

# Dyspnea on Daptomycin: Eosinophilic Pneumonia

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## ABSTRACT

We present a case of drug-induced acute eosinophilic pneumonia with characteristic imaging and bronchioalveolar lavage (BAL) findings. Although not a common diagnosis, it is important to consider in the right clinical scenario, including a patient with presumed pneumonia that does not respond to typical treatment. Diagnosis is confirmed by bronchoscopy with BAL. For drug-induced types, treatment includes removal of the offending agent. Corticosteroids are used if symptoms are severe and can result in rapid clinical improvement.

**KEYWORDS:** Daptomycin, eosinophilic pneumonia, adverse drug event

## CASE REPORT

A 76-year-old man presented to an academic community hospital with complaints of worsening dyspnea on exertion, cough, subjective fevers, nausea and fatigue; gradually increasing over the past week. He denied orthopnea or increase in lower extremity edema. There were no sick contacts and his cough was non-productive. He was a distant former smoker. He had been discharged from the hospital the week before, after treatment for methicillin-resistant *Staph aureus* (MRSA) septic arthritis of the left knee and pacemaker lead vegetation. He had undergone irrigation of his left knee and pacemaker lead extraction. His course was complicated by left leg deep venous thrombosis as well as acute tubular necrosis due to transient hypotension as well as possible vancomycin toxicity. During that admission, at the time of his peak renal failure, he was transitioned to daptomycin to complete his 6-week antibiotic course.

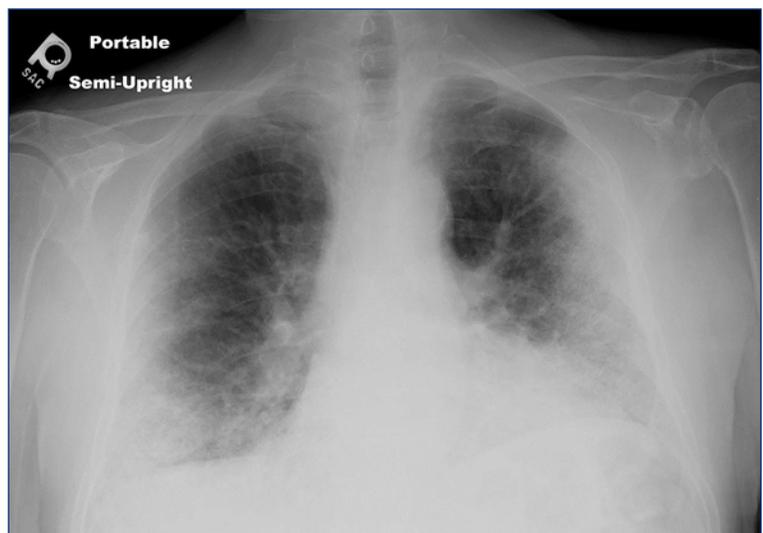
Initial vital signs in the emergency room were T 100.1, BP 134/74, HR 92, RR 20, 88% on RA. He was elderly and chronically ill appearing, but in no acute distress. Mucous membranes were moist, and there was no jugular venous distension. Lung auscultation revealed inspiratory crackles at the right base. Heart rate and rhythm were regular. There were no murmurs. The abdomen was benign and extremity exam showed left calf swelling. His right arm peripherally

inserted catheter site was clean, dry and intact. He had no rash.

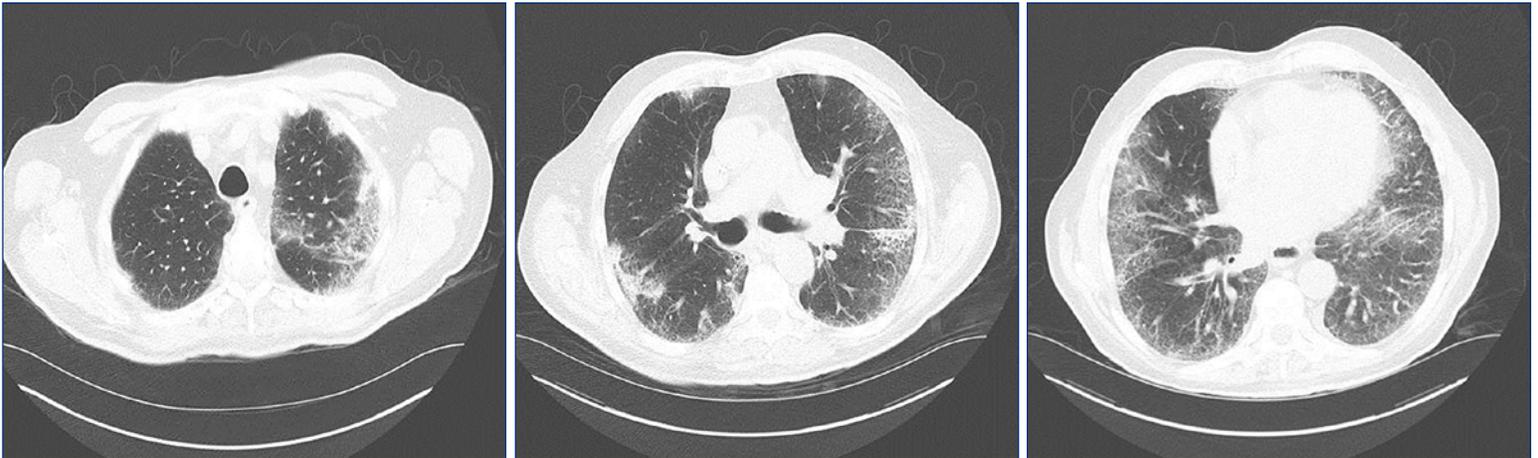
His laboratory studies revealed: Na 136mmol/L, K 4.5mmol/L, Cl 106mmol/L, CO<sub>2</sub> 17mmol/L, BUN 54mg/dL, creatinine 3.9mg/dL, glucose 136mg/dL, WBC count was 11,200/ $\mu$ L with 88.4% neutrophils, 2.1% eosinophils, hemoglobin was 8.3g/dL, platelets 257,000/ $\mu$ L; troponin I was negative. C-reactive protein was profoundly elevated at 230mg/L (normal range 0-10.0mg/L). EKG showed a normal sinus rhythm with a left bundle branch block. Chest x-ray (**Figure 1**) revealed bilateral airspace disease and a chest CT without contrast (**Figure 2A–C**) revealed extensive bilateral areas of ground glass opacity in a peripheral distribution as well as patchy areas of consolidation.

Initially, the patient was treated with broad-spectrum antibiotics for potential healthcare-associated pneumonia (HCAP). Over the first 48 hours of his hospital stay he developed increasing hypoxemia, ultimately requiring 100% oxygen by non-rebreather mask. He also went into atrial fibrillation with rapid ventricular response and was transferred to the ICU for further care. His heart rate was controlled. The patient had historical Chest CT scans as an outpatient from the year prior to admission with findings

**Figure 1.** Portable AP chest radiograph taken the day of admission, revealing bilateral, peripheral airspace disease with sparing of the perihilar regions. This pattern of lung involvement is different from other typical causes of bilateral airspace disease including pulmonary edema and ARDS, which tend to be more central or diffuse respectively.



**Figure 2A-C.** Non-contrast chest CT images from the upper (A), middle (B), and lower (C) lung zones demonstrating ground glass opacities with some areas of more dense consolidation. The CT images, from day 2 of admission, confirm the peripheral distribution of the lung disease. This peripheral predominance is strongly suggestive of eosinophilic pneumonia.



consistent with stable, mild interstitial fibrosis, most likely nonspecific interstitial pneumonia (NSIP). Bronchoalveolar lavage (BAL) was performed. Left lower lobe fluid was pink, with 474 nucleated cells, 31% neutrophils, 7% lymphocytes and 54% eosinophils. Similar findings were present in a right middle lobe BAL. Bacterial, fungal and AFB stains and cultures were negative. Given his exposure to daptomycin over the previous 2 weeks, he was diagnosed with drug-induced acute eosinophilic pneumonia.

Daptomycin was immediately discontinued and intravenous methylprednisolone was administered. His hypoxemia resolved in the 72 hours following initiation of steroid treatment and he was weaned off supplemental oxygen. The patient was transitioned to oral steroids in tapering doses for a total course of 16 days. In follow up, his chest CT showed significant improvement. The patient completed a course of treatment for his MRSA septic arthritis with vancomycin.

## DISCUSSION

Eosinophilic pneumonia should always be considered in the differential diagnosis of acute respiratory failure with bilateral infiltrates, even in the absence of a peripheral blood eosinophilia. As originally described, acute eosinophilic pneumonia is characterized by fever, diffuse pulmonary infiltrates, hypoxemia, and pulmonary eosinophilia.<sup>1</sup> Many drugs have been implicated in potentially triggering eosinophilic pneumonia, the most common classes being NSAIDs and antibiotics; smoking may also be a risk factor.<sup>2</sup> There are at least 24 published case reports of daptomycin-associated eosinophilic pneumonia.<sup>3</sup> Radiographically, a peripheral distribution of airspace disease, as in this case, is characteristic of eosinophilic pneumonia. BAL will confirm the diagnosis. Eosinophils are not normally present in the lungs, so over 1% eosinophils on BAL is considered an eosinophilic pattern, but >25% eosinophils strongly suggests a diagnosis of

either acute or chronic eosinophilic pneumonia.<sup>4</sup> A careful review of medications, toxins and exposures to exclude an etiologic agent should be performed in all cases of suspected or confirmed eosinophilic pneumonia. An online database is available as a reference for drug-induced lung disorders.<sup>5</sup> In addition to cessation of potential offending medications, patients with significant hypoxemia or respiratory failure may benefit from corticosteroid treatment. Steroids have been recommended specifically for lung toxicity secondary to amiodarone, bleomycin, cocaine or mitomycin<sup>6</sup>, and although there are no studies specifically looking at daptomycin, steroids have been used in other case reports<sup>3</sup>. There are also no official guidelines on optimum dose or treatment length, but recent data support a short treatment course of 2 weeks.<sup>7</sup> In our patient, steroids were used given his significant hypoxemia and he did respond well with a short duration of treatment (16 days).

## References

1. Allen JN, Pacht ER, Gadek JE, Davis WB. Acute eosinophilic pneumonia as a reversible cause of noninfectious respiratory failure. *N Engl J Med.* 1989;321(9):569-574
2. Solomon J, Schwartz M. Drug-, toxin-, and radiation therapy-induced eosinophilic pneumonia. *Semin Respir Crit Care Med.* 2006;27(2):192-8
3. Phillips J, Cardile AP, Patterson TF, Lewis JS. Daptomycin-induced acute eosinophilic pneumonia: Analysis of the current data and illustrative case reports. *Scand J Infect Dis.* 2013;45(10):804-8.
4. Meyer KC, et al. An official American Thoracic Society clinical practice guideline: The clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. *Am J Respir Crit Care Med.* 2012;185(9):1004-14.
5. Camus P. Pneumotox online: The drug-induced respiratory disease website. Dijon (France): University Hospital Department of Pulmonary Medicine and Intensive Care. c2012. [cited 2015 Apr 4]. Available from: <http://www.pneumotox.com>.
6. Jantz MA & Sahn SA. Corticosteroids in acute respiratory failure. *Am J Respir Crit Care Med.* 1999;160(4):1079-100.

- Rhee CK, et al. Clinical characteristics and corticosteroid treatment of acute eosinophilic pneumonia. *Eur Respir J*. 2013;41(2):402.

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