SPONTANEOUS PNEUMOTHORAX: WHY ANGER MANAGEMENT IS IMPORTANT

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Pneumothorax

1. Traumatic
2. Spontaneous
   - Primary (PSP)
     - No underlying pulmonary disease
   - Secondary
     - Neoplastic
     - Infectious
     - Parasitic
     - Foreign bodies
     - Congenital cysts
     - Bullous emphysema
3. Iatrogenic
Clinical Signs and Physical Exam
Radiographic Findings

- Increased width of air-filled pleural space
- Retraction of lung margins (follow vascular patterns)
- Partial pulmonary collapse
- Elevated cardiac silhouette (lateral view)

Tension pneumothorax:
- Mediastinal shift
- Flattening of diaphragm
Radiographs vs CT

CT: identifies more lesions, better defines lesion size, location, surrounding structures

Human: radiographs identified bullae/blebs 10-60% of time, CT 88-92%

Bleb: located between visceral pleura and lung parenchyma
Bulla: air space within lung parenchyma
Pulmonary bleb (A), type 1 bulla (B), type 2 bulla (C), and type 3 bulla (D). Note the accumulation of air between the layers of the visceral pleura in the pulmonary bleb and the different connections to the underlying pulmonary parenchyma in B, C, and D.

Treatment Recommendations

Thoracocentesis:
- Mild pneumothorax, no continued leakage of air

Tube thoracostomy:
- >2 thoracocenteses within 24 hrs, thoracocentesis fails to resolve pneumothorax, or tension pneumothorax

Thoracotomy:
- Failed tube thoracostomy, >2 recurrences, bullae noted
- Failed: pneumothorax persists > 48hrs and persistent clinical signs

Median sternotomy unless able to localize
- Lobectomy (focal) vs. pleurodesis (diffuse)
Etiopathogenesis

- **Humans:**
  - **Primary:** Ectomorphic, males > females
    - Increased apical pressure, tall morphology
    - Smoking increases risk
    - Collagen, alpha-1 antitrypsin, folliculin defects
  - **Secondary**
    - Most commonly COPD
      - Emphysema is subset of COPD

- **Dogs:** Secondary most common
  - Bullous emphysema

Folliculin

- Unknown function, possibly tumor suppressor
- Hereditary renal cystadenocarcinoma and nodular dermatofibrosis in GS
- Birt-Hogge-Dubé syndrome
  - Skin disorder, also associated with renal cancer and spontaneous pneumothorax (11.5-32%)
  - Skin disorder and renal cancer typically occur later in life in human patients
  - Some mutations associated with PSP phenotype only, 50 fold higher risk of developing PSP
Alpha-1 Antitrypsin

- Major plasma serine protease inhibitor
  - Lack of exposes lung tissue to uncontrolled proteolytic attack from neutrophil elastase, culminating in alveolar destruction
  - A1AT deficiency is one of the most common autosomal codominant inherited disorder in Caucasians
  - In people, specific genotypes are associated with serum levels which are correlated with severity of emphysema
  - Smoking and A1AT deficiency increase risk and progression of emphysema

Objectives

Objective one

- Perform immunohistochemistry on lung samples from dogs diagnosed with spontaneous pneumothorax

Hypothesis

- Lung tissue from dogs diagnosed with spontaneous pneumothorax would have abnormal staining pattern for folliculin and/or alpha-1 antitrypsin
Objectives

Objective two

- Perform DNA sequencing from dogs diagnosed with spontaneous pneumothorax

Hypothesis

- Dogs diagnosed with spontaneous pneumothorax would have mutations in the folliculin and/or alpha-1 antitrypsin gene that were associated with the trait

Materials and Methods

- Two portions of the study
  - Retrospective evaluation for pathology cases of bullous emphysema (n=10)
  - Prospective clinical spontaneous pneumothorax cases (n=5)
  - Research hounds controls (n=6)

- Selection Criteria
  - No history of trauma
  - No obvious neoplasia or other identified cause of pneumothorax
Histopathology

- H&E
- Trichrome
- Alpha-1 antitrypsin
- Folliculin

affected a1at HE - emphysema-early bulla

affected a1at -subpleural trichrome
Candidate Gene Analyses

- **Folliculin**

  A 4-bp deletion in exon 4 of the *FLCN* gene. 
  
  **A**, Exon 4 sequence. The deletion is underlined. 
  **B**, Unaffected control sequence. 
  **C**, Affected sequence, showing the wild-type and c.733delTCGG alleles.

- **Alpha one antitrypsin**

  exon 5, rs24483703
Results

**Breeds**
- Husky 4
- Golden Retriever 3
- Labrador Retriever 2
- Collie
- English Springer Spaniel
- German Shepherd
- Gordon Setter
- Great Dane
- Lhasa Apso

**Sex**
- 8 females, spayed
- 7 males, neutered

**Age**
- 6.7 years, range 3 to 9.7

**Weight**
- 33.2 kgs, range 11.4 to 47.9
Recurrence, 4/15 = 27%

- 5.8 yo, M/N, Mixed Breed, 6 months later
- 9 yo, F/S, German Shepherd, 38 months later
- 7 yo, F/S Labrador, 2 weeks later
- 7 yo, M/N, Siberian husky, 10.5 months later
Histopathology (7/15 multifocal bulla)

- Emphysema: focal, diffuse, multifocal
- Fibrosis: subpleural > interstitium, mild diffuse/multifocal, moderate diffuse/multifocal, minimally different from controls
- Folliculin: only slight increase in staining intensity in bronchiole epithelium, slight decrease in pleura, no difference in cell distribution
## Alpha 1 Antitrypsin IHC

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<th>a1at</th>
<th>sub-pleural</th>
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<th>perivascular</th>
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- **affected a1at - subpleural**
- **control a1at - subpleural**
### Genotyping Results

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Cases: 2 Labradors, 1 Golden retriever, 1 Alaskan husky
Conclusions

- Focal to multifocal or diffuse emphysema
- No difference in folliculin staining
- Decreased subpleural staining for alpha-1 antitrypsin
- In the mutations studied, no association with the trait
Future Work

- Gene expression analyses
  - qRT-PCR lung samples, folliculin and alpha-1 antitrypsin
- Serum levels of A1AT
  - Correlate with degree of emphysema
- CT lung densitometry
- Evaluate treatment options for SP
Recommendations for SP

- Surgery vs. medical management
  - Higher success rates
  - Lower recurrence rates
  - Lower mortality rates
  - Shorter hospitalization times

- Median sternotomy: multifocal bullae common

- Thoracoscopy

- Pleurodesis for diffuse disease?

- STOP Smoking!!!!

- Stress management
References