Nonspecific Interstitial Pneumonia in the setting of Immunocompromising Medications

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Background

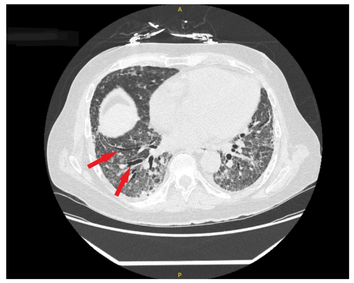
Interstitial lung disease(ILD), also known as diffuse parenchymal lung disease, is a grouping that encompasses several abnormalities of the respiratory system, including both the interstitium as well as the rest of the airway and alveoli. One subtype of ILD is Idiopathic interstitial pneumonia(IIP) which includes diseases that do not have a specific etiology such as drug-induced, rheumatic disease, or granulomatous disease. IIPs include idiopathic pulmonary fibrosis, desquamative interstitial pneumonia, respiratory bronchiolitis interstitial lung disease, acute interstitial pneumonia, and nonspecific interstitial pneumonia (NSIP). NSIP accounts for 14-36% of idiopathic interstitial pneumonia cases and most commonly affects middle-aged women who do not smoke(1).

Case Presentation

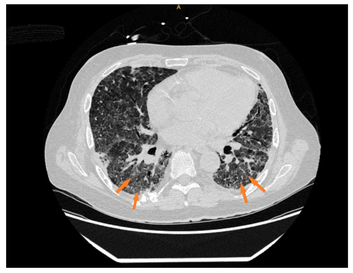
The patient is a 62-year-old male with a past medical history of HTN, HLD, and CKD who presented from home with shortness of breath. He began having trouble breathing a week prior to arrival which included dyspnea at rest, worse with exertion. Denies any recent infection or previous hospitalizations. He was diagnosed with membranous glomerulonephritis about 3 months prior and started on Cyclophosphamide and Prednisone. He stopped these medications just after the symptoms started, thinking they were the cause of his breathing problem. He had no oxygen requirement at home. He is a non-smoker, worked as an analytical chemist, and has no pets at home. No recent travel history. Family history is significant for coronary artery disease only.

Upon arrival at the hospital, he was noted to have SpO2 68% on room air and was placed on a non-rebreather. His oxygen saturation improved, and his symptoms resolved. On physical exam, he was noted to have bilateral lower extremity edema, inspiratory crackles in the lung bases, and increased work of breathing. Labs showed creatinine of 2.1 but were otherwise unremarkable. ABG was within normal limits and COVID/Flu tests were negative. Chest x-ray showed parenchymal opacities in both lungs, edema versus infiltrate. CT Angiogram of the chest showed significant interstitial opacities and possible pneumonia; No PE. Complement levels, ANA, rheumatoid factor, and ANCA were ordered, and he was started on high-dose prednisone for suspected autoimmune causes, but all were within normal limits. He was started on empiric CAP coverage and was eventually transferred to the IMCU for high-flow nasal cannula. Echocardiogram showed normal EF with Grade I diastolic dysfunction. Finally, a high-resolution CT chest was obtained showing scattered bilateral interlobular and intralobular septal thickening with architectural distortion and mild bronchiectasis, predominantly within the lung bases. There is no honeycombing. Findings are most consistent with nonspecific interstitial pneumonia (NSIP).

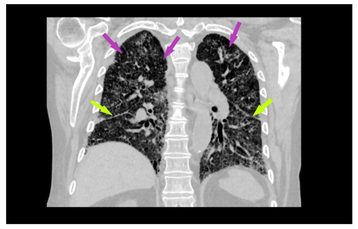
HRCT



Axial HRCT on inspiration: traction bronchiectasis (red arrows) seen on right lung (irreversible dilation of bronchi and bronchioles within areas of pulmonary fibrosis/distorted lung parenchymal architecture)(3)



Axial HRCT on inspiration: intralobular septal thickening as indicated by orange arrows (thickening of the pulmonary interstitium)(3)



Coronal HRCT: Purple arrows indicate interlobular septal thickening. Green arrows show thickening of the fissure lines bilaterally(3)

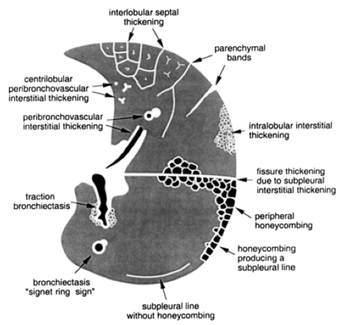


Illustration showing the difference between interlobular v. intralobular septal thickening(4).

Discussion

Diagnosis - Interstitial lung disease can be difficult to diagnose with exacerbations presenting similarly to and concomitantly with pneumonia. Our case was further complicated by the use of immunosuppressive therapy for an unknown reason. It was discovered later in the hospital course that our patient was previously diagnosed with MGN which was the reason he was started on Cyclophosphamide and Prednisone. Ultimately the diagnosis was made once HRCT was ordered. Reducing our threshold for ordering this test may facilitate quicker diagnosis in the future. Despite this delay, the patient was started on appropriate therapy early in his hospital course when his oxygen saturation dropped upon mild exertion despite high-flow nasal cannula.

Pathophysiology - NSIP is often associated with connective tissue disease or other autoimmune process. The pathophysiology revolves around epithelial injury and dysregulated repair which leads to fibrosis. Abnormal fibroblast and myofibroblast function is present which contributes to the excess collagen deposition. Lymphocytes are often found around the alveoli in these patients which suggests some involvement of the immune system(2).

Treatment - When diffuse abnormalities are seen on HRCT or moderate impairment on PFTs, we use systemic glucocorticoids. After 3-6 months we assess the response and add a second immunosuppressive agent. For severe disease, double therapy can be started initially. First-line therapy would include Prednisone 0.5 to 1 mg/kg ideal body weight per day up to 60mg/day for one month followed by 30-40mg/day for an additional two months before starting a new agent. Tapering the medication is recommended if symptoms resolve. Second-line agents to be added include azathioprine and mycophenolate. Cyclophosphamide, rituximab, and calcineurin inhibitors are reserved for refractory therapy. Severe disease may warrant a pulse dose of Prednisone for the first three days to relieve symptoms more quickly(2).

Conclusion

NSIP is a subtype of interstitial lung disease that is associated with connective tissue disease. The gold standard of diagnosis is a high-resolution CT scan. Treatment depends on severity and range from conservative management to high-dose steroids and immunosuppressants. Prompt diagnosis and consistent monitoring can allow for the resolution of symptoms and good quality of life.

References

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