Nitrofurantoin-Induced Pulmonary Toxicity

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Abstract

Background*:** Nitrofurantoin is commonly prescribed to treat and prevent uncomplicated urinary tract infections. Although generally considered safe, one rare but serious side effect is chronic pulmonary toxicity. ***Purpose*:** Describe a single incident of chronic nitrofurantoin-induced pulmonary toxicity that was nearly overlooked, in part, due to poor chart documentation of home medications. ***Case Report: An 89 year old female presented to the emergency department (ED) with a one month history of fatigue, nonproductive cough, and weakness. Chest radiograph demonstrated extensive interstitial changes with bilateral cyst formation or possible cavitation. Because of incomplete medication histories documented in nursing, ED, and pulmonary consult records, prior chronic nitrofurantoin use was not recognized. On day two of hospitalization, a complete home medication list was obtained and all medications resumed. It was then that the use of nitrofurantoin was recognized and a diagnosis of chronic nitrofurantoin-induced pulmonary toxicity was made. A chest radiograph performed 22 months later demonstrated resolution of toxicity. ***Conclusion*:** Poor documentation of home medications coupled with the rarity of occurrence of this adverse reaction and slow insidious onset of symptoms created a diagnostic dilemma for clinicians. Describing this relatively rare adverse reaction to a commonly prescribed antibiotic may remind clinicians to consider drug toxicity in patients who develop new onset of pulmonary symptoms while taking nitrofurantoin. This case also highlights the importance of thorough documentation and awareness of home medications in making accurate diagnoses.

1. Introduction

Nitrofurantoin is an antibiotic commonly prescribed for the treatment and prevention of uncomplicated urinary tract infections. Although generally considered safe, one rare but serious side effect is pulmonary toxicity.[1] Because of the rarity of occurrence and slow, insidious onset of symptoms, chronic nitrofurantoin pulmonary toxicity may be overlooked as a cause of new onset respiratory symptoms.

2. Case Presentation

An 89 year old Caucasian female presented to the emergency department with a one month history of fatigue, nonproductive cough, and weakness, progressing over the past three days to the point where she was unable to attend meals in her assisted living facility's cafeteria. Her nonproductive cough is exacerbated with deep inspiratory effort. The patient denied fever, chills, night sweats, shortness of breath, nausea, vomiting, weight loss, syncope, or chest pain. Past medical history included hypertension, cystocele (fallen bladder), mild dementia and recurrent urinary tract infections. The patient could only recall taking a blood pressure medication, metoprolol, and a sulfa agent for chronic urinary tract infections.

Physical examination: On admission the patient was alert and oriented, pulse was 74 beats per minute; respirations 20 breaths per minute; blood pressure 153/70 mmHg; and room air pulse oximetry saturation was 90%. Pertinent physical exam findings revealed bilateral rales and cough with deep inspiratory effort. Extremities were without clubbing or cyanosis and one centimeter pedal edema was present on the left with tenderness to palpation.

Testing: Chest radiograph demonstrated extensive interstital changes with bilateral cyst formation or possible cavitation. These findings were not present on previous chest radiographs dated three years prior.

Hospital Course: Because of inconsistencies between medication histories documented by nursing, the ED physician and pulmonology physician assistant, the patient's assisted living facility was contacted to reconcile the home medication list. The patient was restarted on her home medications including nitrofurantoin 100 mg once daily. During unrelated medication monitoring, a pharmacist recognized the possibility that nitrofurantoin could be the cause of the pulmonary symptoms and alerted the pulmonologist. The nitrofurantoin was discontinued. A high resolution chest computerized tomography (CT) was obtained which demonstrated extensive septal thickening and periseptal areas of infiltrate throughout all lung fields. Flexible bronchoscopy was performed; airways appeared normal. No malignant cells were identified and all cultures were negative. Transbronchial biopsy revealed chronic interstitial pneumonia, thickened alveolar septa, and increased alveolar macrophages.

The injury pattern was compatible with nitrofurantoin toxicity.

Discussion: Nitrofurantoin-induced pulmonary toxicity is categorized either as acute or chronic in presentation. Pulmonary toxicity is rare; the incidence of acute toxicity is estimated in 1/5000,[2] with the acute presentation out numbering the chronic 9:1.[3] The presentation of acute pulmonary toxicity can be alarming and may include fever, chills, cough, shortness of breath, elevated erythrocyte sedimentation rate, eosinophilia, and chest pain and diffuse pulmonary infiltrates on chest radiograph.[1-3] Development of acute toxicity most often occurs within 3 – 8 days of nitrofurantoin initiation.

Unlike the acute form, *chronic* nitrofurantoin-induced pulmonary toxicity has a slow, insidious onset, often presenting months to years after treatment is initiated.[1,4] Middle aged and older women dominate the patient population likely due to the susceptibility to recurrent urinary tract infections in this sex and age group.[1,4] As in this case, patients typically present with gradually increasing shortness of breath and nonproductive cough with bilateral, scattered crackles on physical exam[3] and diffuse bilateral interstitial infiltrates on chest radiograph and bilateral patchy ground glass attenuation on chest CT.[4] It does not appear that acute toxicity leads to chronic toxicity or that chronic lesions follow an acute reaction to nitrofurantoin.[5] Currently, the mechanism of chronic nitrofurantoin–induced pulmonary toxicity has not fully been elucidated but it is thought to be related to direct oxidative damage to the lungs.[6]

Primary treatment for chronic pulmonary toxicity begins with discontinuation the medication. Early diagnosis and discontinuation of nitrofurantoin is important in preventing irreversible pulmonary fibrosis.[4,5] The majority of patients with chronic pulmonary toxicity will experience improvement in symptoms after cessation of nitrofurantoin.[4,5] In patients with reversible disease, there appears to be a correlation between the duration of symptoms and amount of improvement. There does not appear to be any correlation between the length therapy and the severity of the illness, or its reversibility.[5]

Clinical Significance. Home Medication Documentation upon Hospital Admission*:* Although adverse drug reactions are a frequent cause of emergency department visits and hospital admission, they are commonly over looked. In order for the possibility of adverse drug reactions to be adequately considered in making any clinical diagnosis and treatment decision an accurate medication history must be obtained and clearly documented. This case highlights the importance of recording an accurate and complete medication history as part of the initial patient assessment at hospital admission. Discrepancies in home medication lists at hospital admission occur for a variety of reasons and are not unique to this case. In this case, the pulmonology consultants were unaware of the patient's prior history of nitrofurantoin use due to poor documentation of home medications and therefore, the diagnosis was nearly overlooked. Had the medication not been clarified and restarted days later, it is unknown when the diagnosis would have been made. Thoroughly investigating any vagueness or inconsistencies in the patient's home medication list upon admission to the hospital is important but can be difficult, especially when the patient is unknown to the clinician or is an unreliable historian. Resources to help clarify a patient's home medications include family members and caregivers, other medical records, the patient's retail pharmacy, and the hospital pharmacist.

3. Conclusion:

This case created a diagnostic dilemma for clinicians. The combination of poor documentation of home medications and the slow insidious onset of symptoms associated with chronic nitrofurantoin-induced pulmonary toxicity delayed accurate diagnosis and discontinuation of nitrofurantoin. It remains critical that clinicians carefully document all home medications and remain suspicious of this adverse reaction in patients taking nitrofurantoin, particularly in those who present with pulmonary symptoms. Medication histories upon admission to the hospital are frequently incomplete. This case highlights the importance of thorough documentation and awareness of home medications in making an accurate diagnosis.

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