

PULMONARY HYPERSENSITIVITY TO NITROFURANTOIN

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SYNOPSIS

“Acute, transient, non-cardiac pulmonary oedema” is a new form of drug allergy recently described. A case of such an allergy to nitrofurantoin is reported. The clinical features closely simulated that of cardiac asthma with dyspnoea, tachy-cardia and basal crepitations in the lungs dominating the clinical picture. In view of the benign nature of this condition and the seriousness of the differential diagnoses, it is crucial to be aware of this new entity to avoid instituting unnecessary treatment in this transient and non-fatal condition albeit an alarming clinical presentation.

INTRODUCTION

The induction of pulmonary sensitivity reactions by nitrofurantoin was first described by H.L. Israel and P. Diamond in 1962. Since then some twenty four cases of pulmonary reactions to nitrofurantoin have been described. The purpose of this paper is to report another case of this rare complication in which the clinical presentation was similar to cardiac asthma.

CASE HISTORY

T. C. K., a 68 year old Chinese male was treated by a surgeon for urinary tract infection with nitrofurantoin. About four to five hours after taking the drug, the patient developed severe breathlessness and was admitted to hospital the same day. He had no past history of bronchial asthma or paroxysmal nocturnal dyspnoea but he had a similar attack of breathlessness one year ago after apparently taking the same drug.

On admission, the patient was dyspnoeic with a respiratory rate of 30 per minute. His blood pressure was 170/90 mm. Hg. and his pulse rate, 100 min. Crepitations and rhonchi were heard on auscultation of the lungs. There were no signs of cardiac failure. He was afebrile but his temperature rose to 100°F a few hours after admission.

An electro-cardiogram done immediately after admission did not show any significant changes.

The patient was treated with intravenous aminophylline and his dyspnoea was immediately relieved. He made satisfactory progress during the next five days and his lung signs cleared up.

It was then decided to do a provocative test with nitrofurantoin. He was given 100 mgms. of nitrofurantoin and observed at hourly intervals. At the time of administration of nitrofurantoin, the patient had occasional basal crepitations. One hour later, the crepitations were noted to have increased especially at the base of the left lung. After three hours, the crepitations were markedly increased.

Six hours after the drug was given, he began to complain of breathlessness and on auscultation of the lungs, crepitations and rhonchi were heard. He was given intravenous aminophylline with relief.

Two hours later, he developed rigors. On examination, he had a temperature of 99°F, a pulse rate of 120/min. and his blood pressure was 120/80. He had no skin rash and only a few crepitations were heard in the lungs. He was given intramuscular phenergen and his rigors subsided.

The chest X-ray taken after admission showed large volume lungs with cystic changes in both apices and was consistent with chronic pulmonary lung disease. The heart was not enlarged. A repeat chest X-ray done soon after the provocative test did not show any significant change.

On admission, he had a leucocytosis of 10,500 with a differential count of 91% polymorphonuclears, 5% lymphocytes, 1% monocytes and 3% eosinophils. An absolute eosinophil count done a few days later was 700/cu.mm. After the provocative test, his total white count was 7,400 with 74% polymorphonuclears, 8% lymphocytes, 2% monocytes and 16% eosinophils.

DISCUSSION

Immunological reactions involving the lung are well known. Bronchial asthma is a common example of a hypersensitivity reaction which affects the lung. It is thus not surprising that an allergic response to a drug may involve the lung as the primary site of the adverse reaction.

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Nicklaus (1968) has classified pulmonary reactions to systemically administered drugs into five main groups viz. anaphylactoid reactions, eosinophilic pneumonia, interstitial fibrosis, pulmonary calcification and finally, the pulmonary reaction to nitrofurantoin, aptly described by Nicklaus as an acute, febrile non-cardiac pulmonary oedema.

The precise mechanism of reaction of the latter is unknown but the clinical features suggest an immunological reaction to nitrofurantoin or its breakdown products.

Clinical features of Nitrofurantoin induced Pulmonary Oedema

The clinical picture is strikingly similar in all the reported cases. Symptoms develop after previous sensitization to the drug and the onset is acute, occurring within 30 to 60 minutes after taking the drug and the reaction reaching a peak in two to five hours. This was seen during the provocative test in the above patient.

It has also been noted by other authors (Robinson, 1964) that the interval between the drug administration and the development of symptoms shortens after each exposure and a history of an atopic tendency is often present.

The reaction manifests primarily as an acute onset of severe dyspnoea and cough with fever, chills, chest pain and skin rashes as associated symptoms. On examination, tachycardia and basal crepitations in the lungs are marked. In our patient, rhonchi was also heard. With such symptomatology, the picture of pulmonary oedema is closely simulated especially when the patient is in the elderly age group as well.

The chest X-ray may show diffuse pulmonary infiltrations, pleural effusion, increased bronchial markings or no change at all. The E.C.G. is often normal with sinus tachycardia but signs of a right heart strain have been described. Leucocytosis

and eosinophilis may be present. The latter often increase with each exposure to the drug and may be absent during the initial reaction to the drug. With the above features, the initial diagnosis made in the cases reported are varied and included asthma, pulmonary embolism, pneumonia, pulmonary oedema and myocardial infarction.

The clinical, radiological and haematological reactions are transient and disappears with the withdrawal of the drug. In view of the typical features, the reaction deserves the appropriate descriptive term of "acute transient non-cardiac pulmonary oedema".

Treatment is simple and required only the withdrawal and avoidance of the drug. In the acute stage, the attack has been aborted with adrenaline, antihistamine, steroids and aminophylline. The main problem is one of diagnosis. An awareness of this rare reaction to drugs is essential if one is to avoid invoking potentially dangerous and unnecessary treatment. Satter (1966) has suggested that such a drug reaction should form one of the differential diagnosis of pulmonary oedema especially when there is associated eosinophilia.

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