Case Report

Autopsies are indispensable in the advancement of patient care: Report of an unusual presentation and fatal outcome of an autopsy-diagnosed case of advanced idiopathic interstitial pneumonia

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ABSTRACT

Idiopathic interstitial pneumonias (IIPs) are a group of fibrosing lung disorders conferring significant morbidity and mortality to patients. Most patients with IIP first present with dyspnea and/or cough. Here, we report the case of a 53-year-old male who presented with severe abdominal pain and weight loss of approximately 100 pounds of 3-month duration. Symptoms of mild dyspnea and cough were obtained during additional history taking. Physical examination and computed tomography of the chest were suggestive of pneumonia, and he was placed on multiple antibiotics but developed worsening respiration that necessitated hyperbaric oxygen and died after 10 days. Histopathological examination of autopsy lung specimen, revealed severe lung damage secondary to a mixed IIP pattern of diffuse alveolar damage, superimposed on extensive interstitial fibrosis, with features of honeycombing, consistent with advanced interstitial/end-stage lung disease. This case typifies an unusual and fatal presentation of IIP, which may be useful in clinical practice.

KEY WORDS: Autopsies, diffuse alveolar damage, idiopathic interstitial pneumonia, interstitial lung disease

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/lungindia.lungindia_570_19

How to cite this article: Abada E, Raval K. Autopsies are indispensable in the advancement of patient care: Report of an unusual presentation and fatal outcome of an autopsy-diagnosed case of advanced idiopathic interstitial pneumonia. Lung India 2020;37:333-5.
or cough, and the disease course is characterized by a progressive deterioration in lung function.\cite{5} It is unusual for patients with underlying interstitial lung disease to progress without clinically significant respiratory symptoms, due to the significant amount of inflammation, fibrosis, and parenchymal destruction often seen in the lung, both radiologically and histopathologically. Due to the overlapping clinical, radiological, and histopathological features of the IIPs, diagnosis remains complex and is best approached through a collaboration of clinicians, radiologists, and pathologists, as the treatment and prognosis of these conditions vary greatly.\cite{6} Very few physicians have substantial experience with their diagnosis and management,\cite{6} and as a result of this, many patients are often misdiagnosed with other respiratory diseases.\cite{6}

CASE REPORT

This was a case of a 53-year-old male patient who presented with major complaints of severe abdominal pain and approximately 100 pounds unintended weight loss, over the course of 3 months. Additional history taking revealed the presence of intermittent dyspnea and a productive cough over the same period. He also complained of subjective fevers and night sweats, but was afebrile at presentation. He was a former smoker with 20 pack years smoking history and denied any sick contacts at presentation. He had no history of joint pains, connective tissue, respiratory, or granulomatous disease.

On examination, he was in moderate distress, and his abdomen was tender to light palpation with decreased bowel sounds but without rigidity, guarding, or rebound tenderness. Respiratory examination revealed decreased air entry with poor inspiratory effort, crackles in bilateral lung lower lobes, and decreased tactile vocal fremitus in bilateral lower lung fields. The examination of other systems was noncontributory.

Blood tests revealed an elevated lipase at 220 U/L and an elevated aspartate aminotransferase at 88 U/L. There was no leukocytosis. Blood cultures, respiratory cultures, urinalysis and culture, serum Aspergillus antigen, HIV antibody, tuberculosis, syphilis, C3, C4, erythrocyte sedimentation rate, urine legionella antigen test, cyclic citrullinated peptide, rheumatoid factor, hepatitis A, hepatitis B, and hepatitis C antibodies all returned negative. Autoantibodies, including Anti-ds DNA, ANCA, Anti-JO-1, anti-SM, anti-SSA, anti-SSB, anti-SCL70, myeloperoxidase, and serine protease 3, were also all negative. Bronchoalveolar lavage and fungal cultures were also negative. Computed tomography (CT) of the abdomen revealed no evidence of bowel obstruction. CT of the thorax was performed, and the radiologic impression was suspicious for multifocal pneumonia or aspiration pneumonitis. With the constellation of his symptoms, signs, and radiologic findings, he was diagnosed with pancreatitis and pneumonia and was placed on bowel rest and broad-spectrum antibiotics. In light of his significant weight loss, an additional whole-body CT scan was performed but revealed no covert malignancy.

However, his hospital course quickly deteriorated, and he developed severe respiratory compromise. He was given hyperbaric oxygen, developed acute respiratory distress syndrome and required intubation. Despite optimal ventilator settings and pronation, his condition worsened, and he died after 10 days on admission.

The significant findings at autopsy were bilateral enlarged lungs with bibasilar pulmonary consolidations. Histologically [Figure 1], sections from both lungs showed extensive interstitial fibrosis, with the presence of fibroblastic foci present in multiple lung lobes. There were areas of focal hyaline membranes and dense interstitial inflammatory infiltrates consisting of lymphocytes, neutrophils, and plasma cells. Prominent intra-alveolar macrophages and type 2 pneumocyte hyperplasia were also seen. There were focal areas of interalveolar and interstitial edema, with prominent pulmonary congestion. In addition, focal areas of honeycomb lung were seen in the left lower lobe, right upper lobe, and right lower lobe. However, there was no subpleural honeycombing.

In summary, the patient’s primary cause of death was determined to be severe respiratory failure secondary to a mixed IIP pattern of diffuse alveolar damage (DAD), superimposed on extensive interstitial fibrosis, with features of honeycombing, consistent with advanced interstitial/end-stage lung disease.

DISCUSSION

Most patients with interstitial lung diseases first present with clinically significant symptoms of breathlessness and as a result of this, many patients...
and/or cough, and the disease course is characterized by a progressive deterioration in lung function.\[^{[5]}\] As a group, the IIPs can be distinguished from other forms of diffuse parenchymal lung diseases by clinical methods, including history, physical examination, chest radiology, laboratory studies, and pathology.\[^{[5]}\] Following the histologic classification of an IIP by a pathologist, the clinician needs to do a thorough review of the patient’s medical history to check for antigen exposure that could account for hypersensitivity pneumonitis, laboratory, or clinical features of collagen vascular disease, and possible drug or toxic exposure.\[^{[5]}\] Given the rapid decline in respiratory status and autopsy confirmation of DAD superimposed on extensive lung fibrosis, it is highly suggestive that an acute exacerbation complicated an underlying chronic undiagnosed lung pathology in this patient.

With his rapid decline in respiratory function, the impact of oxygen is not exactly clear here, given the association between the use of oxygen and worsening respiratory status in patients with DAD,\[^{[7]}\] as was seen in this patient. In addition, the presence of significant weight loss may have been related to an underlying undiagnosed IIP\[^{[8]}\]

To date, the processes mediating fibrosis in the lungs of patients with IIP are not completely understood. However, it is believed that recurrent injury to alveolar epithelial cells activates inflammatory cells, which releases fibrogenic growth factors.\[^{[9]}\] These perpetuate a cycle of injury, failed repair, and fibrosis through the activation, proliferation, invasion, and apoptotic resistance of fibroblasts and myofibroblasts.\[^{[9]}\] All these factors culminate in the excess deposition of extracellular matrix/collagen in the lung, resulting in pathologic tissue scarring and ultimately, respiratory failure.\[^{[9]}\]

**CONCLUSION**

Since this patient lacked an antemortem diagnosis/correlation of his lung pathology, a specific IIP pattern was not rendered. However, findings from his lung specimen were highly suggestive of a mixed IIP pattern, with DAD superimposed on a chronic interstitial disease process. The unique presentation of the patient in this case with significant weight loss and severe abdominal pain highlights a subset of patients with IIP who may progress rapidly to end-stage lung disease without significant respiratory symptoms of breathlessness or cough at initial presentation.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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