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CASE REPORT

Sertraline-Induced Acute Eosinophilic Pneumonia

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Abstract: ***Background*:** Acute Eosinophilic Pneumonia (AEP) is a rare, potentially fatal disease often characterized by a short febrile illness, hypoxemic respiratory failure, diffuse pulmonary opacities and evidence of pulmonary eosinophilia. AEP can be idiopathic, but has documented associations with multiple drugs.

***Case Report*:** We present the first case highlighting Sertraline specifically as a cause of drug-induced AEP in the English literature.

Keywords: Sertraline, acute eosinophilic pneumonia, adverse drug reaction, respiratory failure.

1. INTRODUCTION

Acute Eosinophilic Pneumonia is a rare disease that typically occurs in previously healthy, young adults and can lead to rapidly progressive respiratory failure. Patients are found to have bilateral pulmonary infiltrates on imaging and may or may not have peripheral eosinophilia. Almost all patients are hypoxemic on presentation and many cases require mechanical ventilation [1-3]. Eosinophilia on bronchoalveolar lavage (BAL) is typically used for diagnosis, however, lung biopsy is used to confirm in unclear cases [2]. Most cases of acute eosinophilic pneumonia are considered to be idiopathic, but there are several case reports linking AEP to environmental exposures or specific drugs [1-4]. We present a case of sertraline-induced AEP and highlight AEP as a rare side effect of sertraline use.

2. CASE REPORT

A 49-year-old female with a past medical history significant for hypertension, anxiety, and depression presents with a four-day history of progressively worsening dyspnea, malaise, myalgia and a non-productive cough. The patient denied any fevers, chills or pleuritic chest pain. She had never experienced these symptoms before. She denied a history of asthma. She denied any history of tobacco, alcohol or illicit drug use. She denied recent environmental exposures or unusual outdoor activities. She reported no significant travel history. Medications included Sertraline 100 mg once daily, prescribed six months ago, and Lisinopril 10 mg once daily for the past four years. Family history was significant for coronary artery disease. She presented to an urgent care facility, received a chest x-ray, and was diagnosed with bilateral pneumonia. She was given a dose of ceftriaxone, but her respiratory status continued to worsen, and she was transferred to the emergency room.

On admission, she was afebrile and normotensive, but tachycardic. She was dyspneic and hypoxemic with SpO2 of 70% on room air. Lung examination revealed bilateral crackles at the bases. Her chest x-ray showed bilateral pulmonary infiltrates (Fig. **1**). A CT angiogram of the chest was performed which ruled out pulmonary embolus but revealed bilateral pleural effusions and diffuse bilateral interstitial infiltrates (Fig. **2**). Based on her presentation, it was suspected the patient was experiencing an exacerbation of undiagnosed congestive heart failure and was started on IV furosemide. Troponins were initially elevated at 0.14 ng/ml but trended down to 0.04 ng/ml. EKG showed no acute abnormality and a BNP was 63 ng/L. An echocardiogram was performed and revealed normal systolic and diastolic function with no wall motion abnormalities. The patient was subsequently evaluated by pulmonology, which noted a peripheral eosinophilia of 9.5%.

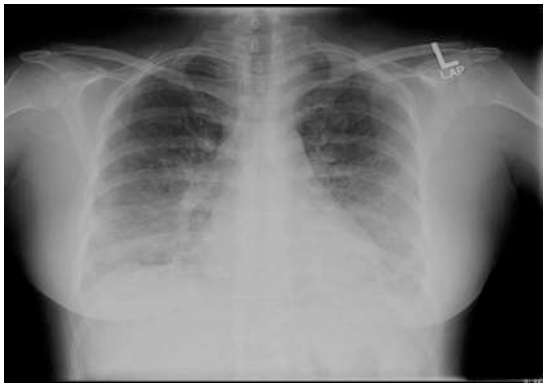


Fig. (1). Chest X-ray on admission with bilateral pulmonary infiltrates.

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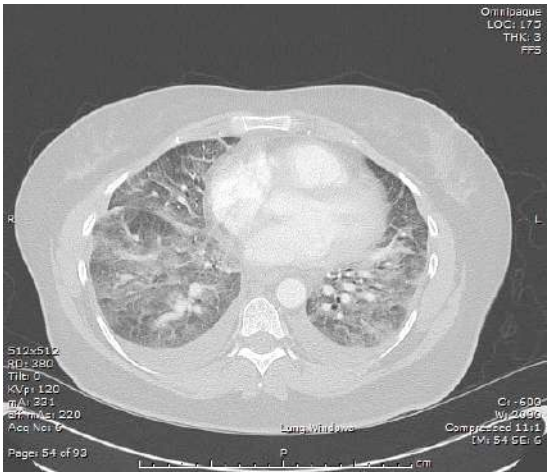


Fig. (2). CT on admission with bilateral pleural effusions and diffuse bilateral interstitial infiltrates.

Eosinophilic pneumonia was suspected, and the patient subsequently underwent a bronchoscopy with a right lower lobe bronchoalveolar lavage (BAL) and a transbronchial lung biopsy. The BAL revealed no purulence but showed a 41% eosinophil count (Fig. **3**), and the lung biopsy revealed interstitial eosinophilic inflammation and intra-alveolar fibrin (Fig. **4**).

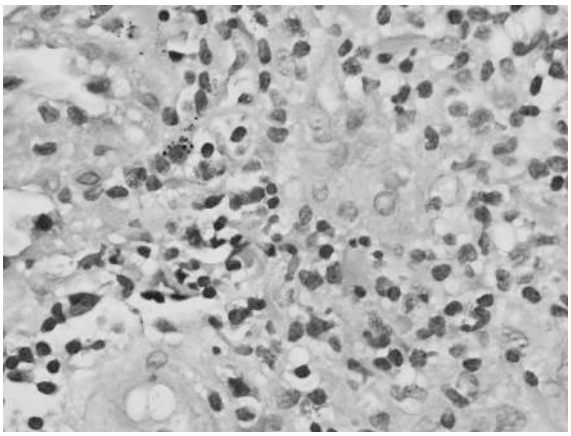


Fig. (3). Bronchoalveolar lavage with increased eosinophils.

Sertraline was discontinued, and on hospital day three she was discharged on prednisone 40 mg once daily with TMP-SMX prophylaxis. The patient was followed up in the clinic ten days following discharge with resolution of lung infiltrates on subsequent chest x-ray (Fig. **5**), eosinophilia, and dyspnea. The patient was then tapered off the prednisone with no recurrence of symptoms on subsequent follow-up.

3. DISCUSSION

AEP is suspected in patients who present with an acute febrile illness for less than a month, hypoxemic respiratory failure, diffuse bilateral pulmonary infiltration on lung imaging and a BAL differential cell count showing eosinophilia > 25% [2]. Patients do not always have peripheral blood eosinophilia at diagnosis.

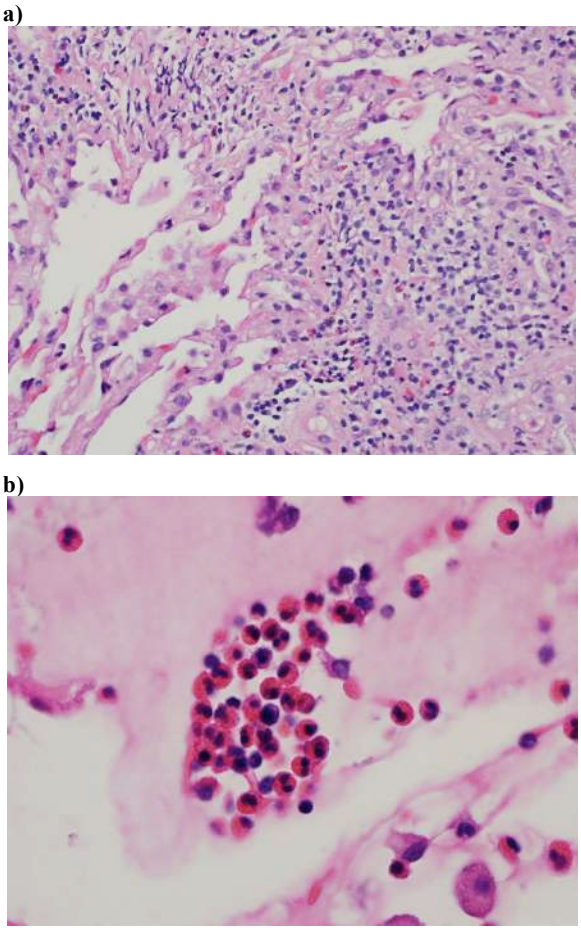


Fig. (4). Lung biopsy with interstitial eosinophilic inflammation and intra-alveolar fibrin.



Fig. (5). Chest X-ray showing resolution of pulmonary infiltrates after treatment with steroids.

Most cases of acute eosinophilic pneumonia are considered to be idiopathic [2]. Smoking history is the only well-documented risk factor, however, there are numerous case reports linking AEP to environmental exposures or specific drugs [1-5] . The most common drugs implicated in causing AEP are chemotherapy drugs, particularly daptomycin.

Other drugs implicated include minocycline, progesterone, and antidepressants [1, 2, 5].

Management includes supportive care with oxygen and ventilation if necessary, empiric antibiotics pending culture results and glucocorticoids, with a hallmark rapid improvement 12-48 hours after initiation. Complete symptomatic and radiographic resolution are expected [2, 6].

The patient above presented with classic symptoms of acute eosinophilic pneumonia. She experienced a milder case than most as she did not require intubation or ICU care. In the context of her lack of pulmonary risk factors or use of confounding medications, sertraline was suspected as the cause of her presentation. It was discontinued with resolution of her symptoms.

To assess causality, the WHO-UMC criteria for adverse drug reactions were applied and resulted in a "certain" score. The Naranjo score was calculated and resulted in a "probable" category rather than "definite" given that the patient was not re-challenged with the drug.

There have been a few case reports documenting acute eosinophilic pneumonia as a rare side effect of antidepressant use, however, this is the first case in the English literature implicating sertraline specifically as a cause. One report documented a case of AEP in the context of clomipramine and sertraline use. Both medications were discontinued simultaneously with resolution of the patient's symptoms [7]. Another case reported a patient who developed AEP secondary to venlafaxine use. Upon discontinuation, her symptoms resolved. This same patient was reported to have AEP secondary to sertraline use in her past medical history [8] . There have been several other case reports implicating venlafaxine alone as a cause of AEP [9, 10].

The precise pathophysiology behind AEP in the setting of SSRIs in unknown. However, increasing research has demonstrated serotonin's central role as a peripheral hormone as well as an immune modulator, with almost all immune cells expressing at least one serotonin receptor [11]. Serotonin modulates cytokine secretion, neutrophil recruitment as well as T-cell activation [11]. It acts as a chemotactic factor for eosinophils [12] which express multiple serotonin receptors. The most common receptor is 5-HT2A through which eosinophil recruitment is mediated with resultant airway inflammation and hyperresponsiveness in diseases like asthma [11]. Furthermore, serotonin's role in airway smooth muscle constriction is well established [13]. It is possible that SSRI administration caused an aberrant immune response to increased levels of serotonin which contributed to the patient's presentation.

Our patient was also on Lisinopril, however, this was thought to be unlikely to be related to her presentation for several reasons. Firstly, the patient had been asymptomatic on Lisinopril for many years. Secondly, her symptoms did not recur when Lisinopril was reintroduced. Thirdly, to our knowledge, there are no cases of AEP associated with Lisinopril or ACE-inhibitors in general, whereas AEP has been documented with various antidepressants as discussed above.

CONCLUSION

Although rare, AEP can be associated with various drugs and toxins. It may initially be confused with infectious pneumonia or ARDS, and failure to improve clinically should prompt clinicians to consider AEP as a diagnosis and undertake the appropriate steps for further diagnosis and treatment.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

REFERENCES

[1] Janz DR, O'Neal HR, Jr., Ely EW. Acute eosinophilic pneumonia: A case report and review of the literature. Crit Care Med 2009; 37(4): 1470-4.

[2] Allen J. Acute eosinophilic pneumonia. Semin Respir Crit Care Med 2006; 27(2): 142-7.

[3] Sohn JW. Acute Eosinophilic pneumonia. Tuberc Respir Dis 2013; 74(2): 51-5.

[4] Allen JN. Drug-induced eosinophilic lung disease. Clin Chest Med 2004; 25(1): 77-88.

[5] Bartal C, Sagy I, Barski L. Drug-induced eosinophilic pneumonia: A review of 196 case reports. Medicine 2018; 97(4): e9688.

[6] Rhee CK, Min KH, Yim NY, *et al*. Clinical characteristics and corticosteroid treatment of acute eosinophilic pneumonia. Eur Respir J 2013; 41(2): 402-9.

[7] Barnes MT, Bascunana J, Garcia B, Alvarez-Sala JL. Acute eosinophilic pneumonia associated with antidepressant agents. Pharm World Sci 1999; 21(5): 241-2.

[8] Tsigkaropoulou E, Hatzilia D, Rizos E, *et al*. Venlafaxine-induced acute eosinophilic pneumonia. Gen Hosp Psychiatry 2011; 33(4): 411.e7-9.

[9] Fleisch MC, Blauer F, Gubler JG, Kuhn M, Scherer TA. Eosinophilic pneumonia and respiratory failure associated with venlafaxine treatment. Eur Respir J Suppl 2000; 15(1): 205-8.

[10] Paparrigopoulos T, Tzavellas E, Karaiskos D, Ilias I, Liappas I. Acute eosinophilic pneumonia after venlafaxine overdose. J Clin Psychopharmacol 2011; 31(2): 258-9.

[11] Herr N, Bode C, Duerschmied D. The effects of serotonin in immune cells. Front Cardiovasc Med 2017; 4: 48.

[12] Boehme SA, Lio FM, Sikora L, *et al*. Cutting edge: Serotonin is a chemotactic factor for eosinophils and functions additively with eotaxin. J Immunol 2004; 173(6): 3599-603.

[13] Keshavarz M, Schwarz H, Hartmann P, *et al*. Caveolin-1: Functional insights into its role in muscarine- and serotonin-induced smooth muscle constriction in murine airways. lectronic) ; 1664-042X (Linking). Front Physiol 2017; 8: 295.

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