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Transient reverse ventilation-perfusion mismatch in acute pulmonary nitrofurantoin reaction

Tarık BAŞOĞLU,* Levent ERKAN,** Fevziye CANBAZ,* İrem BERNAY,* Tuncay ÖNEN,* Murathan ŞAHIN,* Funda FURTUN*** and Türkay YALIN****

*Departments of *Nuclear Medicine, **Pulmonology, ***Microbiology and ****Radiology, Ondokuz Mayıs University Hospital, Samsun, Turkey*

A 67-yr-old woman with a history of myocardial infarct was admitted to emergency for marked dyspnea, nonproductive cough, nausea and fever. The thorax X-ray revealed a bilateral alveolar and interstitial infiltration pattern with basal accentuation. The cardiac examinations were normal. Technegas ventilation and Tc-99m-macroaggregated albumin (MAA) perfusion scans were performed to rule out pulmonary embolism. Bilateral multiple ventilation defects with normal perfusion was observed. The patient had been taking nitrofurantoin for four days for a bladder infection. Hypersensitivity to nitrofurantoin was suspected and the drug was discontinued. An antihistaminic and anxiolytic medication was started. The majority of the clinical symptoms disappeared within 24 hours. The control chest X-rays disclosed a marked improvement. Ventilation and perfusion scans obtained 48 hours after nitrofurantoin withdrawal were normal. The drug-related pulmonary reactions should be taken into account in patients on medication. Reversible ventilation defects can be the only lung-scintigraphic finding encountered in acute pulmonary nitrofurantoin reaction.

Key words: acute pulmonary nitrofurantoin reaction, lung scintigraphy

INTRODUCTION

THE INCIDENCE of the acute pulmonary nitrofurantoin reaction (APNR) is once in every 5,000 first administrations and fibrosis in one of every 750 long-term users.[1] Typically, the acute reaction begins from several hours to 8 to 10 days after commencement of the therapy. It is manifested by the sudden onset of dyspnea, cough, fever, chills and malaise. Chest pain, often pleuritic in character, may be present. The patient is often hospitalized with a presumptive diagnosis of infectious pneumonia in the presence of bilateral pulmonary infiltrates, fever, and hypoxemia. Only a few deaths have occurred after the acute reaction.[2] Among the reported cases, a limited number of authors described lung scintigraphic findings in this disorder.[3-5] Perfusion and ventilation-perfusion defects have been reported. We report a case of acute pulmonary nitrofurantoin reaction with an abnormal ventilation and normal perfusion scan.

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For reprint contact: Tarık Başoğlu, M.D., Ondokuz Mayıs University Hospital, Department of Nuclear Medicine, 55139 Samsun, TURKEY.

CASE REPORT

A 67-yr-old female smoker (20 cigarettes/day for 30 yrs.) with a previous myocardial infarction (3 yrs. ago) was admitted to emergency for marked dyspnea, nonproductive cough, nausea and fever. Although she had no angina, the patient has first undergone a complete cardiac examination because of her infarction history, that was unremarkable. Chest auscultation disclosed a bilateral decrease in breath sounds. Left basal rales were present. Blood examinations detected peripheral eosinophilia (9.6%). The chest X-ray (Fig. 1A) revealed a bilateral alveolar and interstitial infiltration pattern with basal accentuation.

Technegas ventilation and perfusion scans with Tc 99m labeled macroaggregated albumin (MAA) were conducted approximately 12 hours after the onset of

symptoms to rule out pulmonary embolism. For the preparation of Technegas, a 370 MBq Tc-99m loaded graphite crucible was heated to 2,700°C in an atmosphere of 100% argon. After gas delivery to the patient 200,000 cnts. images were obtained in conventional projections. The perfusion study was performed with 111 MBq of Tc-99m-MAA with 400,000 cnts. images. In the left lung, ventilation defects were detected in the superior and lateral basal segments of the lower lobe, as well as in the superior and inferior lingular segments of the upper lobe. In the right lung, there were ventilation abnormalities in the posterior basal and lateral basal segments of the lower lobe, as well as lateral segments of the upper lobe. No perfusion defects were observed (Fig. 2). A possible broncho-spastic reaction was suspected. During a second questionnaire, the patient remembered that she had been taking nitrofurantoin (On the advice of one of her friends without medical prescription) for her bladder infection for four days. Acute nitrofurantoin reaction was highly suspected. After the immediate withdrawal of the drug, the patient began an antihistaminic and an anxiolytic medication. Almost all clinical symptoms disappeared within 24 hours. The control chest X-rays disclosed a marked improvement (Fig. 1B, C). Ventilation and perfusion (Fig. 3) scans obtained 48 hours after nitrofurantoin withdrawal were normal.

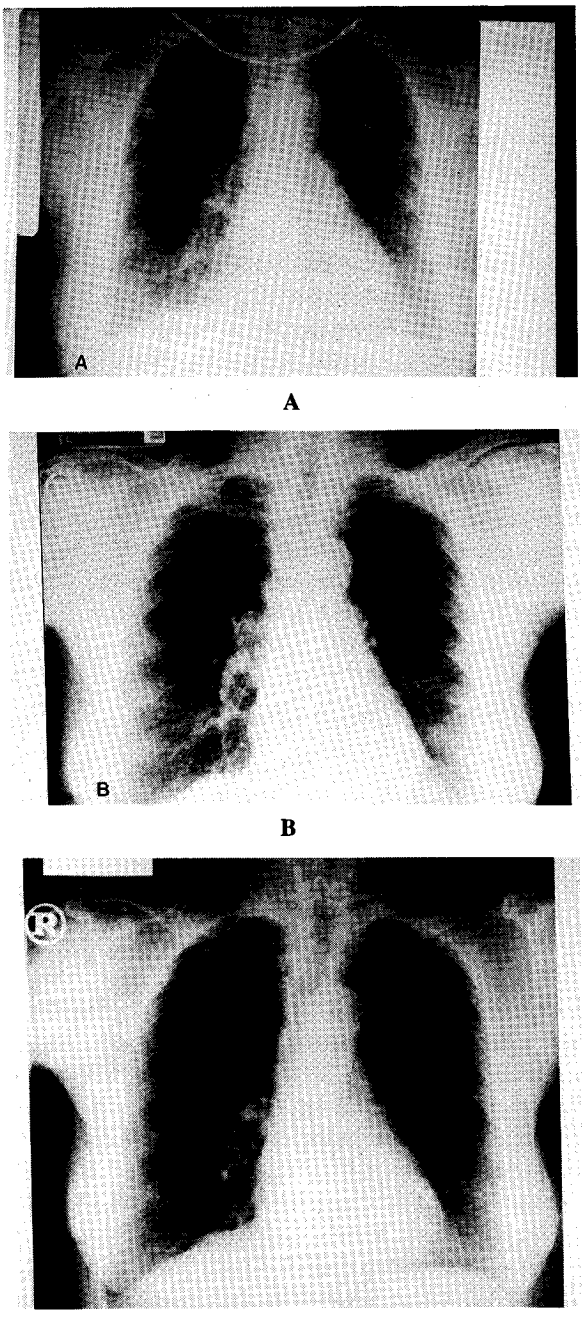

Fig. 1 Initial chest x-ray showing a diffuse alveolar and interstitial infiltration pattern with basal accentuation (A). Chest x-rays 24 hours (B) and 6 Days (C) after drug withdrawal showing marked improvement.

DISCUSSION

Nitrofurantoin is an antimicrobial drug with a widespread use and has been associated with numerous reactions such as skin rashes, acute and chronic lung reactions, hepatitis, neuropathy and hemolytic anemia. In acute cases, immediate drug discontinuation with or without adjacent anti-inflammatory medication is generally sufficient for full patient recovery.[6] There are only a few lung-scan descriptions of this relatively rare disorder.[3–5] Crook et al.[7] have reported gallium uptake in a patient with nitrofurantoin hypersensitivity. Norman et al.[5] have published for the first time ventilation and perfusion images in APNR. These authors have demonstrated significant alterations both in ventilation and perfusion studies. In our case, we could demonstrate abnormal ventilation with a normal perfusion pattern. In nitrofurantoin lung reaction, interstitial and alveolar mononuclear and polymorphonuclear infiltration with varying degrees of eosinophilia were described on lung biopsies.[8] Granuloma formation, sometimes with an appearance resembling allergic alveolitis also has been reported.[9] A predominant alveolar alteration with significant ventilation deterioration was presumably responsible for the acute respiratory symptoms and abnormal ventilation lung scan in our patient. Although no report describing primary vascular effects such as vasculitis in nitrofurantoin reaction could be found in the literature, abnormal perfusion lung scan findings have been described.[5] One acceptable explanation for the disturbed perfusion is, that the vascular structures are affected of by edema and interstitial infiltration.

It is possible that this presumed type of perfusion alteration depends on the stage and/or intensity of the allergic reaction. Relatively rapid lung scanning after the onset of symptoms in our patient could have been the reason for the normal perfusion findings despite significantly disturbed ventilation. Rule-out lung scans for pul-

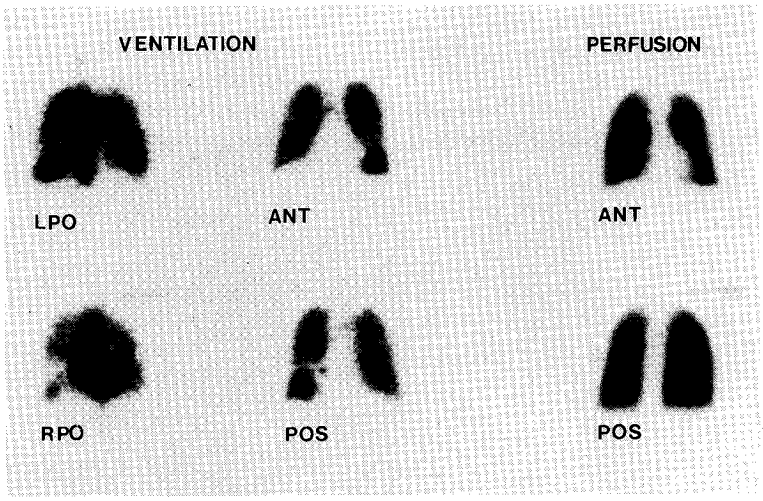

Fig. 2 Initial Technegas ventilation images with multiple defects in both lungs and normal Tc-99m-MAA perfusion images.

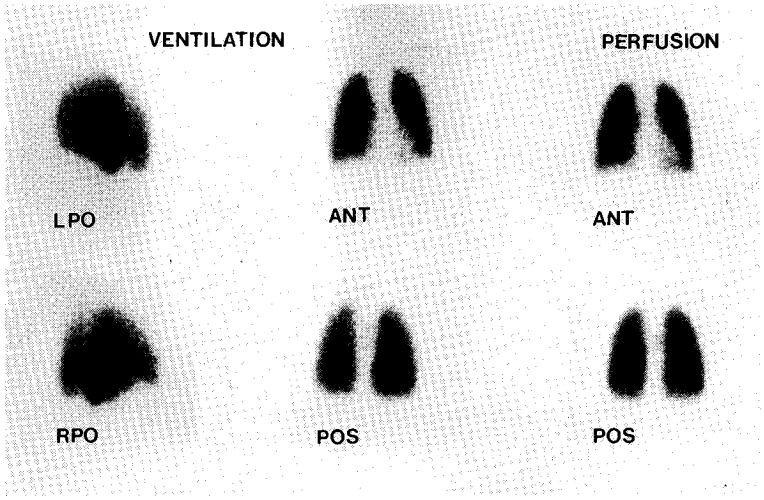

Fig. 3 Normal Technegas ventilation and Tc-99m-MAA perfusion images 48 hours after nitrofurantoin withdrawal.

monary embolism (PE) in patients presenting with acute respiratory symptoms are frequently performed. Physicians of the departments performing "first perfusion/ventilation if necessary" protocols would answer negative for PE but also would be incapable of detecting such anomalies. In the presence of an incomplete medical history or insufficient patient cooperation, routine Ventilation/Perfusion lung scanning beginning with the ventilation study can even contribute to the final diagnosis, as it did to some degree in our case. It should be kept in mind that ventilation defects can be the only lung-scintigraphic finding encountered in acute pulmonary nitrofurantoin reaction. This finding may also be reduced to the spectrum of so-called "reverse ventilation-perfusion mismatch" in radionuclide lung imaging.

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