AABIP JOURNAL CLUB

How non-specific is non-specific pleuritis? Insights from International Collaborative Effusion Database

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The clinical question

Can the rate of malignancy in the setting of idiopathic nonspecific pleuritis be better defined?

Take Home Message

Further analysis of the idiopathic NSP patient population is required at this time as some of these patients do develop malignancy later on. These patients likely require routine monitoring as a result, but the duration of monitoring is unclear. A shared decision model may be beneficial for approaching follow up of these patients.

Background

Patients with nonspecific pleuritis (NSP) may have this condition for one of several dozen reasons. At this time over 60 different conditions can be attributed to NSP, however there is still a large percentage (approximately 48%) that may be due to an idiopathic cause. Single center studies have shown that about 8% of the idiopathic NSP patients go on to develop cancer but there is no prospective data on this population. More concerningly, is the idea that these initial biopsies may not be true negatives, due to this malignancy rate that has been observed. Finally, there is no consensus on the approach to monitoring or managing NSP post initial diagnosis.

Study Design

Study design: Multicenter retrospective cohort study
Primary outcome: Rate of idiopathic NSIP
Secondary Outcome(s): Rate of malignancy within the idiopathic NSIP group
Intervention (s): Identification of malignancy in idiopathic NSIP

Population

I**nclusion criteria**: All patients who were submitted to the International Collaborative Effusion database project (ICE) between October 2019 and July 2021. They were obtained from retrospective chart review of hospital records for patients diagnosed with NSP between 2009 and 2020.

Exclusion criteria: Patients with another histologic diagnosis.

Baseline characteristics

- Total subjects: 175
- Median age: 72 (62-75)
- Male: 142 (81)
- Smoking status
  - Current 27 (15)
  - Previous 66 (38)
  - Never 82 (47)
- Asbestos exposure: 52 (30)
- Comorbidities
  - Cardiovascular 105 (60)
  - Respiratory 42 (20)
  - Gastrointestinal/hepatic 18 (10.3)
  - Renal 11 (6,3)
  - Malignancy 26 (14.9)
  - Other 54 (30.9)
- Cardiovascular
  - Ischemic heart disease 31 (17.7)
  - Heart failure 20 (11.4)
  - Hypertension 74 (42.3)
  - Atrial fibrillation 42 (24)
  - Cerebrovascular disease 17 (9.7)
- Respiratory
  - Asthma 9 (5.1)
  - COPD 20 (11.4)
  - Interstitial lung disease 2 (1.1)
  - Bronchiectasis 1 (0.6)
  - Tuberculosis 3 (1.7)
- Other
  - Type 1 diabetes mellitus 1 (0.6)
  - Type 2 diabetes mellitus 31 (17.7)
  - Rheumatoid arthritis 8 (4.6)
  - Connective tissue disease 1 (0.6)
  - Hypothyroidism 5 (2.9)
- **Procedure**
  - Open surgical biopsy 1 (0.6)
  - VATS 11 (6.3)
  - LAT biopsy 136 (77)
  - US guided biopsy 18 (10.3)
  - CT guided biopsy 5 (2.9)
  - Abrams (blind) 4 (2.3)
- **Outcomes**
  - Eventual pleural based malignancy 11 (6.3)
  - Length of follow up months (N=95) 18 (1-80)
  - Time to development of malignancy months (N=9) 12.2 (0.8-32)
- **Eventual etiology of NSP**
  - Idiopathic 80 (44.2)
  - Pleural infection 27 (14.9)
  - Benign asbestos related 22 (12.2)
  - Cardiac failure 11 (6.1)
  - Malignancy 11 (6.1)
  - Autoimmune 7 (3.9)
  - Rheumatoid arthritis 4 (2.2)
  - Drug reaction 4 (2.2)
  - Post traumatic 3 (1.7)
  - Renal failure 2 (1.1)
  - Occupational exposure (non-asbestos) 2 (1.1)
  - Hemothorax 2 (1.1)
  - Post-operative 2 (1.1)
  - Chronic pancreatitis 1 (0.6)
  - Thymoma 1 (0.6)
  - Cirrhotic liver disease 1 (0.6)

Outcomes

Primary outcome

- Cases of idiopathic NSP: 80
- Age 72 (63-78)
- Male 64 (80)
- Requiring >1 thoracentesis following NSP biopsy finding 26/80 (33)
- Follow up performed 76/80 (96)
- Duration of follow up months 24 (12-36)
- Deceased 23/80 (29)
- Survival months 93.4 (65-109)

Secondary outcomes

Benign disease course following a histological result of NSP
Cases 164
Age 72 (62-78)
Male 133 (81)
Smoking status
Current 25 (15)
Previous 60 (37)
Asbestos exposure 45 (27)
History of malignancy 24 (15)
Requiring >1 thoracentesis (following NSP biopsy finding) 51/159 (32)
Follow up performed 139/164 (85)
Duration of follow up months 18 (11-33)
Survival months 67 (32-10)
Eventual malignant etiology following a histological result of NSP
Cases 11
Age 76 (68-77)
Male 9 (81)
Smoking status
Current 2 (18)
Previous 6 (55)
Asbestos exposure 7 (63)
History of malignancy 2 (18)
Requiring >1 thoracentesis (following NSP biopsy finding) 5/11 (46)
Follow up performed 11/11 (100)
Duration of follow up months 22 (5-36)
Survival months 57 (24-70)

Adverse events: None

Commentary

This was the first multicenter, international data set developed to identify NSP cases at multiple sites that also had the intention of evaluating the rates of malignancy in idiopathic NSP patients. It was found that the rate of idiopathic NSP was similar to previous reports, and the malignancy rate amongst idiopathic cases was similar but slightly lower (6% vs 8%). The factors assessed including smoking status, asbestos exposure, history of malignancy, all were not clinically significant for determining associations for the idiopathic NSIP cases that later developed a malignancy. There still remains concern as to whether or not some of these initially negative samples could have been due to poor initial specimens. Notably, there were also cases in this series that were diagnosed with malignancy only clinically, not by repeat biopsy. Further, the timing of the evolution of pleural malignancy was not known in 2 of the 11 cases. With this information, idiopathic NSP patients likely require routine monitoring to detect malignancies at a later point, but the duration for which they should be followed is unclear. A shared decision model should be considered for approaching follow up for these patients.

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Suggested reading

Bhatnagar R, Janssen J, Maskell N. The International Collaborative Effusion (ICE) database: an ERS Clinical Research Collaboration. Eur Respir J 2019; 53: 1900591.

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Article citation

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