

Resolution of Organizing Pneumonia Secondary to Nitrofurantoin without Immunosuppression

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Abstract

Organizing pneumonia (OP) is an interstitial lung disease (ILD) that can be a primary process or secondary to a wide variety of medical conditions or medications, including nitrofurantoin. A prolonged course of corticosteroids is the mainstay of treatment for OP. We present a novel case of nitrofurantoin induced OP in an 82-year-old woman in which there was complete resolution clinical and radiographic findings following discontinuation of the drug and without the use of corticosteroids. This case highlights the potential role for watchful waiting when there is a clear modifiable trigger of OP in a stable patient in the outpatient setting.

Keywords

Organizing pneumonia, Interstitial lung disease, Drug reaction

Introduction

Organizing pneumonia is an ILD that affects the distal bronchioles, respiratory bronchioles, and alveoli. It can be idiopathic or associated with connective tissue diseases, malignancy, other ILD or drugs [1]. Nitrofurantoin has been linked with a spectrum of pulmonary toxicities including OP [2-4]. The prognosis of OP is good, yet case reports of nitrofurantoin related OP demonstrate a trend of high rates of mortality, extended corticosteroid courses, and additional immunosuppressive agents [1, 5]. This case highlights the potential role for watchful waiting when there is a clear modifiable precipitant of OP in a stable patient in the outpatient setting.

Case Report

An 82-year-old woman was referred to the respiratory clinic by her family doctor with a 4 month-history of dry cough, dyspnea (MRC 3/5) and unintentional weight loss of 12 kg, despite having received two courses of oral antibiotics.

The patient's past medical history was significant for pneumonia 3 years prior, osteoarthritis with lumbar spondylosis, gastroesophageal reflux disease, diabetes mellitus and frequent urinary tract infections for which she had been taking prophylactic nitrofurantoin 100 mg once daily for the past 5 months. No details regarding the reasons for the recurrent urinary tract infections were provided by the referring physician, but the patient had a previous normal cystoscopy. She had smoked 10 pack/years, quit 40 years ago. She had no recent travel nor exposure to chemicals, fumes, organic or inorganic dusts or to other drugs associated with ILD. Her family history was positive for rheumatoid arthritis.

At presentation, her weight was 67.5 kg, heart rate of 87 beats/minute, blood pressure 133/71 mmHg, respiratory rate 18 per minute, and oxygen saturation of 96% on room air at rest and 93% on exertion. Chest examination revealed coarse inspiratory crackles at the bases bilaterally, with no wheezes or squeaks. There was no clubbing, and the remainder of the physical exam was unremarkable.

Blood work showed normal hemoglobin (14.5 g/dl), platelets (261,000/ μ l), white blood cell count (6,600/ μ l) and differential. ESR was high (72 mm/h) and CRP mildly elevated (5.5 mg/L). Her rheumatoid factor, anti-cyclic citrullinated peptide antibodies and antineutrophil cytoplasmic antibodies were negative. She had an antinuclear antibody of 1:160 titre by indirect immunofluorescence on Hep2 cells, positive anti-double stranded DNA (Crithidia luciliae lysate test), negative extractable nuclear antigen antibodies panel (Bioplex panel), normal complement (C3 and C4) levels, normal creatinine, and no proteinuria or hematuria. The patient had no skin rash, oral ulcerations, photosensitivity, alopecia, serositis, gottron's papules, mechanic hands or joint swellings as manifestations of a connective tissue disease, however, given the positive anti-double stranded DNA, she was assessed by Rheumatology who did not find evidence of connective tissue disease.

The CT (Computerized tomography) chest demonstrated emphysema as well as bilateral ground-glass opacities, several of them with the atoll sign (Figure 1).

The nature and temporal relationship of the patient's symptoms after initiation of nitrofurantoin as well as the classic appearance of the CT suggested OP secondary to nitrofurantoin. This was further supported by a score of 6 in the Naranjo probability scale of drug reaction [6]. Given the pa-

tient's stability, age, and the high pre-test probability for the diagnosis, we did not pursue a lung biopsy. She was instructed to discontinue nitrofurantoin and no steroids or immunosuppressants were prescribed.

Upon reassessment 3 months later, her symptoms had entirely resolved, and a repeat CT showed almost complete resolution of the ground-glass opacities (Figure 2).

Discussion

This novel report highlights a patient in whom the clinical presentation and chest CT findings consistent with OP resolved completely by discontinuing the triggering agent without requiring systemic corticosteroids. The diagnosis of OP can be difficult when patients present with non-specific symptoms [5]. However, nitrofurantoin associated OP typically has more constitutional symptoms [4, 7]. CT chest can support the diagnosis with findings such as focal consolidations, or bilateral, patchy infiltrates, classically subpleural or peribronchial. Atoll sign (also known as reversed halo sign) consistent of ground-glass opacities surrounded by a well demarcated, denser, crescent shaped opacity can also be seen in OP [8]. Atoll sign was initially considered to be pathognomonic for OP, although it is present in only 15 - 20% of cases; the differential has since been expanded to include other disease entities such as fungal and bacterial infections, as well as inflammatory conditions such as granulomatosis with polyangiitis.

The patient also had a positive dsDNA in association with positive ANA which is a specific for systemic lupus erythematosus; therefore, it was important to rule out a connective tissue disorder as a possible cause, specifically systemic lupus erythematosus. Rheumatology found no evidence of connec-

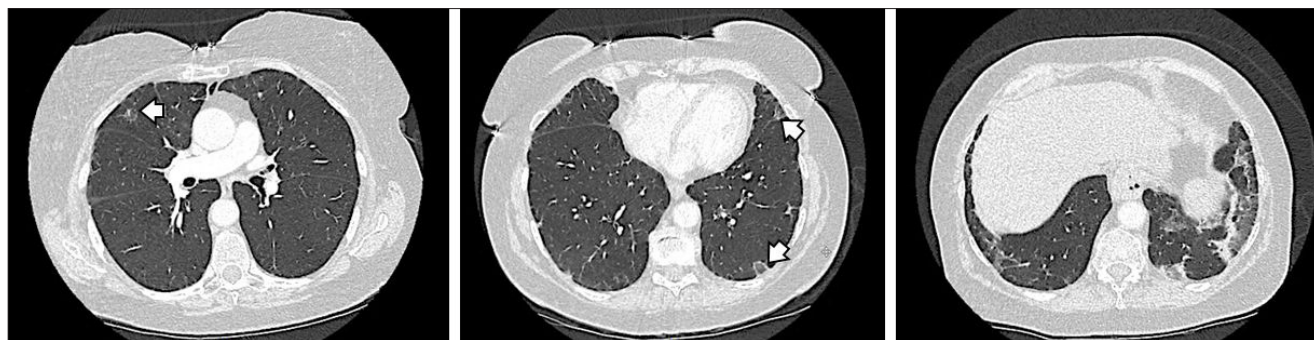


Figure 1: Initial CT chest demonstrating areas of bilateral ground-glass opacities, several surrounded by a denser rim "atoll sign" (arrows).

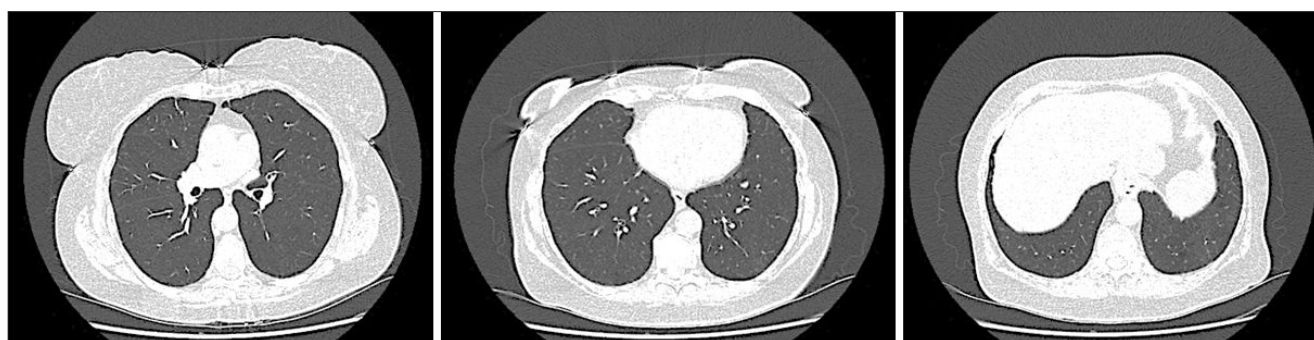


Figure 2: CT chest 3 months after discontinuation of nitrofurantoin shows near complete resolution of the ground-glass opacities.

tive tissue disease; thus, this likely represented a positive biomarker in normal population [9].

In summary, this novel case demonstrates a case in whom nitrofurantoin induced OP can be treated solely by stopping the medication and closely monitoring the patient. This approach may be appropriate in patients with no significant dyspnea or hypoxemia, but clinical judgement and discussion with the patient may be required. In cases of drug induced pulmonary disease, avoiding further use of the culprit drug is key; instead, using drugs not previously associated with lung disease (e.g., by consulting pneumotox.com) is advisable. Additionally, this highlights the fact that not all patients with mild disease and typical findings of OP on chest CT require transbronchial or surgical lung biopsies to confirm a diagnosis; this can spare patients from the morbidity and mortality associated to invasive procedures. This approach is particularly relevant in the management of nitrofurantoin induced OP in older patients with multiple comorbidities, who may require nitrofurantoin prophylaxis for recurrent urinary tract infections and in whom the risks of lung biopsies and the side effects of corticosteroids may have significant consequences.

Acknowledgements

None.

Conflict of Interest

The authors have no conflicts of interest to declare.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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