

Acute Eosinophilic Pneumonia Associated with Amitriptyline in a Hemodialysis Patient

Hyunjin Noh¹, Young Kyu Lee², Shin Wook Kang^{1,3}, Kyu Hun Choi^{1,3}, Dae Suk Han^{1,3}, and Ho Yung Lee^{1,3}

¹Institute of Kidney Disease, ³Department of Internal Medicine, Yonsei University College of Medicine, Seoul;

²Department of Internal Medicine, Eulji University College of Medicine, Taejeon, Korea.

Drugs are well known causes of eosinophilic lung disease. In many patients, drug-induced eosinophilic lung disease presents with transient eosinophilic infiltrates that disappear after discontinuation of the drug. Some patients, however, experience a fulminant, acute eosinophilia-like disease. Recently, we experienced a case of amitriptyline-associated acute eosinophilic pneumonia with respiratory failure in a diabetic hemodialysis patient. Eight days after treatment with amitriptyline, sudden fever, chill, dry cough and dyspnea developed. Subsequently, multiple patch consolidations appeared on the chest radiographs. Bronchoalveolar lavage (BAL), established a diagnosis of acute eosinophilic pneumonia. After immediate discontinuation of amitriptyline, a rapid clinical and radiological improvement was observed. The present case indicates that the possibility of acute eosinophilic pneumonia should be fully considered in dialysis patients developing unexplained respiratory symptoms while on amitriptyline therapy.

Key Words: Amitriptyline, eosinophilic pneumonia, hemodialysis

INTRODUCTION

Drug-induced eosinophilic lung disease commonly presents as a simple pulmonary eosinophilia-like syndrome consisting of transient pulmonary infiltrates, mild pulmonary symptoms, and peripheral eosinophilia that resolve upon withdrawal of the offending agent. Rarely, the disease presents with acute symptom onset and rapidly progressing infiltrates, which may be associated with respiratory failure. This report describes a case of amitriptyline-associated acute

eosinophilic pneumonia confirmed by BAL in a hemodialysis patient. Rapid clinical and radiological improvement was observed solely by withholding the drug. Although tricyclic antidepressants (TCA) are known to cause eosinophilic pneumonia,¹⁻⁴ to our knowledge, this is the first reported case in a dialysis patient.

CASE REPORT

A 26-year-old female patient was admitted to the hospital because of generalized edema and dyspnea. She had a 7-year history of diabetes mellitus (DM) and had been on insulin therapy. At the time of admission, she complained of dyspnea on rest, orthopnea, anorexia and vomiting. Physical examination revealed high blood pressure (240/150 mmHg), inspiratory fine crackles over the middle one-third and attenuated breath sounds over the lower one-third of both lungs, a distended abdomen and bilateral pretibial edema (grade 3). Third and fourth heart sounds were inaudible. Chest radiographs showed cardiomegaly and bilateral pulmonary congestion with bilateral pleural effusions. The echocardiogram showed mild pericardial effusion. Kidney ultrasonography revealed a poorly differentiated corticomedullary junction, but the size was not decreased. Initial laboratory data revealed hemoglobin 8.6 g/dl, hematocrit 26%, white blood cells 5100/ μ l, platelets 234000/l, blood urea nitrogen 33 mg/dl, creatinine 3.9 mg/dl, albumin 1.7g/dl and total cholesterol 342 mg/dl. Daily excretion of urine protein was 6.6g and creatinine clearance 11 ml/min. Calculated renal Kt/Vurea was 0.36. A

Received October 20, 2000

Accepted February 3, 2001

diagnosis of nephrotic syndrome secondary to DM was made clinically. Because the patient did not respond to diuretics, maintenance hemodialysis was started, and the clinical course was uneventful. However, on the 30th hospital day, sudden fever (39°C), chill, dry cough and dyspnea developed. Four days later, multiple patch consolidations appeared on the chest radiographs and rapidly progressed (Fig. 1). Laboratory tests showed no evidence of acute infection and there was no peripheral eosinophilia. Arterial blood gas analysis showed PaO₂ 55.6 mmHg, PaCO₂ 32.7 mmHg and HCO₃ 26.4 mmol/l. Serum IgE was within the normal range. A computed tomographic scan of the chest performed on the 35th hospital day disclosed patchy areas of ground-glass attenuation in both lung fields (Fig. 2). BAL was performed on the 36th hospital day and revealed 38% eosinophils, 7% neutrophils, 19% lymphocytes and 36% monophagocytic cells. At that time, the patient's medication regimen consisted of cilazapril (10 mg/day), amlodipine (10 mg/day), furosemide (160 mg/day), erythropoietin (6000 units/week), insulatard (18 units/day) and amitriptyline (5 mg/day). Amitriptyline had been started on the 23rd hospital day for painful neuropathy and the total dose administered was 70 mg. Upon immediate discontinuation of the

amitriptyline the patient improved and was afebrile after the 39th hospital day. The chest radiograph cleared markedly within 5 days of the discontinuation of amitriptyline (Fig. 3), and the patient was discharged and placed under the care of the outpatient hemodialysis clinic without chest symptoms.

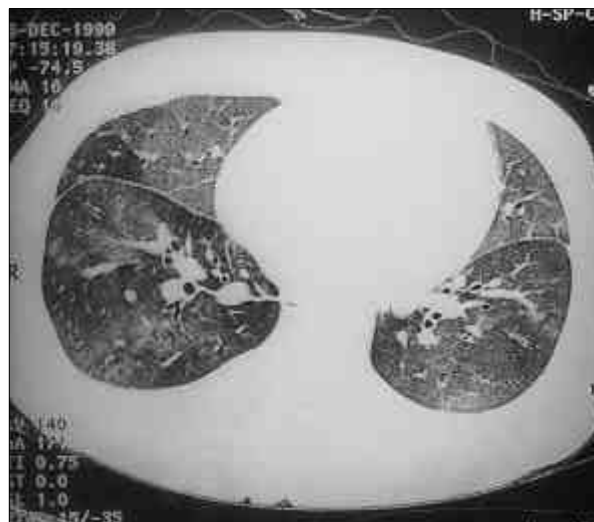


Fig. 2. Chest computed tomography scan showing bilateral ground-glass opacities and focal patch consolidations.



Fig. 1. Chest radiograph taken on the 34th hospital day showing bilateral multiple patchy consolidations.



Fig. 3. Chest radiograph taken 5 days after discontinuation of the amitriptyline treatment showing resolution of the consolidation.

DISCUSSION

Eosinophilic pneumonia is a pulmonary disorder characterized by the accumulation of eosinophils in the lung interstitium and alveoli, radiographic alveolitis, and clinical pulmonary symptoms with or without peripheral eosinophilia varying in chronicity and severity. Drugs are well-known causes of eosinophilic pneumonia. In many cases, drug-induced eosinophilic lung disease presents with transient eosinophilic infiltrates that resolve after drug withdrawal. However, a more fulminant presentation more resembling acute eosinophilic pneumonia has been reported.^{5,6} The diagnostic criteria for acute eosinophilic pneumonia suggested by Pope-Harman et al. are as follows⁷: 1) acute onset of any symptoms (within 7 days) before presentation, 2) fever 37.2°C, 3) bilateral infiltrates in the chest film, 4) severe hypoxemia, 5) lung eosinophilia (BAL differential with $\geq 25\%$ or predominance of eosinophils in open lung biopsy). The disease onset of the presented case closely resembled acute eosinophilic pneumonia.

Several cases of drug-induced acute pulmonary eosinophilia-like syndrome have been reported in the literature. The causative drugs were trazodone and venlafaxine, 5-hydroxytryptamine reuptake inhibitors, minocycline, ampicillin, acetaminophen, nitrofurantoin and pyrimethamine-sulphadoxine.

TCA is also known to be associated with the development of eosinophilic lung disease, and four reports were identified.^{1,4} However, most of the cases were not confirmed by BAL or lung biopsy. In only one case of nomifensine associated pneumonia, lung biopsy was performed. However, there was no evidence of eosinophilic infiltrates. The present case confirmed amitriptyline associated acute eosinophilic pneumonia by BAL. Because the patient completely recovered after the discontinuation of the drug, corticosteroid therapy was unnecessary.

It is well known that TCA undergo 1st pass metabolism in the liver when administered orally. Patients with renal insufficiency were found to have lower concentrations of amitriptyline, nortriptyline, and their unconjugated hydroxymetabolites than patients with normal renal function. However, the plasma levels of the conjugated products were extremely high (500% to 1500%) in

patients with renal failure.^{8,9} It has been suggested that although the latter metabolites are pharmacologically less active, the apparent hypersensitivity to the side effects of TCA might be attributed to the high concentrations of conjugated drug forms.⁸ This report describes a case of amitriptyline associated acute eosinophilic pneumonia in a hemodialysis patient. Considering the widespread use of this class of drug in dialysis patients, it is important that renal physicians are aware of this complication.

Ho Yung Lee, M.D.

Division of Nephrology,

Department of Internal Medicine,

Yonsei University College of Medicine,

C.P.O. Box 8044, Seoul 120-752, Korea.

Tel: 82-2-361-5423, Fax: 82-2-364-7655,

E-mail: hyl@yumc.yonsei.ac.kr

REFERENCES

1. Mutnick A, Schneiweiss F. Desipramine-induced pulmonary interstitial eosinophilia. *Drug Intell Clin Pharm* 1982;16:966-7.
2. Kraus RP, Clarke RJ, Remick RA. Massive eosinophilic reaction to desipramine in conjunction with pneumonia. *Can J Psychiatry* 1984;29:142-4.
3. Hamm H, Aumiller J, Bohmer R, Missmahl HP, Fullbrandt U, Frenzel H. Alveolitis associated with nomifensine. *Lancet* 1985;1:1328-9.
4. Amsterdam JD. Loeffler's syndrome. an uncommon adverse reaction to imipramine. *Int Clin Psychopharmacol* 1986;1:260-2.
5. Allen JN, Davis WB, Pacht ER. Diagnostic significance of increased bronchoalveolar lavage fluid eosinophils. *Am Rev Respir Dis* 1990;142:642-7.
6. Kelly KJ, Ruffing R. Acute eosinophilic pneumonia following intentional inhalation of Scotchguard. *Ann Allergy* 1993;71:358-61.
7. Pope-Harman AL, Davis WB, Allen ED, Christoforidis AJ, Allen JN. Acute eosinophilic pneumonia. A summary of 15 cases and review of the literature. *Medicine* 1996;75:334-42.
8. Lieberman JA, Cooper TB, Suckow RF, Steinberg H, Borenstein M, Brenner R, et al. Tricyclic antidepressant and metabolite levels in chronic renal failure. *Clin Pharmacol Ther* 1985;37:301-7.
9. Sandoz M, Vandel S, Vandel B, Bonin B, Hory B, St. Hillier Y, et al. Metabolism of amitriptyline in patients with chronic renal failure. *Eur J Clin Pharmacol* 1984;26:227-32.