Acute eosinophilic pneumonitis (AEP) is also known as a Pneumonia-like pulmonary infiltrate with eosinophilia.  
Most common causes of secondary eosinophilic pneumonitis are drug-induced and idiopathic causes (primary eosinophilic pneumonitis).  
Common drug-induced causes in daptomycin.  
Symptoms are vague and include respiratory distress, fever, and dry cough that can be confused with a myriad of other diagnoses.  
Pulmonary toxicity is time-dependent with an average time of symptoms onset to diagnosis of 9.8 days.

Risk factors:  
• Male sex  
• Prior prosthetic joint infection  
• Age greater than 65  
• Renal failure  
• Treatment of osteoradionecrosis and diabetes mellitus type 2

Diagnosis:
• Multifocal pneumonia appearance, ground glass opacities, peripheral or pleural-based bilateral alveolar opacities of the upper lobes, interstitial finding  
• Pleural effusions  

Laboratory findings:  
• Acute eosinophilic pneumonitis complicated by Multicentric-resistant Streptococcus aureus (MRSA) bacteraemia.
• Received fifteen days of IV vancomycin prior to switching to IV daptomycin, one day prior to discharge.  
• Received a right hilar amputation and a right pleural stent placement.  
• Discharged to subacute rehabilitation on IV daptomycin through a peripherally inserted central catheter to complete a twenty-eight-day course.

Imaging findings:  
• Increased bilateral reticular markings, peribronchial thickening, and non-preferring densities to the right leg with an ACE wedge to the right foot.  

Etiology of pulmonary toxicity:  
• Unclear  
• Caused by drug binding to and blocking up on pulmonary surfactant leading to alveolar inflammation  
• Drug causes disruption of lipid integrity leading to alveolar inflammation  
• Oxidant-induced injury  

• Only seen in daptomycin and nitrofurantoin-induced injury  
• Oxidant-induced injury  

Vital signs:  
• Oxygen saturation of 80% on room air, BP 182/76, HR 90 beats per minute, RR 26 breaths per minute, and temp 98.9°F. Placed on four liters nasal cannula with improvement.

Physical exam:  
• No acute distress with mucous secretions, coarse breath sounds, mild cor pulmonale, and non-preferring rales to the right leg with an ACE wedge to the right foot.

Laboratory workup (Table 1):  
• EKG revealed rate-controlled atrial fibrillation with chronic atrial fibrillation right bundle branch block.
• Chest x-ray: Increased bilateral reticular markings, peribronchial thickening, and small pleural effusions.  

CT chest angiography:  
• Atelectasis, ill-defined nodular type densities of the upper lobes, moderate aeration throughout her lungs on physical exam.  

Pulmonary function test:  

We present the case involving an 84-year-old female with a medical history of severe atherosclerotic disease, type 2 diabetes mellitus complicated by chronic kidney disease and neuropathy, atrial fibrillation, and hypertension.

Initial Hospitalization:
• Admitted for right great toe osteomyelitis complicated by Multicentric-resistant Streptococcus aureus (MRSA) bacteraemia.
• Received fifteen days of IV vancomycin prior to switching to IV daptomycin, one day prior to discharge.  
• Received a right hilar amputation and a right pleural stent placement.  
• Discharged to subacute rehabilitation on IV daptomycin through a peripherally inserted central catheter to complete a twenty-eight-day course.

Return to the Emergency Department:  
• Retained eight days post-discharge with four days of dyspnea on exertion, right leg swelling, chest tightness, dry cough, and hypoxia.

Second Hospital Course:
• Hypoxia and started methylprednisolone 40 mg every eight hours given concern for AEP.
• Seven days into her hospitalization, she had a chest CT which revealed progressive multifocal irregular ground glass consolidation opacities throughout both lungs with compressive atelectasis, and small bilateral pleural effusions.

Conclusions:
• Expansive use of outpatient IV antibiotics and increased prevalence of resistant bacteria should drive a broad differential diagnosis for dyspnea.
• Diagnostic findings vary from symptoms, increased oxygen requirements, new imaging findings, and improvement after cessation of the offending agent.
• As symptoms evolve or do not improve, the clinicians’ suspicion of alternative diagnoses should also evolve.
• Based on the clinical diagnostic criteria, her symptoms progressed from possible to probable.
• This case had several factors that muddled her final diagnosis, including initial presentation more concerning for heart failure rather than pneumonitis, completion of daptomycin during her second hospitalization before a probable diagnosis, and transient, delayed peripheral eosinophilia.

Jefferson Health Northeast Internal & Emergency Medicine
Broadening the Dyspnea Differential: Daptomycin-induced acute eosinophilic pneumonitis

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