Common Variable Immune Deficiency & Granulomatous – Lymphocytic Interstitial Lung Disease

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National Jewish Health & University of Colorado, Denver
May 2018
Disclosures:

- I have been involved in pharmaceutical-sponsored trials and investigator initiated studies:
  - Boehringer Ingelheim
  - Genentech
  - NJH and CO advanced industry grant programs

- Non-FDA approved therapies will be discussed.
Objectives:

- Describe the prevalence of ILD in patients with CVID.
- Describe the imaging findings and underlying pathologic patterns in GL-ILD.
- Describe (non-FDA approved) therapies that have been used for the treatment of GL-ILD.
Case

• PS is a 34 y/o male h/o hand vitiligo
  – Age 15 dx with ITP
    • Treated with intermittently steroids
  – Age 30 through 34 dx with increasing number of infections
    • Treated with antimicrobials, sinus sx, tympanostomy
  – Age 34 seen by A/I for unifying diagnosis
• He has no pulmonary complaints
Case

- Splenomegaly was noted on exam
- Laboratory studies
  - WBC = 4.1, HCT = 42.1, Plt = 112
  - Comprehensive panel was normal
  - IgG 293, IgM normal, IgA low
  - Abnormal response to vaccination with pneumococcus
- **HRCT imaging was abnormal …**
CVID

- The most common primary immune deficiency
  - 1:25,000 to 1:50,000
- Reduced serum immunoglobulin
  - IgG, IgA and/or IgM
  - Reduced or absent specific antibody response
- Diagnosed between 20 to 40 years of age
- Recurrent sinopulmonary infections …
Pulmonary complications of CVID

• **Infectious disorders**
  - Primary infections
  - Recurrent or post-infectious (e.g. bronchitis)

• **Non-infectious disorders**
  - ILD (e.g. GLILD)
  - Neoplastic disorders
  - Primary airway-centered disorders
  - Benign local or diffuse lymphoproliferative disorders

• **Mixed infectious and non-infectious disorders**
CVID Mortality in US: 2001-2014

Number of Deaths

Age-adjusted Mortality Rate per 1 Million

N = 248
Race: W=235, B=9, H=4
Mean age: 49 yrs. (CI 47-51)
Mean crude: 1.4 per 100,000 (CI 1.1-1.8)
Mean rate: 0.20 (CI 0.18-0.22)
Mortality rate % change from 2001: 44%

Unpublished Data: ICD-10 D83.9 from NCHS.
Contributing Causes of Death in CVID: 2001-2014

- Respiratory: 35.8%
- Other: 13.2%
- Infection: 12.8%
- Ca: 6.1%
- BM, anemia: 5.5%
- Metabolic: 4.6%
- Psych: 2.5%
- CNS: 2.3%
- GI: 4.5%

Unpublished Data: ICD-10 D83.9 from NCHS.
Contributing Causes of Death in CVID: 2001-2014

N = 248
Respiratory = 246

- Respiratory failure & ARDS 25%
- Bronchiectasis 15%
- PNA 14%
- COPD 13%
- ILD & Pulmonary fibrosis 7%

Unpublished Data: ICD-10 D83.9 from NCHS.
What is the prevalence of ILD in CVID?

Morbidity and mortality in common variable immune deficiency over 4 decades

Elena S. Resnick,¹² Erin L. Moshier,³ James H. Godbold,³ and Charlotte Cunningham-Rundles¹²⁴

¹Immunology Institute and Departments of ²Medicine, ³Preventative Medicine, and ⁴Pediatrics, Mount Sinai School of Medicine, New York, NY
68% had one or more autoimmune/inflammatory complication from CVID

* 473 patients, followed over 40 years

### Selected Complications

<table>
<thead>
<tr>
<th>Associated Complication</th>
<th>No.</th>
<th>% of Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections Only</td>
<td>151</td>
<td>31.9%</td>
</tr>
<tr>
<td><strong>Pulmonary Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>135</td>
<td>28.5%</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>53</td>
<td>11.2%</td>
</tr>
<tr>
<td><strong>Autoimmunity</strong></td>
<td>136</td>
<td>28.6%</td>
</tr>
<tr>
<td>Gastrointestinal Disease</td>
<td>73</td>
<td>15.4%</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>43</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

* 473 patients, followed over 40 years

Granulomatous Disease (GD)

- Of those 473 patients, 46 (9.7%) had biopsy-proven GD.
- Of those with GD, >50% had lung involvement.

<table>
<thead>
<tr>
<th>Location</th>
<th>No. (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>20</td>
</tr>
<tr>
<td>Multiple sites (ie, liver, lung, spleen)</td>
<td>7</td>
</tr>
<tr>
<td>Lymph node</td>
<td>6</td>
</tr>
<tr>
<td>Liver</td>
<td>4</td>
</tr>
<tr>
<td>Skin</td>
<td>3</td>
</tr>
<tr>
<td>Spleen</td>
<td>2</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>1</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
</tr>
<tr>
<td>Neck tissue</td>
<td>1</td>
</tr>
<tr>
<td>Operative site</td>
<td>1</td>
</tr>
</tbody>
</table>

Prognosis:

• Of 411 patients followed over 4 decades, 93 died (19.6%)
• The most common cause of death was pulmonary-related (36.6%)
• Chronic lung disease was associated with reduced survival
  – (HR = 2.06, p =0.022)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>No. (n = 93)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung failure</td>
<td>34</td>
<td>14 of these from respiratory failure, 3 after lung transplant</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>17</td>
<td>2 cases with coexistent lung disease and 1 with coexistent liver disease contributing to death</td>
</tr>
<tr>
<td>Cancers</td>
<td>10</td>
<td>2 lung, 2 stomach, 1 ovarian, 1 esophageal, 1 carcinoid, 1 oral, 1 breast, 1 colon</td>
</tr>
<tr>
<td>Liver disease</td>
<td>8</td>
<td>1 after liver transplant, 4 infectious hepatitis</td>
</tr>
<tr>
<td>Other infections</td>
<td>5</td>
<td>Pneumocystis pneumonia, measles, nocardia brain abscess, multiple anaerobes, meningitis</td>
</tr>
<tr>
<td>Heart disease</td>
<td>4</td>
<td>1 with coexisting lung disease</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>4</td>
<td>1 with coexisting neurodegenerative disease</td>
</tr>
<tr>
<td>Unknown cause of death</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Progressive multifocal leukoencephalopathy</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Vasculitis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Neurodegenerative</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Autonomic</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sudden death</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Suicide</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

CVID & ILD

• In CVID, “chronic lung disease” is common occurring in ~ 25% of patients
• Granulomatous disease occurs in ~ 10% of patients, > 50% of the time involves the lung.

What is this form of interstitial lung disease?
In patients with low immunoglobulins:

- Lymphoid Interstitial Pneumonia (LIP) had been long recognized.

- Granulomas in this setting had also been identified.

- “Sarcoidosis” (granulomatous lung disease) had also been recognized.

Granulomatous-lymphocytic lung disease shortens survival in common variable immunodeficiency

Christopher A. Bates, MD, a Misoo C. Ellison, PhD, a,e David A. Lynch, MD, a,f Carlyne D. Cool, MD, a,d Kevin K. Brown, MD, a and John M. Routes, MD a,b,c Denver, Colo
Retrospective analysis of 69 patients from National Jewish Health; ~ 25% ILD.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2 Airways Dz</th>
<th>Group 3A GL-ILD</th>
<th>Group 3B Other ILD/ Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pulmonary disease</td>
<td>Bronchiectasis Asthma</td>
<td><strong>Granulomatous Disease</strong></td>
<td>Organizing Pneumonia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LIP Follicular Bronchiolitis</td>
<td>Hypersensitivity Pneumonitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lymphoid Hyperplasia MALT-lymphoma</td>
<td>Metastatic Gastric CA</td>
</tr>
<tr>
<td>29/69 (42%)</td>
<td>23/69 (33%)</td>
<td>13/69 (19%)</td>
<td>5/69 (7%)</td>
</tr>
</tbody>
</table>

ILD in CVID: GLILD and others

- Lymphoid Interstitial Pneumonia
- GLILD
- Follicular Bronchiolitis Bronchitis
- Granulomatous Lung Disease
- Lymphoid Hyperplasia
- Other ILDs/ Malignancy
Pathologic features GLILD

- Benign Lymphoproliferative patterns
  - LIP
  - Follicular bronchiolitis
Pathologic features GLILD

- Benign Lymphoproliferative patterns
  Lymphoid hyperplasia

• **Granulomas**
  - Giant cells, histiocytes, and lymphocytes
  - Non-necrotizing
  - “Sarcoid-like”
    - Loose vs. well defined granulomas of sarcoid
  - Alone or with LP features
Pathogenesis?

Impaired T-cell function

Disregulated lymphoproliferation

Lymphoid Interstitial Pneumonia

Lymphoid Hyperplasia

Follicular Bronchiolitis Bronchitis

Granulomatous Lung Disease

GLILD
Increased Risk for Granulomas

- Dysregulated T-cell function/cytokine production:
  - ↓ T-cell proliferation to mitogens\(^1\)
  - ↓ CD4+ CD45RA+ naïve T cells\(^2,3\)
  - ↓ CD4+ CD127 low regulatory T cells\(^3\)
  - ↑ CD8+ CD57+ activated T cells\(^2,3\)
  - Associated with TNF +488A allele\(^2\)
  - Associated with autoimmunity\(^1\), splenomegaly, and LAD \(^2,3,4\)

- B-cells
  - Low memory (switched) B-cells

GLILD Lymphoproliferation

- Lymphoproliferation
  - HHV8+
  - B-cell role
    - Case report of tx with rituximab alone → ↑ T-regs
  - Age associated B cells?

ABC

- BCR
  - TLR7
  - TLR9
  - IFNγR other?

T-bet

ABC-like phenotype
CD11c+, CD11b+, CD21-, CD23-
IgG2a/c production
Ag-presentation

Rutsova K et al. J Imm 2015; 195(5) 1933-37
What is our evaluation for presence these diseases?

GLILD

- Lymphoid Interstitial Pneumonia
- Follicular Bronchiolitis Bronchitis
- Granulomatous Lung Disease
- Lymphoid Hyperplasia

Other ILDs/Malignancy
150+ ILDs

Many ILDs share similar symptoms, physiology and radiologic findings

Idiopathic  Known causes  Other forms
Making the diagnosis in GLILD, requires that you become a detective:

- History
- Physical Exam
- Pulmonary physiology
- Radiography
- +/- Surgical lung biopsy
• History
  – Symptoms
    • Constitutional/Infectious (malignancy, active infection)
    • Pulmonary (airways disease, ILD)
      – Cough & Dyspnea
    • Gastrointestinal (malabsorption, IBD, infection)
    • Musculoskeletal (polyarthritis)
    • Hematologic (cytopenias)
    • Reticular (LAD/splenomegaly)
  – Medications
  – Occupational & Environmental Exposures
    • Hypersensitivity Pneumonitis
– Physical examination
  • VS: Oxygen saturation (at rest and w/ambulation)
  • SKIN and FINGERS
  • LYMPH: LAD
  • PULM: Crackles
  • ABD: Splenomegaly
  • EXT: Synovitis, clubbing
• Laboratory Testing
  – Immunology:
    • Immunoglobulins
    • Lymphocyte enumeration: T & B cell numbers/subsets and NK cells
    • Post-vaccination antibody response
  – Other:
    • CBC, comprehensive metabolic panel
  – Microbiologic:
    • Evidence of infection?
    • Microbiologic testing w/possible bronchoscopy
Pulmonary Function Tests

- Lung Volumes & Spirometry
  - Typically restrictive
  - Obstructive
  - Mixed patterns
  - Normal
- Diffusion (DLCO)
  - Typically reduced
  - Normal
- Normal PFTs do not rule out disease
Our Evaluation: Pulmonary Evaluation

- **Physiology**
  - Pulmonary Function Testing

- **Gas Exchange**
  - ABG and Walk Oximetry
  - Cardiopulmonary Exercise Testing

- **Imaging**
  - Chest radiographs are not sensitive
  - High-resolution Computed Tomography
Clinical Predictors of a Diagnosis of Common Variable Immunodeficiency-related Granulomatous-Lymphocytic Interstitial Lung Disease

Amar Mannina¹, Jonathan H. Chung², Jeffrey J. Swigris¹, Joshua J. Solomon¹, Tristan J. Huie¹, Zulma X. Yunt¹, Tho Q. Truong³, Kevin K. Brown¹, Rosane Duarte Achcar⁴, Amy L. Olson¹, Christian W. Cox⁵, Seth J. Kligerman⁶, Douglas Curran-Everett⁷, and Evans R. Fernández Pérez¹
Clinical History ...

Assessed for eligibility:
NJH cohort
N = 345 patients

Excluded:
Secondary hypogammaglobulinemia, N = 173
CVID with other lung diseases, N = 29

CVID
N = 143 patients

CVID controls with no pulmonary complications
N = 109

CVID-GLILD
N = 34

Age- and sex-matched controls
N = 52

### Clinical History

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytopenia</td>
<td>26.62</td>
<td>6.63–181.40</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypersplenism</td>
<td>31.91</td>
<td>10.05–120.87</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>4.91</td>
<td>1.43–19.75</td>
<td>0.01</td>
</tr>
<tr>
<td>Dyspnea score*</td>
<td>1.77</td>
<td>1.31–2.55</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dosage IVIG†</td>
<td>1.01</td>
<td>1.01–1.07</td>
<td>0.01</td>
</tr>
<tr>
<td>IgA‡</td>
<td>0.95</td>
<td>0.89–0.98</td>
<td>0.01</td>
</tr>
<tr>
<td>IgE</td>
<td>0.99</td>
<td>0.96–1.00</td>
<td>0.09</td>
</tr>
<tr>
<td>IgG‡</td>
<td>0.99</td>
<td>0.98–0.99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IgM</td>
<td>0.99</td>
<td>0.97–1.00</td>
<td>0.09</td>
</tr>
<tr>
<td>IgD⁺CD27⁺ B cells,§ %</td>
<td>0.95</td>
<td>0.90–0.99</td>
<td>0.02</td>
</tr>
<tr>
<td>IgD⁻CD27⁺ B cells,§ %</td>
<td>0.91</td>
<td>0.82–0.99</td>
<td>0.02</td>
</tr>
<tr>
<td>FVC % predicted‖</td>
<td>0.96</td>
<td>0.93–0.98</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FEV₁, % predicted‖</td>
<td>0.96</td>
<td>0.94–0.99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>D_LCO % predicted‖</td>
<td>0.92</td>
<td>0.88–0.95</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Mannina et al. Annals ATS 2016 (7):1042-9
Clinical History ...

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersplenism</td>
<td>23.9</td>
<td>4.5–179.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>18.7</td>
<td>2.3–206.86</td>
<td>0.01</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>0.93</td>
<td>0.87–0.98</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Positive Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>84.5 (68.1–94.8)</td>
<td>90.2 (78.6–96.7)</td>
<td>84.8 (68.1–94.8)</td>
<td>90.2 (78.6–96.7)</td>
<td>8.7 (3.7–20.1)</td>
</tr>
</tbody>
</table>

• For Quality Imaging: slice thickness ≤ 2 mm, non-contrast, full inspiration, expiration, prone
HRCT imaging in GL-ILD

- Micronodules & nodules, randomly distributed
- Patchy ground glass opacities & consolidation
- Interlobular septal thickening
- Mid-lower lung zone predominant

http://www.ufrgs.br/imunovet/molecular_immunology/lungs.html
GLILD HRCT Findings

Pattern
HRCT Findings

Advanced disease

- Reticular Abnormalities
- Traction Bronchiectasis
- Honeycombing
GLILD HRCT

Findings

Distribution

Associated findings
• Thin cysts
• Bronchovascular and diffuse

Occasionally, we see these cysts in GL-ILD.
More common in autoimmune-associated ILD.
Sarcoidosis HRCT

- Nodules
- Upper lung
- Bronchovascular and perilymphatic
**Hypersensitivity Pneumonitis**

**HRCT**

- Centrilobular nodules
- Ground glass
- **Mosiacism/Air trapping**
- Rarely reported
- Overlap between
  - CTD & HP
  - CVID & HP

- **Inspiratory mosaic attenuation**
- **Ground glass opacities**
- **Poorly defined centrilobular nodules**
- **Expiratory air trapping**
Organizing Pneumonia

- OP looks like PNA
  - Consolidation
  - Air bronchograms
- Injury pattern →

<table>
<thead>
<tr>
<th>Table 1. Causes of SOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated with connective tissue disorders</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Sjogren syndrome</td>
</tr>
<tr>
<td>Polymyositis-dermatomyositis</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
</tr>
<tr>
<td>Systemic sclerosis</td>
</tr>
<tr>
<td>Behcet’s disease</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td>Mixed connective tissue disease</td>
</tr>
<tr>
<td>Associated with immunological disorders</td>
</tr>
<tr>
<td>Common variable immunodeficiency syndrome</td>
</tr>
<tr>
<td>Essential mixed cryoglobulinemia</td>
</tr>
<tr>
<td>Associated with infectious disease</td>
</tr>
<tr>
<td>Bacterial</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
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<tr>
<td>Mycoplasma pneumoniae</td>
</tr>
<tr>
<td>Coxiella burnetti</td>
</tr>
<tr>
<td>Nocardia asteroides</td>
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<tr>
<td>Chlamydia pneumoniae</td>
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<td>Staphylococcus aureus</td>
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<td>Viral</td>
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<td>Adenovirus</td>
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<td>Influenza and parainfluenza</td>
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<td>Parasites</td>
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<td>Plasmodium vivax</td>
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<tr>
<td>Associated with aspiration pneumonia</td>
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<td>Associated with radiation therapy for breast cancer</td>
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<td>Associated with organ transplantation</td>
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<td>Bone marrow</td>
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<td>Lung</td>
</tr>
<tr>
<td>Renal</td>
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<td>Liver</td>
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<tr>
<td>Drug-related (see Table 2)</td>
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<tr>
<td>Miscellaneous</td>
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<tr>
<td>Inflammatory bowel disease</td>
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<tr>
<td>Primary biliary cirrhosis</td>
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<tr>
<td>Polyarteritis nodosa</td>
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<tr>
<td>Chronic thyroiditis</td>
</tr>
<tr>
<td>Hematological malignancies (myelodysplastic syndrome, T-cell leukemia, lymphoma)</td>
</tr>
<tr>
<td>Coronary artery bypass graft surgery</td>
</tr>
<tr>
<td>Environmental exposure (textile printing dye, house fire, cocaine abuse)</td>
</tr>
<tr>
<td>Sweet’s syndrome</td>
</tr>
</tbody>
</table>

Pulmonary nodules in GLILD

• Mucus plugging
• Organizing pneumonia
• Granulomas
• Benign Lymphoproliferation
Which is benign vs. malignant?

MALT Lymphoma

Nodular Lymphoid Hyperplasia

Treatment?

• At present, there is no established standard of care for the treatment of patients with CVID & GLILD

• Not all patients need to be treated
  – Severity of symptoms/physiologic impairment
  – Pace of disease
  – Comorbid conditions

• If you are going to treat, pre-define what you want to make better
  – Imaging changes ≠ clinical changes
The Usual Suspects...

- Steroids
- Cyclosporine or Cyclophosphamide
- Azathioprine
- Mycophenolate mofetil
- Rituximab
Case Reports

- Lymphoproliferative
  - Glucocorticoids
  - Cyclophosphamide
  - Cyclosporine
  - Azathioprine
  - Mycophenolate mofetil
  - Rituximab

- Granulomatous Disease
  - " Agents +
  - Methotrexate
  - TNF-α antagonists
    - (infliximab)
  - Hydroxychloroquine
Use of Combination Chemotherapy for Treatment of Granulomatous and Lymphocytic Interstitial Lung Disease (GLILD) in Patients with Common Variable Immunodeficiency (CVID)

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Our Algorithm...

Abnormal HRCT

Evaluation: Clinical Features, Physiology, Gas Exchange

Findings c/w GL-ILD?

- No clinically significant symptoms, physiology, gas exchange = Monitor
- With symptoms/abnl = Consider bronchoscopy

Findings not c/w GL-ILD?

- Biopsy

C/W GL-ILD

Trial of steroids IVIG, comorbid tx, supportive care
Case:

• 34 y/o male with ITP, and diagnosis of CVID
• Abnormal HRCT
• He has no pulmonary complaints
## Pulmonary Function Tests

![Pulmonary Function Test Graph]

### Lung Volumes

<table>
<thead>
<tr>
<th></th>
<th>Pred Baseline</th>
<th>%Pred</th>
<th>Post</th>
<th>%Pred</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC</td>
<td>5.68 [L]</td>
<td>102</td>
<td>5.84</td>
<td>103</td>
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<tr>
<td>FRC-PL</td>
<td>3.09 [L]</td>
<td>96</td>
<td>3.04</td>
<td>98</td>
<td>3</td>
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<tr>
<td>RV</td>
<td>1.36 [L]</td>
<td>139</td>
<td>2.21</td>
<td>163</td>
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</table>

### Forced Expiration

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<th>Pred Baseline</th>
<th>%Pred</th>
<th>Post</th>
<th>%Pred</th>
<th>%Change</th>
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<tbody>
<tr>
<td>FVC</td>
<td>3.35 [L]</td>
<td>4.10</td>
<td>91</td>
<td>3.63</td>
<td>88</td>
<td>-3</td>
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<tr>
<td>FEV 1</td>
<td>2.91 [L]</td>
<td>3.54</td>
<td>100</td>
<td>3.48</td>
<td>98</td>
<td>-2</td>
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<tr>
<td>FEV 1 / FVC</td>
<td>76</td>
<td>86</td>
<td>94</td>
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### Additional Studies

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<th>%Pred</th>
<th>Post</th>
<th>%Pred</th>
<th>%Change</th>
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<tbody>
<tr>
<td>Raw</td>
<td>1.42 [cmH2O*s/L]</td>
<td>136</td>
<td>1.58</td>
<td>112</td>
<td>-18</td>
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<tr>
<td>sGaw</td>
<td>0.228 [L/(cmH2O*s)]</td>
<td>77</td>
<td>0.207</td>
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<td>DLCO SB</td>
<td>31.74 [ml/min/mmHg]</td>
<td>77</td>
<td>31.75</td>
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<tr>
<td>VA</td>
<td>5.26 [L]</td>
<td>5.10</td>
<td>97</td>
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<td>DLCO/VA</td>
<td>6.03 [ml/min/mmHg/L]</td>
<td>6.22</td>
<td>103</td>
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Gas Exchange

- No desaturation on walk oximetry
- CPET study suggesting no ventilatory or gas exchange abnormalities; possible deconditioning
Case:

• A/I is starting IVIG therapy.
• From a pulmonary perspective, for treatment:
  – A.) Monitor Closely
  – B.) Bronchoscopy
  – C.) Surgical Lung Biopsy
  – D.) Empiric Trial of Glucocorticoids
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• In CVID …
  – GL-ILD is common
  – GL-ILD portends a worse prognosis
  – If we see granulomatous disease or lymphoproliferative disease, we check immunoglobulin levels
• ILD requires a …
  – Multidisciplinary diagnosis
  – Clinician(s), Radiologist, Pathologist
• CVID & ILD
  – Multidisciplinary treatment
  – Frequent re-evaluation
Thank you