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Case report

Nitrofurantoin-induced acute respiratory distress syndrome during pregnancy: A case report

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Abstract Acute respiratory distress syndrome (ARDS) is a rarely seen complication with nitrfurantoin. We report improvement of a parturient who was admitted to our hospital's obstetrical unit with life threatening nitrofurantoin-induced acute respiratory failure. She had been taking nitrofurantoin for one week for urinary tract infection (UTI). Her chest radiography showed bilateral parenchymal infiltrates of the lung. The patient responded well to nitrofurantoin discontinuation and methylprednisolone infusion 1 mg/kg/day.

Nitrofurantoin-induced pulmonary complications occur in about 1:100,000 during course of the therapy [1]. These pulmonary adverse effects were first reported in 1962 [2]. In between 1966 and 1976, 447 cases had been reported from Sweden and several other reports thereafter [3–6].

1. Case report

A twenty three years old parturient at 33 weeks' gestation visited our hospital's obstetrical clinic complaining of right sided loin pain. Her routine urine analysis revealed leucocytes, so nitrofurantoin (a 100 mg capsule, twice per day) was prescribed for treatment of UTI. One week later, the patient was admitted to our intensive care unit with dyspnea, tachypnea, nonproductive cough, and low O_2 saturation (82%). Her antenatal care history was unremarkable. Her past medical history was free from previous history of recurrent miscarriage, thromboembolic disease, or deep venous thrombosis. She denied smoking and had not recently travelled or exposed to animals before. Her respiratory rate was 45 breath/min, blood pressure 90/60 mmHg, hear rate 118 beat/min with regular rhythm, and temperature 38 °C. Chest auscultation revealed only harsh vesicular breathing, equal air entry with bilateral pulmonary crackles, and normal heart sounds. Neck veins were not congested, and examination of abdomen and lower limbs was unremarkable. Initial arterial blood gas analysis revealed hypocapnea ($PaCo_2$ = 3.3 Kpa) and hypoxaemia (PaO_2 = 7.3 Kpa on O_2 mask 6 L/min), so that possibilities of pulmonary embolism was not excluded. A prophylactic dose unfractionated heparin (enoxaparin 40 mg s.c) was prescribed and patient was connected to noninvasive mechanical ventilation (CPAP of 10 cmH_2O with FIO_2 of 60%) to maintain $SO_2 \geqslant 90\%$. The patient was monitored by five-lead ECG, arterial line, central venous catheter, pulse oximeter, Flowtrac (Edwards lifesciences vigilio monitor, USA) connected to arte-

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rial line (for measurements of cardiac output, cardiac index, stoke volume, and systemic vascular resistance), urinary catheter, and continuous fetal monitoring with cardiotocography (CTG). Her ECG showed only sinus tachycardia. Lung video scan showed no probability of pulmonary embolism. Bed-side transthoracic echocardiography showed no pathological finding, LVEF = 50%, pulmonary artery systolic pressure of 20 mmHg and normal Rt. ventricle size. Her chest radiography showed bilateral parenchymal infiltrates of lung. Abdominal ultrasound was normal. A complete blood count revealed leukocytosis with eosinophilia (WBCs = 14,300/mm^3, eosinophil = 2860/mm^3), normal platelet count (PLT = 156,000/mm^3), and microcytic anemia (Hg = 9.8 gm/dl). Hepatic profile was within normal range except for high level of lactate dehydrogenase (256 IU/L). The rest of blood chemistry profile and cardiac markers were within normal range. Her urine analysis revealed proteinuria (+2). All cultures and sensitivities for blood, sputum, urine, and viral studies were negative. Based on clinical, radiographic and arterial blood gas findings, the patient was diagnosed as ARDS. A 48-h after admission, the patient showed no improvement which necessitates endotracheal intubation and mechanical ventilation using synchronized intermittent mandatory ventilation with low tidal volume (Vt = 6 ml/kg, RR = 12/min, PEEP = 10 cmH_2O, pressure support = 15 cmH_2O and FIO_2 = 60%). She was kept sedated on remifentanil 0.05–0.1 μg/kg/min and propofol = 50 mg/h infusions. Nitrofurantoin was discontinued and infusion of methylprednisolone 1 mg/kg/day was started. Enteral feeding was commenced within 24 h, with conservative fluid management strategy, with deep venous thrombosis prophylaxis. On day 10, her follow-up chest X-ray showed a marked resolution of previous infiltrates with successful weaning and extubation. Patient was discharged to the ward and delivered after 3 days a healthy boy by spontaneous vaginal delivery.

2. Discussion

Nitrofurantoin is commonly prescribed for prophylaxis and treatment of UTI. Nitrofurantoin adverse reactions include interstitial pulmonary disease, hepatic toxicity as well as peripheral neuropathy [7] and few reports described concomitant pulmonary reactions and hepatic toxicity [8–10]. Despite of the known pulmonary side effects of nitrofurantoin, this toxicity is rarely reported in pregnant patients [11]. Nitrofurantoin-induced pulmonary reactions may be presented in there types: acute, subacute, and chronic. Acute toxicity may develop within few days [4], subacute type may develop after one month, while chronic type may appear after 6 months or more. Acute presentation is characterized by fever, cough, dyspnea, rash, cyanosis, and chest pain [3,7]; meanwhile, chronic presentation is manifested with dyspnea, dry cough, and fatigue, but fever is uncommon [3]. Diagnosis is made by clinical suspension and exclusion of other causes of respiratory compromise. An increase in broncho-alveolar lavage fluid eosinophils is suggestive of drug induced toxicity. The exact mechanism of acute reactions is still undetermined [12]. The presence of peripheral blood eosinophilia in 83% of cases is highly suggestive of hypersensitivity reaction [1]. Nitrofurantoin-induced hepatotoxicity is postulated to be due a break down product of the drug being combined to an endogenous peptide; this complex is identified by class I-HLA antigen [13]. Although our case showed dramatic improvement after 10 days, prompt improvement within 24 h had been reported [14]. In fact, management of ARDS is extremely difficult when dealing with two lives: mother and fetus. CTG allowed safe monitoring of the fetus and sharing decision with obstetrician, and we decided to continue pregnancy unless fetal distress was documented. The fundamental strategy in treatment was drug discontinuation, supportive treatment, and corticosteroid therapy. In conclusion, although acute pulmonary reactions to nitrofurantoin are uncommon; life threatening respiratory failure may be encountered. Physician and obstetrician should be aware of this adverse reaction and its management.

Conflict of Interest

None declared

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