**CASE STUDY**

Eosinophilic pneumonia and respiratory failure associated with venlafaxine treatment

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ABSTRACT: Drugs are well known causes of eosinophilic lung disease. In many patients, symptoms increase slowly, pulmonary infiltrates and eosinophilia progress over weeks, and resolve upon withdrawal of the offending agent. Rarely, the disease presents like acute eosinophilic pneumonia with acute onset of symptoms and rapidly progressing infiltrates which may be associated with respiratory failure. This report describes a case of venlafaxine-induced acute eosinophilic pneumonia causing respiratory insufficiency that rapidly resolved upon institution of corticosteroid treatment. This 5-hydroxytryptamine and noradrenaline reuptake inhibitor was previously known to cause lung or peripheral blood eosinophilia. Considering the increasing use of this class of medication physicians have to be aware of this life-threatening and fully reversible complication.


Drug reactions rank highly among the causes of pulmonary infiltrates with blood and/or alveolar eosinophilia [1]. In many cases, drug-induced eosinophilic lung disease presents with transient eosinophilic infiltrates that disappear after discontinuation of the drug. Some patients, however, experience a fulminant, acute eosinophilic pneumonia-like disease, and require corticosteroid treatment. Acute eosinophilic pneumonia (AEP) differs from chronic eosinophilic pneumonia (CEP) in several important aspects. The onset is within a few days, may lead to respiratory failure, and it usually does not recur after discontinuing corticosteroid treatment [1, 2]. CEP has an insidious onset, responds promptly to corticosteroids, but the relapse rate after discontinuing corticosteroids is quite high, although most patients are eventually able to come off corticosteroids [3]. This report describes a case with acute eosinophilic lung disease, resembling AEP, associated with venlafaxine treatment, a new antidepressant with 5-hydroxytryptamine and noradrenaline reuptake inhibiting actions [4].

**Case report**

A 41-yr-old Caucasian male was transferred from another hospital because of fever up to 38.9°C, increasing shortness of breath, dry cough, chest pain, and myalgias, which had occurred over the previous 2 days.

Because of major depression he had been admitted to the psychiatry department 3 weeks prior to transfer to the authors’ hospital. Five days after admission to psychiatric treatment, venlafaxine was started at a dose of 37.5 mg daily for 9 days and 75 mg daily for the following 8 days. He was put on no other medication.

He had stopped smoking 8 yrs previously but restarted 2 weeks prior to admission (total of 8 pack-years) and took 3–4 glasses of beer per day. He had never consumed illicit drugs, had no allergies, and had not visited a foreign country during the previous 5 yrs. He worked as a dentist in private practice.

On admission, the patient was in moderate respiratory distress, with a blood pressure of 170/100 mmHg, a heart rate of 112 beats per minute, and a respiratory rate of 30 breaths per minute. On examination he had bibasilar crackles and rales and dullness to percussion with otherwise normal findings. An arterial blood gas analysis on room air revealed an oxygen tension in arterial blood (PaO₂) of 7.0 kPa, a carbon dioxide tension in arterial blood (PaCO₂) of 4.77 kPa, a pH of 7.48, and an oxygen saturation of 89.4%. Except for a white blood cell count of 19.7 × 10⁹/mm³ with 32.5% bands and 1% eosinophils and a C-reactive protein of 239 mg·L⁻¹ (normal: <3 mg·L⁻¹) laboratory results including human immunodeficiency virus (HIV) testing, serological screening for vasculitis (autoantibodies to deoxyribonucleic acid (DNA), double stranded DNA, proteinase 3, myeloperoxidase, rheumatoid factor, and circulating immune complexes) and various pulmonary pathogens (*Strongyloides stercoralis*, *Toxocara canis*, *Schinococcus species*, and *Trichinella spiralis*), urinalysis, and stool tests for ova and parasites were normal. Total serum immunoglobulin (Ig)E was 5 kU·L⁻¹ (within normal limits).

A chest radiograph revealed bilateral interstitial infiltrates with prominent Kerley B lines and airspace opacities in the right lower lung field (fig. 1).
The patient was admitted to the intensive care unit and underwent bronchoscopy. The bronchi appeared inflamed and contained increased secretions. Gram stain and cultures of the bronchial washings did not reveal any infectious organism and cytological examination showed 30% eosinophils. Treatment with high dose corticosteroids (i.v. methylprednisolone 1000 mg per day for 3 days) and clarithromycin 500 mg p.o. b.i.d was instituted.

A computed tomographic (CT) scan of the chest 3 days after admission disclosed patchy areas of ground-glass attenuation accentuated in both upper lung fields, thickened interlobular septae, and bilateral pleural effusions (fig. 2). The following day bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsy was performed. Total cell count on BAL was 177 cells/µL with 25% eosinophils, 7% neutrophils, 57% macrophages, and 10% lymphocytes. Transbronchial biopsies revealed an accumulation of eosinophils and neutrophils within alveolar vessels and intra-alveolar accumulation of eosinophils, macrophages, and neutrophils (fig. 3). No bronchiolitis, intra-alveolar fibrous tissue plugs, granulomas, vasculitis, virus-associated changes, or fibrosis were detected. Special stains and cultures for mycobacteria, *Pneumocystis carinii*, fungi, *Legionella pneumophila*, *claydia*, and mycoplasma were negative. On tapering doses of corticosteroids the patient improved and remained afebrile after the third hospital day. The chest radiograph cleared markedly within 5 days of steroid treatment. Clarithromycin was stopped after 7 days of treatment. Pulmonary function tests (PFT) 9 days after admission showed a moderate restrictive ventilatory defect with a vital capacity (VC) of 3.47 L (71% predicted), an FEV1 of 2.76 L (72% predicted), a total lung capacity (TLC) of 4.81 L (70% predicted), and a residual volume (RV) of 1.34 L (68% predicted).

The patient was discharged 10 days after admission. Follow-up examinations 1 and 3 weeks after discharge revealed normal laboratory results and a normal chest radiograph. The prednisone was discontinued after 4 weeks. PFT 1 week after discharge showed some residual restriction with a VC of 4.08 L (84% predicted), an FEV1 of 3.2 L (83% predicted), a TLC of 5.58 L (81% predicted), and an RV of 1.5 L (77% predicted).

Five months after discharge the patient was examined in the authors’ emergency room for signs of upper respiratory tract infection with cough and increased sputum production. The chest radiograph had remained normal and his symptoms disappeared within 6 days of symptomatic treatment. Eleven months after discharge the patient was contacted by phone. He had resumed his work as a dentist 2 months after discharge, was free of respiratory symptoms, continued to smoke, and was later put on trazodone without adverse effects.

**Discussion**

Acute eosinophilic pneumonia is a recently described disease entity [2] and involves acute onset of symptoms within ≤5–7 days, fever ≥37.2 °C, hypoxaemia, bilateral alveolar or mixed alveolar and interstitial infiltrates, and lung eosinophilia (BAL cell differential ≥25% eosinophils and/or predominance of eosinophils in open lung biopsy), without any history of hypersensitivity to drugs, no evidence of infection, and no other known cause of eosinophilic lung disease [1, 5]. The histopathological features are characterized by diffuse alveolar damage with interstitial and alveolar eosinophils [6]. Radiological examination reveals diffuse interstitial and acinar opacities, ground-glass attenuation, and pleural effusion.
the reported disease presentations do not completely fulfil heroin can also cause acute eosinophilic lung disease, but stimulating factor (GM-CSF) [28], piroxicam [29], and carbamazepine [26], and chloroquine [27] have to be incl-...


