Respiratory Medicine Case Reports 27 (2019) 100856

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Eosinophilic pneumonia: A rare manifestation of amiodarone toxicity diagnosed using traditional bronchoscopy

Alexis LeVee[a,*], Megan Trieu[b], Sarathi Bhattacharyya[b], Gurveen Sandhu[b]

[a] Department of Medicine, Tufts University School of Medicine, Boston, MA, USA
[b] Department of Medicine, Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA

ARTICLE INFO

Keywords:
Amiodarone
Eosinophilic
Pneumonia
Toxicity
Adverse effects

ABSTRACT

Amiodarone is an antiarrhythmic agent used primarily to treat atrial and ventricular arrhythmias. However, the drug also has many adverse effects, including pulmonary toxicity, and a wide range of pulmonary diseases have been reported. Amiodarone-induced eosinophilic pneumonia is a relatively rare adverse effect with an incidence ranging between 5 and 13% [1]. The majority of cases have been diagnosed with lung biopsy, with only one prior reported case diagnosed by bronchoalveolar lavage (BAL) [2]. This report describes the second documented case of amiodarone-induced eosinophilic pneumonia diagnosed by eosinophilia on BAL cytology. In this case, complete cessation of symptoms occurred after discontinuation of amiodarone and treatment with corticosteroids. An updated review of the literature of amiodarone-induced eosinophilic pneumonia is also detailed.

1. Introduction

Amiodarone is a potent antiarrhythmic agent commonly used to treat a variety of tachyarrhythmias; however, its use is associated with a number of adverse effects. These include pulmonary toxicity, pulmonary fibrosis, diffuse interstitial pneumonia, organizing pneumonia, and diffuse alveolar damage. Amiodarone-induced eosinophilic pneumonia is an extremely rare toxicity, with only one prior reported case diagnosed by eosinophilia on bronchoalveolar lavage (BAL). We describe a case of amiodarone-induced eosinophilic pneumonia that presented as a subacute nonproductive cough and was diagnosed by eosinophilia on BAL.

2. Case report

A 75-year-old male presented with a three-week history of nonproductive cough. His medical history was notable for coronary artery disease for which he had undergone coronary artery bypass grafting (CABG) and left atrial ligation four weeks earlier. His medical history was also significant for a 9-pack/year smoking history but he had no known allergic or respiratory disease. His post-operative hospital course had been complicated by atrial fibrillation with rapid ventricular rate. Intravenous amiodarone was initiated and later transitioned to oral amiodarone after the patient converted to normal sinus rhythm. The patient was discharged on amiodarone.

Approximately one week post discharge the patient developed a non-productive cough without associated fever, chills, or shortness of breath. A chest X-ray obtained at his surgery follow-up appointment demonstrated a new opacity in the peripheral right upper lobe. Amiodarone was discontinued two days later out of concern for possible pulmonary toxicity. The patient then presented to his outpatient pulmonologist for persistent cough, and a repeat chest X-ray at that time revealed an interval increase in the size and distribution of the consolidation. He was started on levofloxacin for presumed pneumonia.

After completion of a seven day course of levofloxacin, the patient presented to the emergency department with progressively worsening cough and pleuritic chest pain. On admission, he was afebrile with normal oxygen saturation on room air. His physical exam was significant for bibasilar crackles without wheezing, rhonchi, or accessory muscle use. Laboratory findings were remarkable for platelet count of 542,000, normal white blood cell count, and absolute eosinophil count of 360. All bacterial, viral, and fungal studies were negative. Chest X-ray demonstrated persistent multifocal opacities, and a chest CT showed bilateral peripheral ground-glass opacities with a possible reverse halo sign of the left lower lobe (Fig. 1). He underwent bronchoscopy with bronchoalveolar lavage (BAL), which revealed a cell count of 400 cells/μl with 80% eosinophils. Gram stain showed few gram-positive bacilli, rare gram-positive cocci, rare yeast, and moderate white blood cells. Bacterial and viral cultures were negative. The fungal culture grew Candida albicans, which was thought to be a contaminant.

* Corresponding author. Tufts University School of Medicine, 145 Harrison Avenue, Boston, MA 02111, USA.
E-mail address: alexis.levee@tufts.edu (A. LeVee).

https://doi.org/10.1016/j.rmcr.2019.100856
Received 20 February 2019; Received in revised form 8 May 2019; Accepted 13 May 2019

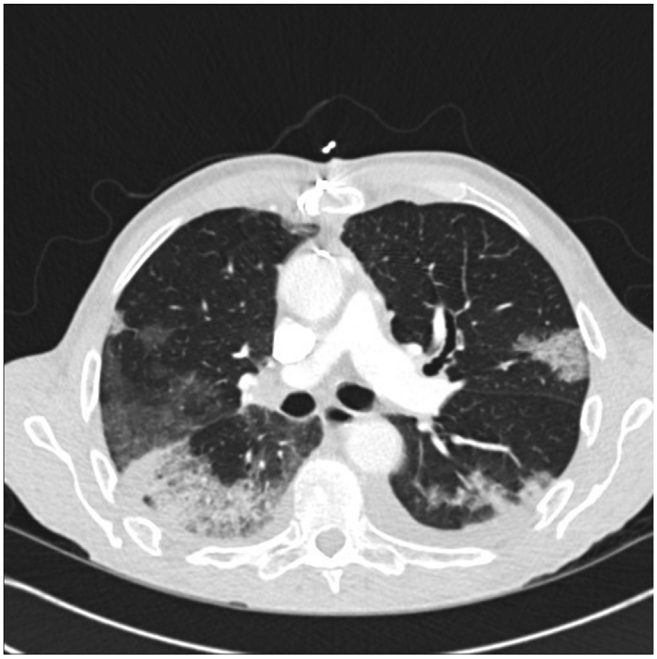

Fig. 1. Chest CT-Angiogram obtained 31 days after the initial administration of amiodarone. Bilateral peripheral ground-glass opacities are seen with a possible reverse halo sign in the left lower lobe.

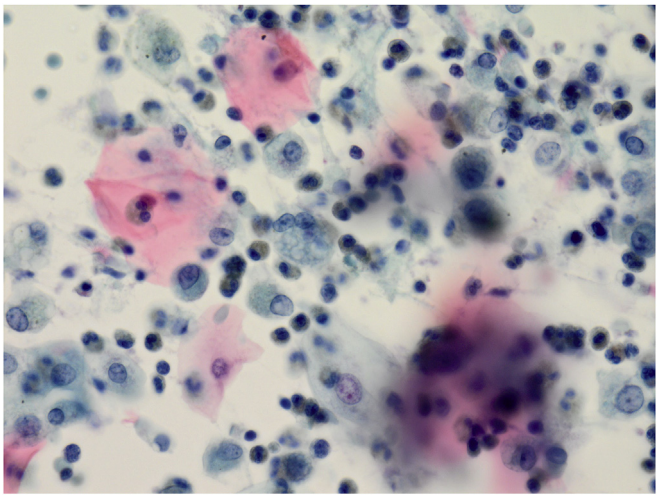

Fig. 2. Cytology of bronchoalveolar lavage which revealed foamy macrophages with surrounding eosinophils (Papanicolaou stain, original magnification ×600).

Cytology ultimately demonstrated occasional foamy macrophages and an increased number of eosinophils (Fig. 2), leading to the diagnosis of amiodarone-induced eosinophilic pneumonia. The patient began treatment with prednisone 40 mg/day, resulting in rapid resolution of symptoms.

3. Discussion

Pulmonary toxicity is a well-established adverse effect of amiodarone use, with an incidence ranging between 5 and 13% [1]. A wide variety of acute and chronic lung diseases have been reported, affecting both the alveolar and interstitial compartments. Symptoms are not specific, and often include dyspnea, non-productive cough, and pleuritic chest pain. Chest radiograph and CT scan findings related to amiodarone toxicity vary depending on the disease process, but typically show alveolar or interstitial opacities in a bilateral patchy, peripheral, or diffuse pattern. Discontinuation of the drug and administration of corticosteroids are the mainstay of treatment. Although a number of lung toxicities have been reported related to amiodarone use, there are few reports of amiodarone-induced eosinophilic pneumonia [3].

Eosinophilic pneumonias result in a wide array of lung pathology, but are primarily characterized by prominent infiltration of the lung parenchyma by eosinophils. The presentation can range from acute to chronic, and the diagnosis requires the demonstration of alveolar and/or peripheral blood eosinophilia. Diagnostic criteria include $> 1 \times 10^9$ eosinophils/l in peripheral blood, $\geq$ 25% eosinophils on BAL cell count, and/or demonstration of lung tissue eosinophilia on lung biopsy [4]. The diagnosis also requires careful review of the medication history and exclusion of other possible etiologies, such as infections or other toxins.

Though amiodarone-induced eosinophilic pneumonia is rare, mild eosinophilia may be present in both peripheral blood and BAL in patients with other forms of amiodarone-induced pulmonary toxicity [3]. In 1992, Coudert et al. reported the BAL findings in fifteen patients with amiodarone pneumonitis and found that the average eosinophil percent was 5.4% and the highest was 16% [5]. Despite the increased eosinophil counts in these patients, none met the criteria for eosinophilic pneumonia.

There are a few cases of amiodarone-induced eosinophilic pneumonia that have been diagnosed using lung biopsy. In a case review of 75 cases of probable amiodarone-induced pneumonia, Larsen et al. found four cases of eosinophilic pneumonia based on lung wedge biopsy [6]. There is also one case report of probable amiodarone-induced eosinophilic bronchiolitis [7].

On the other hand, there are limited reports of amiodarone-induced eosinophilic pneumonia diagnosed by peripheral eosinophilia or alveolar eosinophilia using BAL. There are two known cases that diagnosed amiodarone-induced eosinophilic pneumonia using peripheral eosinophilia, and one of these demonstrated 20% eosinophils on BAL [8,9]. There is only one documented case of amiodarone-induced eosinophilic pneumonia diagnosed by BAL that demonstrated 81% eosinophils [2].

The pathophysiology of amiodarone-induced eosinophilic pneumonia is currently unknown. However, it is speculated that amiodarone causes lung injury through several mechanisms including cytotoxicity to type II pneumocytes and other lung parenchymal cells, activation of the angiotensin enzyme system (which enhances apoptosis of alveolar epithelial cells), and inflammation with a predominance of T helper lymphocytes and cytokines [3]. More research is needed to elucidate the specific mechanism by which amiodarone induces eosinophilic pneumonia.

The diagnosis of amiodarone-induced eosinophilic pneumonia was established in this patient based on the strong temporal relationship of amiodarone initiation and a BAL demonstrating 80% eosinophils in the setting of typical radiographic findings. The patient also responded well after discontinuation of amiodarone and initiation of prednisone.

A differential diagnosis was considered to make this diagnosis of exclusion, which included community-acquired pneumonia, idiopathic interstitial pneumonias, sarcoidosis, and adverse effects of other drugs. Community-acquired pneumonia was ruled out based on negative cultures and no response to antibiotics. Idiopathic interstitial pneumonias, such as cryptogenic organizing pneumonia (COP) or nonspecific interstitial pneumonia (NSIP), could cause a similar clinical and radiologic presentation as seen in this case, and both can be idiopathic or caused by other diseases (such as amiodarone toxicity). However, the BAL profile of COP and NSIP reveals elevated lymphocytes with a normal or minimally elevated eosinophil count [10]. Sarcoidosis was considered given that the disease is commonly associated with the CT finding of a reverse halo sign, but the characteristic BAL profile in sarcoidosis is 0.5% eosinophils and the lack of plasma cells and “foamy” macrophages

[11]. Lastly, the patient's remaining medications, including acetaminophen, clopidogrel, aspirin, dextromethorphan-guaifenesin, docusate, levofloxacin, metoprolol tartrate, rosuvastatin, tramadol, and zolpidem, were considered unlikely causes of eosinophilic pneumonia.

As such, this case highlights the importance of considering amiodarone as a rare but identifiable cause of eosinophilic pneumonia in patients that present with pulmonary symptoms and radiographic findings after exclusion of other etiologies.

Declarations of interest

None.

Conflicts of interest

The authors have no financial or grant support conflicts of interest. There are no sources of funding.

Acknowledgements

We would like to acknowledge the expert pulmonologist Dr. Eric Kleerup, as well as the expert pathologist Dr. David Lu involved in this case.

References

[1] M. Schwaiblmair, T. Berghaus, T. Haeckel, T. Wagner, W. Von Scheidt, Amiodarone-induced pulmonary toxicity: an under-recognized and severe adverse effect? Clin. Res. Cardiol. 99 (2010) 693–700.

[2] S. Sato, K. Watanabe, T. Ishida, M. Yoshikawa, K. Kanazawa, J. Saito, et al., Amiodarone-induced pneumonitis associated with marked eosinophilia in BALF, [in Japanese], 95 (2) (2006) 356–358.

[3] S.A. Papiris, C. Triantafillidou, L. Kolilekas, D. Markoulaki, E.D. Manali, Amiodarone: review of pulmonary effects and toxicity, Drug Saf. 33 (6) (2010) 539–558.

[4] V. Cottin, F.J. Cordier, Eosinophilic pneumonias, Allergy 60 (7) (2005 Jul) 841–857.

[5] B. Coudert, F. Bailly, J.N. Lombard, F. Andre, P. Camus, Amiodarone pneumonitis: bronchoalveolar lavage findings in 15 patients and review of the literature, Chest 102 (4) (1992 Oct) 1005–1012.

[6] B.T. Larsen, L.T. Vaszar, T.V. Colby, H.D. Tazelaar, Lymphoid hyperplasia and eosinophilic pneumonia as histologic manifestations of amiodarone-induced lung toxicity, Am. J. Surg. Pathol. 34 (4) (2012) 509–516.

[7] F.R. Costa-Jussa, B. Corrin, J.M. Jacobs, Amiodarone lung toxicity: a human and experimental study, J. Pathol. 144 (2) (1984) 73–79.

[8] A. Alqaud, G. Baskaran, C. Dougherty, Amiodarone-induced lung injury with bilateral lung pneumonitis and peripheral eosinohplia, Am. J. Therapeut. 23 (4) (2016) e1121–e1123.

[9] F. Lavaud, C. Cossart, V. Tack, G. Bonnaud, Follow-up of blood and alveolar hypereosinophilia in pneumopathy induced by amiodarone, Therapie 45 (1) (1990) 49–51.

[10] S. Nagai, Tm Handa, Y. Ito, M. Takeuchi, Takateru Izumi, Bronchoalveolar lavage in idiopathic interstitial lung diseases, Semin. Respir. Crit. Care Med. 28 (5) (2007) 496–503.

[11] M. Drent, K. Mansour, C. Linssen, Bronchoalveolar lavage in sarcoidosis, Semin. Respir. Crit. Care Med. 28 (5) (2007) 486–495.