Introduction

- First introduced in 1994
- Used to describe pattern of inflammation and fibrosis that did not meet criteria of other idiopathic interstitial pneumonias
- Variable clinical, radiologic, and histologic patterns make accurate diagnosis difficult

NSIP Clinical

- Age
  - Younger patients than IPF
  - Age of onset 40-50 y/o
- Gender
  - Idiopathic NSIP equal gender distribution
  - NSIP much more common in women due to association with CVD
- Smoking
  - Not know association

NSIP Causes

- Idiopathic (NSIP)
- Secondary
  - CVD
    - Scleroderma
    - Mixed connective tissue disease
    - Dermatomyositis/polymyositis
  - Drug toxicity
  - Occupational Exposure
  - Hypersensitivity Pneumonitis

Histologic Subtypes

- Three main subtypes
  - Cellular
    - Nearly 100% survival
    - Much less common (near 10-15%)
  - Fibrotic
    - Much worse survival
    - More common
  - Mixed
    - Both cellular and fibrotic components
    - Similar survival to fibrotic group
    - Classified as fibrotic
- No reliable way to differentiate radiologically

Cellular NSIP

- Temporally and spatially homogenous
- Alveolar septa expanded by chronic inflammation
- Cells lining the septa (pneumocytes) show mild reactive changes
- Absent
  - Significant collagen deposition
  - Fibroelastic tissue
  - Honeycombing

NSIP Clinical

- Causes
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**Cellular NSIP**
- Mixed cellular and fibrotic changes
- +CVD
  - Associated lymphoid aggregates

**Mixed NSIP**
- Mixed cellular and fibrotic changes

**Fibrotic NSIP**
- Diffuse interstitial thickening by mature collagen
- Honeycombing, fibroblastic foci absent
- Inflammatory cells absent

**NSIP Radiology**
- Distribution
  - Symmetric
  - Lower lobe predominant
    - Can be diffuse
  - Peripheral
    - Subpleural sparing may be present
  - Can have peribronchovascular component
    - Organizing Pneumonia?

**Parenchymal Findings**
- Ground Glass Opacity (GGO)
- Reticulation
- Traction Bronchiectasis
- Consolidation may be present
  - Organizing Pneumonia?

**NSIP GGO**

**Cellular NSIP**
- GGO
Cellular NSIP
GGO and reticulation

Fibrotic NSIP
GGO and Reticulation

NSIP
GGO and Bronchiectasis

NSIP
Distribution

NSIP
Reticulation
Findings Suggesting Alternate Diagnosis
- Upper lobe predominance
- Honeycombing
- Dense Consolidation
- Nodules
- Prominent Mosaicism
- Cysts

Differentiation between UIP and NSIP
- Subspecialized thoracic radiologists only correct 40-68% of the time
- Interobserver variability high
- Biopsy needed if classic signs of UIP (honeycombing) are absent

Why does it matter?
- NSIP survival better than IPF
- Effective treatments for NSIP
- No effective treatments for IPF


DIP, Cellular NSIP
- Fibrotic NSIP
- UIP (IPF)

UIP or NSIP? UIP
Secondary causes of NSIP
- Collagen Vascular Disease
- Drug Toxicity
- Hypersensitivity Pneumonitis

Collagen Vascular Disease
- NSIP most common pattern in CVD
  - Scleroderma/Systemic Sclerosis
    - NSIP>UIP
  - Mixed Connective Tissue Disease
    - NSIP>UIP
  - Polymyositis/Dermatomyositis
    - NSIP>OP>UIP
  - RA
    - UIP>NSIP
- Lung disease major cause of mortality in patients with CVD

38 year-old woman with Scleroderma

NSIP
NSIP
Secondary Signs of CVD

51 year-old woman with RA

Reclassified as MCTD

31 year-old woman with polymyositis
A 44-year-old woman with polymyositis.

**Idiopathic vs CVD: Does it Matter?**


**Drug Toxicity**

- Multiple histologic patterns in drug toxicity
  - NSIP
  - Organizing Pneumonia
  - Diffuse Alveolar Damage
  - Hypersensitivity Pneumonitis
  - Eosinophilic Pneumonia

**Drug Toxicity**

- Drugs associated with NSIP
  - Methotrexate
  - Amiodarone
  - Carmustine
  - Bleomycin
  - Nitrofurantoin
  - Hydrochlorothiazide

**NSIP Methotrexate Toxicity**

**NSIP Taxotere**
NSIP
Bleomycin toxicity

Hypersensitivity Pneumonitis
- Chronic HP can be mistaken for NSIP on pathology
- Imaging and clinical history helpful differentiating HP from NSIP

Hypersensitivity Pneumonitis

Hypersensitivity Pneumonitis

NSIP Outcomes
- Potential Outcomes
  - Improvement
  - Progression
  - Acute Exacerbation

NSIP Improvement
NSIP Progression

NSIP Acute Exacerbation

- 4.2%/year in patients with NSIP
- Recent study showed that all patients with idiopathic NSIP survived acute exacerbation and all patients with NSIP associated with CVD died.

Radiology vs. Pathology

- Interobserver agreement between pathologists low in NSIP
  - Kappa value low
- Intrapatient variability high
  - Biopsy of different sites reveals different disease processes in 26% of patients

Consensus Approach

- ATS/ERS recommends joint approach utilizing all clinical, pathologic, and radiologic information to create a consensus diagnosis
- Clinical and pathologic information leads to a change in radiologic diagnosis in over 50% of cases.
- Radiologic and clinical diagnosis leads to a change in pathologic diagnosis in 19% of presumed pathologic NSIP cases

Controversies with NSIP

- Is it a distinct entity?
  - Often associated with other abnormalities
    - OP
    - UIP
    - Smoking-related lung disease
- Does it turn into UIP?
- Does it represent a common end point to different causes of lung injury?

Summary

- NSIP is the second most common IIP
- Associated with CVD, drug toxicity, HP
- Heterogeneous radiologic presentation
  - Most commonly lower lobe predominant ground glass opacity with associated reticulation and traction bronchiectasis
  - Biopsy suggested if classic signs of UIP absent
- Consensus approach provides best chance of making correct diagnosis