CASE 2

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Clinical History:
A 56 year old woman with past medical history of migraines, coronary artery disease, and depression. She presented to her primary care physician with complaint of shortness of breath for four months. She developed increasing dyspnea and edema. She was diagnosed with pulmonary arterial hypertension, but continuous intravenous prostacyclin therapy failed to alleviate her symptoms, and she died soon after initiating treatment.
Diagnosis?

Pulmonary Capillary Hemangiomatosis

PCH - Clinical

- Sporadic, although familial and congenital forms have been reported
- Rare: 4 cases/million
- Age group: all, most commonly 20-40
- M = F
- Indolent onset of dyspnea and cough
- Hemoptyisis (30%) and hemorrhagic pleural effusions (25%)

PCH - Clinical

- Often misdiagnosed as idiopathic pulmonary arterial hypertension or pulmonary veno-occlusive disease
- Median survival of 3 years (from the time of diagnosis)
- Death occurs due to cor pulmonale
- Treatment: Transplantation
- Clinical clue: elevated pulmonary arterial pressures and normal or low pulmonary capillary wedge pressures on right heart catheterization

CT findings:

- Poorly defined small nodular opacities
- Thickened interlobular septa
- Areas of ground-glass opacity

Pathologic findings:

- At autopsy
  - Punctate areas of red congestion

Image courtesy of Dr. D. Lynch, AJRC
**Histopathologic findings:**

- Low magnification
  - Patchy congestion

**Histopathologic findings:**

- Higher magnification
  - Proliferation of capillary-like channels within alveolar walls

**Histopathologic findings:**

- **Secondary findings:**
  - Hemosiderosis with secondary ‘endogenous pneumoconiosis’
  - Proliferation of capillaries around bronchovascular bundles and in pleura
  - Secondary veno-occlusion
  - Medial hypertrophy of pulmonary arteries

**Endogenous pneumoconiosis:**

**Bronchovascular bundle involvement**

**Pleural involvement**
Secondary veno-occlusion

PCH – Differential Diagnosis

- PVOD
  - Widespread venous occlusion with patchy areas of capillary dilatation
  - Passive congestion can lead to hemosiderin-laden macrophages, hemosiderosis and endogenous pneumoconiosis (with giant cell reaction)

PVOD histology

Endogenous pneumoconiosis

Elastic tissue stain

PCH – Differential Diagnosis

- Congestion
  - Diffuse, not patchy, prominence of capillaries
  - Maintenance of single capillary layer within septa, lacks the increased density of PCH

- Atelectasis
  - At low power, patchy atelectasis can be a mimic, but high power examination reveals the lack of capillary proliferation

Congestion

PCH
PCH – Discussion

Pathogenesis is unknown

? Reactive, neoplastic, congenital?

WHO classification: Evian, 1998

PCH – Discussion

1. Pulmonary Arterial Hypertension
2. Pulmonary Venous Hypertension
   - Pulmonary Veno-Occlusive Disease
3. Pulmonary Hypertension Associated with Disorders of the Respiratory System and/or Hypoxemia
4. Pulmonary Hypertension due to Chronic Thrombotic and/or Embolic Disease
5. Pulmonary Hypertension due to Disorders Directly Affecting the Pulmonary Vasculature
   - Pulmonary Capillary Hemangiomatosis

PCH – Discussion

Pulmonary Arterial Hypertension (PAH)
1. Idiopathic (IPA)
2. Familial (FP)
3. Associated with...
4. Associated with significant venous or capillary involvement
   - Pulmonary veno-occlusive disease
   - Pulmonary capillary hemangiomatosis
5. Pulmonary venous hypertension
6. Pulmonary hypertension associated with hypoxemia
7. Pulmonary hypertension due to chronic thrombotic and/or embolic disease
8. Miscellaneous

WHO classification: Venice, 2003

Relationship to PVOD?

Lanteaume et al. hypothesize that PVOD and PCH are related. Postcapillary (venous) occlusion leads to the excessive growth of new capillaries and the location of the new capillaries reflects the attempt to bypass the postcapillary occlusions. i.e. PCH is a secondary angio proliferative response to PVOD, not a separate entity.

**PCH – Discussion**

IHC comparison between PCH and IPAH demonstrates that the endothelial cells of both are proliferative (Ki-67) and express angiogenic markers (VEGF), but that the endothelial cells of PCH, unlike IPAH, retain markers of cell growth suppression (PPARγ, caveolin-1).


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**Cell growth suppressor (caveolin)**

**PCH – Discussion**

- Reduced endothelial NOS
- Upregulation of PDGF-B and PDGFR-B genes in microdissected lesions of PCH

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**Key points**

- Not all causes of severe pulmonary hypertension are arterial
- PCH is a rare disease that affects a broad age group, with a mean age of 30 years and no sex predilection
- Survival is dismal without lung transplantation (rare reports of response to antiangiogenic therapies)
- Difficult diagnosis to make clinically, radiographically and histologically
- Diagnosis is often delayed and may not be made until post-mortem examination.