Crazy-Paving on CT: Pulmonary alveolar proteinosis and other causes
Definition: Crazy-Paving

- Crazy-Paving is a pattern seen at thin section CT of the lungs.
- It appears as thickened interlobular septa superimposed on a background of ground-glass attenuation.

Axial CT of the lungs showing the typical features of Crazy-Paving.
Index Patient: EA

- 60 y/o male with Shortness of Breath

- The radiograph shows extensive airspace opacity in both lungs
- The axial CT of the lungs shows the characteristic features of Crazy-Paving
Differential Diagnosis of Crazy-Paving

Causes

SANGUINEOUS
Acute Respiratory Distress Syndrome
Pulmonary Hemorrhage Syndromes

INFECTION
Pneumocystis Pneumonia

NEOPLASM
Bronchioloalveolar Carcinoma

INHALATION
Lipoid Pneumonia

IDIOPATHIC
Pulmonary alveolar proteinosis
Nonspecific Interstitial Pneumonia
Organizing Pneumonia
Additional notes about Crazy-Paving

1. Crazy-Paving was originally described in patients with pulmonary alveolar proteinosis and is very characteristic for this disease.

2. But Crazy-Paving is really a very nonspecific finding and can been seen in a variety of diffuse lung diseases.

3. Note that most diseases on the differential list don’t necessarily present with Crazy-Paving.
Infection

- Common pulmonary infection in severely immunocompromised patients
- CD4-cell counts < 200 cells/???
- Patient presents with acute onset of fever, cough and progressive dyspnea
- Typically bilateral, perihilar ground-glass opacities due to foamy nature of the alveolar exudates
- Interlobular septal thickening due to edema and cellular infiltrates

Pneumocystis Pneumonia

Coronal CT of the lungs showing ground glass opacities and septal thickening in a perihilar distribution

Typical pneumocystis cyst forms in a bronchoalveolar lavage specimen stained with Gomori methenamine

PACS, BIDMC

Patients present with cough, shortness of breath, hemoptysis, weight loss, and fever

**Lepidic growth pattern** (along intact alveolar septa) with preservation of the underlying lung architecture

Ground-glass attenuation reflects the intra-alveolar glycoprotein secreted by the tumor cells; septal thickening is due to infiltration with tumor cells and inflammatory cells

**Multicentric development of lesions due to aerogenous and lymphatic spread**

Rossi, S. E. et al. Radiographics 2003;23:1509-1519

Axial CT of the lungs showing bilateral BAC

Rossi, S. E. et al. Radiographics 2003;23:1509-1519

Mucinous tumor cells infiltrate the alveolar wall
Lipoid Pneumonia

- Results from chronic aspiration of (mineral, vegetable, animal) oils into the lungs
- Predisposing factors: neuromuscular disorders, structural disorders of the pharynx, esophageal disorders, chronic illness
- Most common location are the dependent portions of the lungs
- Most characteristic finding on CT is lung consolidation with fat attenuation
ARDS is a form of pulmonary edema.

Acute and persistent lung inflammation with increased vascular permeability.

Causes/predisposing factors: Shock, sepsis, aspiration, infection, trauma, drug/alcohol abuse etc.

Bilateral infiltrates ground-glass opacities and septal thickening represent edema of the alveoli and the perivascular spaces and filling of the alveoli with protein-rich fluid.
Patients present with hemoptysis, dyspnea, fever and anemia
Onset of symptoms is most often acute or of short duration
Important causes are: systemic vasculitides (Wegener’s granulomatosis), connective tissue disease (SLE, Goodpasture’s syndrome) drugs (anticoagulant therapy, amiodarone, crack cocaine), infection (opportunistic infections, viral), etc.
## Causes of diffuse alveolar hemorrhage syndromes (DAH) based on histologic appearance

<table>
<thead>
<tr>
<th>Capillaritis</th>
<th>Diffuse alveolar damage</th>
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<tbody>
<tr>
<td>Systemic vasculitides</td>
<td>Infection</td>
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<td>Beh&quot;et's syndrome</td>
<td>Any infection causing ARDS</td>
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<td>Cryoglobulinemia</td>
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<td>Henoch-Schoenlein purpura</td>
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<td>Connective tissue disease</td>
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<td>Pauci-immune glomerulonephritis</td>
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<tr>
<td>Wegener’s granulomatosis</td>
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<td>Connective tissue disease</td>
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<tr>
<td>Mixed connective tissue disease</td>
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<td>Goodpasture's syndrome*</td>
<td>Platelet glycoprotein IIA/IIIB</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>Other</td>
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<tr>
<td>Primary antiphospholipid antibody syndrome</td>
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<td>Rheumatoid arthritis</td>
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<td>Systemic lupus erythematosis*</td>
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<tr>
<td>Systemic sclerosis</td>
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<tr>
<td>Drugs</td>
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<tr>
<td>Diphenylhydantoin</td>
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<td>Propylthiouracil</td>
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<td>Retinoic acid syndrome</td>
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<tr>
<td>Other</td>
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<td>Autologous hematopoietic cell transplantation</td>
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<tr>
<td>Idiopathic pulmonary hemosiderosis</td>
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<td>Infective endocarditis</td>
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<td>Isolated pulmonary capillaritis</td>
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<tr>
<td>Leptospirosis</td>
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<tr>
<td>Lung transplant rejection</td>
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</tbody>
</table>

## More Causes of diffuse Alveolar Hemorrhage Syndromes

- Bland Hemorrhage
- Connective tissue disease
- Goodpasture's syndrome*
- Systemic lupus erythematosis*
- Drugs
- Anticoagulant therapy
- Platelet glycoprotein IIA/IIIB
- Other
- Idiopathic pulmonary hemosiderosis
- Leptospirosis
- Mitral stenosis
- Pulmonary veno-occlusive disease
- Diffuse alveolar damage
- Infection
- Any infection causing ARDS
- Opportunistic infections in immunocompromised host
- Viral
- Connective tissue disease
- Polymyositis
- Systemic lupus erythematosis
- Drugs
- Amiodarone
- Crack cocaine
- Cytotoxic drugs
- Nitrofurantoin
- Penicillamine
- Propylthiouracil
- Sirolimus
- Other
- Acute respiratory distress syndrome (any cause)
- Pulmonary capillary hemangiomatosis
- Pulmonary infarction
- Trimellitic anhydride
- Tuberous sclerosis

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1. 60-year-old male with history of ILD who presented with acute shortness of breath for several days that rapidly progressed to hypoxic respiratory failure
2. No improvement despite being on steroids for several weeks
3. Tobacco: 50 pack-years
4. No recent changes in weight. No fatigue, fever, chills or night sweats
Pulmonary Alveolar Proteinosis

**Idiopathic**

- Accumulation of PAS-positive lipoproteinaceous material in the distal air spaces
- Impaired processing of surfactant by alveolar macrophages
- Patients present with dyspnea and nonproductive cough
- Interlobular thickening is due to type II epithelial cell hyperplasia
- Radiologic findings: Diffuse bilateral ground-glass opacity, with superimposed intra/ and interlobular septal thickening (Crazy-Paving)

*Coronal CT of the lungs (patient EA) showing extensive bilateral Crazy-Paving*
Making the Diagnosis of Pulmonary Alveolar Proteinosis

Patient with suspected PAP
- Clinical manifestations
- Elevated LDH
- Abnormal chest radiograph

HRCT: Typical findings

Fiberoptic bronchoscopy

Bronchoalveolar lavage
- PAS stain
  - Negative: Open or VATS lung biopsy
  - Positive: Diagnosis of PAP

Transbronchial biopsy
- PAS stain
  - Negative: Open or VATS lung biopsy
  - Positive: Diagnosis of PAP
Making the Diagnosis of Pulmonary Alveolar Proteinosis

Bronchoalveolar lavage:

- A thick layer of dense proteinaceous material at the bottom


Transbronchial biopsy

- The alveoli are filled with a flocculent and granular lipoproteinaceous material that stains pink with PAS stain

Talmadge E King, Jr, MD

➤ A biopsy was taken in patient EA and it proved to be PAP
Therapy of Pulmonary Alveolar Proteinosis

- The most widely accepted and effective form of treatment is a therapeutic whole lung lavage via a double-lumen endotracheal tube.

- A therapeutic lung lavage was performed in patient EA.
- The post-lavage lung CT shows marked improvement in the diffuse ground-glass opacity and intervening interlobular septal thickening.
Some patients are asymptomatic with little or no physiologic impairment despite extensive radiographic abnormalities.

Approximately 25% of patients experience spontaneous remission.

30 to 40 percent of patients require only one lavage.

Most patients will require repeat lung lavages at intervals of 6-12 months.
Questions that may guide you to the right diagnosis:

✓ Is the condition acute or chronic?

✓ Is the patient immunocompromised?

✓ Is the patient ventilated?

✓ Does the patient have an underlying condition that puts him at risk for diffuse alveolar bleeding?

✓ Does the patient present with any symptoms that make you think about neoplasm?
Summary

1. Crazy-Paving appearance consists of interlobular septal thickening superimposed on an area of ground-glass opacity on CT of the lungs.

2. Crazy-Paving is characteristic for PAP, yet many other diseases can show this appearance on CT; Crazy-paving is a nonspecific finding.

3. The various disease entities that cause crazy paving can often be distinguished by their clinical findings and patient history.
References:

- Holbert, et al. CT features of pulmonary alveolar proteinosis. AJR Am J Roentgenol 2001; 176:1287
- Gruden, et al. High-Resolution CT in the evaluation of clinically suspected Pneumocystis carinii pneumonia in AIDS patients with normal, equivocal, or nonspecific radiographic findings. AJR Am J Roentgenol 1997;169:967
Acknowledgments

Paul W. Spirn, MD
Michael G. Geary, MD
Gillian Lieberman, MD
Maria Levantakis