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CASE REPORT

Case Report: Nitrofurantoin-induced interstitial lung disease

[version 1; peer review: 1 approved, 1 not approved]

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Abstract

Nitrofurantoin is widely used for urinary tract infection (UTI) prophylaxis. Long-term use is known to be able to cause serious adverse effects including pulmonary and hepatic toxicity. The prevalence of nitrofurantoin-induced pulmonary injury is on the increase again as the drug regains popularity as a urinary antiseptic. We describe a previously healthy 83-year-old woman who presented to our emergency department in early 2012 with progressive dyspnoea since two weeks. This was not preceded by cough. She had no fever, wheezing, chest pain, or sputum production. She was a 50 pack per year ex-smoker. She had no previous exposure to tuberculosis or industrial chemicals. However, she suffered from recurrent symptomatic UTIs and was on a long-term prescription of nitrofurantoin for prophylaxis.

Respiratory examination revealed dullness on percussion at both lung bases and widespread fine inspiratory crackles throughout both lungs. Arterial blood gas analysis showed hypoxia and complete compensation of respiratory acidosis.

Initial treatment with co-amoxiclavulanic acid was initiated. CT scanning of the chest showed widespread ground-glass appearance in both lungs with organising pneumonia. A diagnosis of nitrofurantoin-induced interstitial lung disease (NIILD) was suspected. Nitrofurantoin was subsequently stopped and prednisone treatment at 30 mg OD was initiated. Follow-up chest X-ray showed marked improvement.

Keywords

Nitrofurantoin , urinary tract infection , pulmonary injury
 nitrofurantoin-induced interstitial lung disease , NIILD

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Any reports and responses or comments on the article can be found at the end of the article.

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Case report

A previously healthy 83-year-old Caucasian woman presented with progressive dyspnoea. She was a 50 pack per year ex-smoker. She suffered from recurrent symptomatic urinary tract infections (UTIs) and was prescribed long-term nitrofurantoin 50 mg daily for prophylaxis by her GP.

On examination she appeared dyspnoeic. She was afebrile and normotensive with respiratory rate of 31 per minute and oxygen saturation was 91% while receiving supplementary oxygen at a flow of 5 liter per minute. Respiratory examination revealed fine inspiratory crackles throughout both lungs. Arterial blood gas showed hypoxia with PaO₂ 5.4 kPa (without oxygen supplementation), PaO₂ 8.3 kPa (with 5 liter/min oxygen supplementation) and complete compensation of respiratory acidosis with pH 7.37, and PaCO₂ 6.9 kPa on 5 liter oxygen supplementation with base excess 2.9 mmol/l [Figure 1]. Laboratory findings showed increased leucocytes and C-reactive protein level [Figure 2]. Auto-immune laboratory findings including the antinuclear antibody and rheumatoid factor tests were negative. Chest X-ray revealed diffuse bilateral interstitial infiltrates [Figure 3]. CT scanning of the chest showed widespread ground-glass appearance with organizing pneumonia [Figure 4]. Initial treatment with co-amoxiclavulanic acid was started at a dose of 1.2 gram 4 times daily.

Figure 1. The course of FiO₂/PaO₂ (y axis) during admission days (x axis).

Figure 2. The course of C-reactive protein (CRP)/leucocytes (y axis) during admission days (x axis).

Figure 3. Chest X-ray on admission showed diffuse bilateral interstitial infiltrates on both sides.

Figure 4. High-resolution computed tomography (HRCT) on admission showed widespread ground-glass appearance with organizing pneumonia.

Course

Nitrofurantoin was subsequently stopped and prednisolone treatment at 30 mg OD was initiated. She had a short hospital course of 12 days and was finally discharged without long term oxygen treatment. Follow up chest X-ray before discharge and after withdrawal of nitrofurantoin (Figure 5) showed marked improvement compared to the X-ray upon admission.

The patient was seen after two months during outpatient control; her symptoms had improved dramatically and a follow-up chest X-ray showed further normalization.

Discussion

The differential diagnosis of nitrofurantoin induced interstitial lung disease (NIILD) includes pulmonary edema, cryptogenic organizing pneumonia and idiopathic interstitial pneumonias¹. The

Figure 5. Chest X-ray before discharge and after nitrofurantoin withdrawal.

auto-immune markers tested, antinuclear antibody and rheumatoid factor, were negative indicating a reaction to nitrofurantoin rather than an underlying systemic pathology.

Prompt resolution following the discontinuation of nitrofurantoin further supports the diagnosis^{2,3}. The diagnosis is based on the history of nitrofurantoin use and the absence of another explanation for the patient's symptoms and radiographic abnormalities.

Discontinuation of nitrofurantoin results in the regression of symptoms and radiographic abnormalities³. Systemic corticosteroids

are occasionally administered and it remains unclear how much corticosteroids contribute to improvement beyond drug cessation alone⁴.

Conclusion

Long-term use of nitrofurantoin as prophylaxis for UTIs can cause serious pulmonary side effects. Our patient received antibiotics and corticosteroids because of diagnostic uncertainty. This may represent frequent clinical practice, however there are no specific symptoms to separate NIILD from other interstitial lung diseases¹.

Informed consent

Written informed consent for publication of clinical details and clinical images was obtained from the next of kin.

Author contributions

Suhail Basunaid: data collection, drafting and revising the manuscript for intellectual content. Pilate Helena: clinician assessing and looking after the patient. Schoutteten Melanie: clinician assessing and looking after the patient. Sprooten Rooy: the chief clinician looking after the ward.

Competing interests

No competing interests were disclosed.

Grant information

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At the completion of this case study, I am very thankful for Dr. Rohde Gernot's help, and without his support this case study would have never come into its present form.

References

1. Camus P, Fanton A, Bonniaud P, *et al.*: **Interstitial lung disease induced by drugs and radiation.** *Respiration*. 2004; **71**(4): 301–26.
[PubMed Abstract](#) | [Publisher Full Text](#)
2. Mendez JL, Nadrous HF, Hartman TE, *et al.*: **Chronic nitrofurantoin-induced lung disease.** *Mayo Clin Proc*. 2005; **80**(10): 1298–302.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Peall AF, Hodges A: **Concomitant pulmonary and hepatic toxicity secondary to nitrofurantoin: a case report.** *J Med Case Rep*. 2007; **1**: 59.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Sheehan RE, Wells AU, Milne DG, *et al.*: **Nitrofurantoin-induced lung disease: two cases demonstrating resolution of apparently irreversible CT abnormalities.** *J Comput Assist Tomogr*. 2000; **24**(2): 259–61.
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A case of drug-induced ILD after Nitrofurantoin Treatment due to recurrent UTIs is presented. Although there are some questions left (DD pulmonary infection, documentation on the CT scan shown) the report seems plausible. This is an important topic since NF use is increasing due to changes in international recommendations regarding antimicrobial treatment of UTIs (restriction of other antibiotic classes such as Co-trimoxazole and quinolones). I would however, recommend in comparable cases to perform a BAL for excluding infection and confirming the aetiology by a BAL cytology compatible with drug induced ILD (typically mixed pattern with lymphocytosis, eosinophilia and some PMN).

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 April 2015

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The authors describe a case of Nitrofurantoin-induced interstitial lung disease. However a lot of important data are missing from this review.

1. The authors do not report the duration of nitrofurantoin therapy. This is of utmost importance as there are 3 types of reactions regarding nitrofurantoin related lung toxicity: acute, subacute and chronic. Determining the type of reaction is critical as this is associated with the clinical features of the patient, the radiographic findings and the time needed for their resolution after nitrofurantoin withdrawal.
2. The authors report: "CT scanning of the chest showed widespread ground-glass appearance in both lungs with organising pneumonia".

First, in the CT image provided (figure 4) is of poor quality and the prominent pattern is not that of ground glass opacities (GGO). Second, organizing pneumonia is a histology pattern. No radiology pattern is conclusive of organizing pneumonia. It is important not to confuse histology with radiology patterns.

3. There are two CXR presented in the article, on admission and at discharge (figure 3 and 5). The second CXR shows marked (almost complete improvement). Given the fact that the patient received co-amoxiclav (1.2gr x 4 iv), a likely scenario is that of lower respiratory tract infection.
4. The patient presented with hypercarbia. In the chronic form of nitrofurantoin related lung toxicity there is usually underlying fibrosis. This leads to a rapid shallow pattern of breathing causing hypocarbia and not hypercarbia. The history of smoking (50 pack years) in this context favors the possibility of lower respiratory tract infection.
5. No data are given regarding pulmonary function tests. Based on the above, a diagnosis of nitrofurantoin related lung toxicity cannot be robustly proven.
6. This case refers to a well known drug-induced ILD in patients taking nitrofurantoin. The first sentence into discussion is erroneous. ---COP is included in the idiopathic interstitial pneumonias! It should be termed as non cryptogenic if the cause is known...

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 17 May 2015

Suhail Basunaid, Mayo University Hospital,, Ireland

Thank you very much for the feedback regarding this case report.

1. Our patient had nitrofurantoin therapy several times for a recurrent UTI. The last one was longer than normal. I am not sure if this was mentioned in my abstract. I could

revise it and include this. For sure it was not a chronic use due the self-discontinuation by the patient every time her UTI was cured. The aim of this article was to raise awareness regarding lung toxicity due to some medications like nitrofurantoin.

2. I believe that the term organizing pneumonia could be also mentioned by radiologists in describing X-rays or CT-scans. I am familiar that this term is a pathologic finding but this was the description of our radiologist, together with associated GGO during the acute presentation. However this latter is usually not specific and could be seen in many differential diagnoses like superinfection, pulmonary edema and many others. I will try to find a better quality CT scan in my next revise, however I am sure that the case here has nothing to do with an organizing pneumonia due to the quick improvement and evidence of recurrent scenario after tapering of the steroids.
3. Unfortunately, I am not sure of your intended meaning here. In most cases as I said there is a superinfection and in most situations adding a broad spectrum antibiotic is a pragmatic issue. Or is the practice in your country different from here in the Netherlands?
4. As I said the case was not a chronic scenario, otherwise the patient would not have improved so quickly. Again the prognosis was very good and did not lead to fibrosis. I was not familiar with term hypercarbia, thank you for the added information.
5. Due to the quick response in the case and the fact that the patient was discharged within 1 week there was no pulmonary function test performed. This was done later during the follow up and was surprisingly good despite the fact that our patient is an ex-smoker.
6. Unfortunately, again, I am not sure of your intended meaning here. Are you trying to add some information, because I do not believe that this is a COP case, - the term drug induced ILD is a general term and might refer to the use of nitrofurantoin.

Competing Interests: I believe I disclose any competing interests that might influence my judgment of this article.

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