 3

Granulomas are present !!
What are you considering?
   Infection, sarcoid, HP, other?
You can’t pose a reasonable Dx/Dx without knowing the question, ie.
   What is the history ???
You have to know why you are looking at the slides; why was the biopsy done?
Back to Case 3

More clues from the pathology…….
Lots of organizing pneumonia.....
Giant cells; some fibrosis/organization.....
....with polarizable material