Reversible Lansoprazole-Induced Interstitial Lung Disease Showing Improvement after Drug Cessation

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Lansoprazole is an acid proton-pump inhibiting drug that is used for the treatment of duodenal or gastric ulcers, H. pylori infection, gastroesophageal reflux disease or Zollinger-Ellison syndrome. Although lansoprazole is well known for its gastrointestinal and dermatologic adverse effects, mild pulmonary symptoms are also known to develop from taking this drug. There have been no reports about lansoprazole-induced interstitial lung disease. We report here a case of lansoprazole-induced interstitial lung disease that developed in a 66-year-old man.

CASE REPORT

The patient was a 66-year-old man without a smoking history. The patient had been previously healthy until he was diagnosed with GERD a month prior, and began treatment with lansoprazole. He had a history of working at a dusty place several weeks before hospitalization, where he did not experience any respiratory symptoms. However, a few days after initiation of lansoprazole treatment, cough and dyspnea developed along with a febrile sense. After suffering from a progressively aggravating cough and dyspnea for a month, the patient visited our hospital.

Vital signs of the patient were stable and the laboratory studies including eosinophil count were all in the normal ranges. An initial chest radiograph showed diffuse ground-glass opacities in both lungs with upper lobe predominance, and we diagnosed differentiated diffuse interstitial lung disease or interstitial pneumonia, such as Pneumocystis carinii pneumoniae pneumonia (Fig. 1A). High-resolution computed tomographic scans (HRCT) showed focal areas of diffuse ground-glass opacity in both
lungs with upper lung predominance, similar to those of the plain radiographs (Figs. 1B, C). The patient was hospitalized for further evaluation and treatment. A transbronchial lung biopsy was performed, and the histopathological result was acute lung injury with marked type II pneumocyte hyperplasia, interstitial edema and interstitial infiltration of lymphocytes. After only one day of symptomatic treatment, both the clinical symptoms and

Fig. 1. Lansoprazole-induced interstitial lung disease.
A. Posteroanterior chest radiograph shows diffuse ground-glass opacities in both lungs, which are predominant in upper lung zones.
B, C. Axial (B) and coronal (C) reconstruction high-resolution CT images show areas of diffuse ground-glass opacity in both lungs with upper lung predominance, similar to those seen in chest radiograph (A).
D. Histopathological specimen shows mixed interstitial infiltration of lymphocytes and plasma cells, suggestive of nonspecific interstitial pneumonia pattern. Note active hyperplasia of type II pneumocytes (arrows) and Massons’ body (arrowheads).
E. Follow-up high resolution CT image shows markedly improved opacities in both lungs. Faint areas of ground-glass opacity still remain.
Drug-induced interstitial lung disease (DI-ILD) shows various clinicoradiographical findings that range from nonsymptomatic infiltration to severe acute respiratory distress syndrome (ARDS). For example, amiodarone or methotrexate treatment may lead to nonspecific interstitial pneumonia (NSIP), treatment with bleomycin, nitrofurantoin or sulfasalazine to acute organizing pneumonia (alternatively called bronchiolitis obliterans organizing pneumonia [BOOP]), and treatment with nonsteroidal antiinflammatory drugs NSAIDs (nonsteroidal antiinflammatory drugs) or some antibiotics to acute eosinophilic pneumonia. These manifestations can lead to the clinicoradiographically gas-exchange pattern of ARDS (1, 4).

Drug-induced interstitial lung disease may present several hours to several weeks after the introduction of the causative drug. The clinical findings of DI-ILD include very nonspecific symptoms such as a nonproductive cough, dyspnea and fever, or crackles upon auscultation. The laboratory results can show a range of findings from normal to eosinophilia and/or leukocytosis (2). The radiological findings of DI-ILD are also highly variable (3). Although it is not pathognomonic, the radiological findings are sometimes very suggestive for certain types of DI-ILD. Invasive diagnostic examinations (bronchoalveolar lavage, transbronchial or thoracoscopic biopsy) are sometimes needed to rule out other lung diseases, especially when the medication history does not clearly meet the criteria of drug-induced lung diseases (1). Among many types of DI-ILD, NSIP is the second most common form of a histopathological pattern, after usual interstitial pneumonia. Clinically, NSIP usually starts as insidious dyspnea and dry cough. Diffuse, heterogeneous ground-glass opacities in both lungs, predominantly in the lower lobes are a typical finding on chest radiography. An HRCT scan shows focal or diffuse areas of ground-glass opacities with interstitial fibrosis (4). In our case, despite the histopathological findings consistent with NSIP, it was difficult to diagnose our patient as having drug-induced NSIP, due to the clinical and radiological differences when compared to typical cases of the disease.

In fact, although a large number of drugs are known to cause pulmonary complications, it is difficult to diagnosis drug-induced lung disease (5). There are several reasons that make such a diagnosis difficult. First, the clinical and radiological findings are nonspecific and they can mimic other pulmonary diseases (6). Many new drugs are being developed and their adverse effects are have not been fully characterized. Sometimes, both patients and clinicians do not consider the adverse effects of a drug as a cause of pulmonary symptoms. In some cases, there is no clear temporal relationship between the initiation of a drug and the onset of symptoms.

To the best of our knowledge, this is the first description of DI-ILD caused by lansoprazole. The diagnosis was made by considering the radiological, histopathological and clinical findings, including the close temporal relationship between lansoprazole exposure and symptom severity. Other possible causes were excluded due to a lack of a temporal relationship between the symptoms and work history or prednisolone therapy, and no other history of...
specific allergen exposure.

When there is diffuse interstitial lung disease with an unknown etiology, it is important to remember that drugs can be the cause of pulmonary symptoms and it is crucial to take a careful patient history. If there is a recent history of taking lansoprazole in a patient with clinical and radiological findings of diffuse interstitial lung disease, we recommend stopping the medication to see if there is clinical and radiological improvement. That way, one can avoid using invasive procedures to diagnose a lansoprazole-induced interstitial lung disease.

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