

Rare Case of Theophylline Toxicity due to Influenza A Infection in an Adult With Asthma

To the Editor:

Theophylline is less commonly used for the management of asthma these days because of the newer drugs with a better safety profile. Some patients continue to take theophylline and are hesitant to discontinue or switch it because of the good control of symptoms. The steady state serum concentration for theophylline ranges from 10 to 20 $\mu\text{g/mL}$ in patients treated for asthma.¹ Theophylline has a narrow clinical therapeutic index of 1–1.5.² Various drugs and disease conditions interfere with theophylline clearance and lead to toxicity. Here, we report a rare case of theophylline toxicity due to influenza A infection in an adult with asthma.

A 50-year-old woman with obesity, known to have hypertension, coronary artery disease, asthma, bipolar disorder, stable diastolic dysfunction, and 20 pack-years of smoking history, presented to the emergency

room with complaints of flu-like symptoms including nasal congestion, dry cough, myalgia, fatigue, fever, shortness of breath, and chest tightness for 2 days. Her home medication list included theophylline 200 mg PO twice daily (BID), furosemide 40 mg PO daily, gabapentin 200 mg PO BID, aripiprazole 5 mg PO daily, clopidogrel 75 mg PO daily, fluoxetine 40 mg PO daily, atorvastatin 40 mg PO daily, carvedilol 6.25 mg PO BID, and prazosin 2 mg PO daily. Her nasal swab tested positive for influenza A. Rest of the diagnostic workup was within normal limits. She was given IV fluids and was discharged on oseltamivir. She returned to the emergency room in 24 hours with symptoms of shortness of breath, chest pain, palpitations, headache, tremors, nausea, and vomiting. Her heart rate was 140/min and blood pressure was low. Her theophylline level was 32.1 $\mu\text{g/mL}$. She was started on IV fluids and theophylline was discontinued.

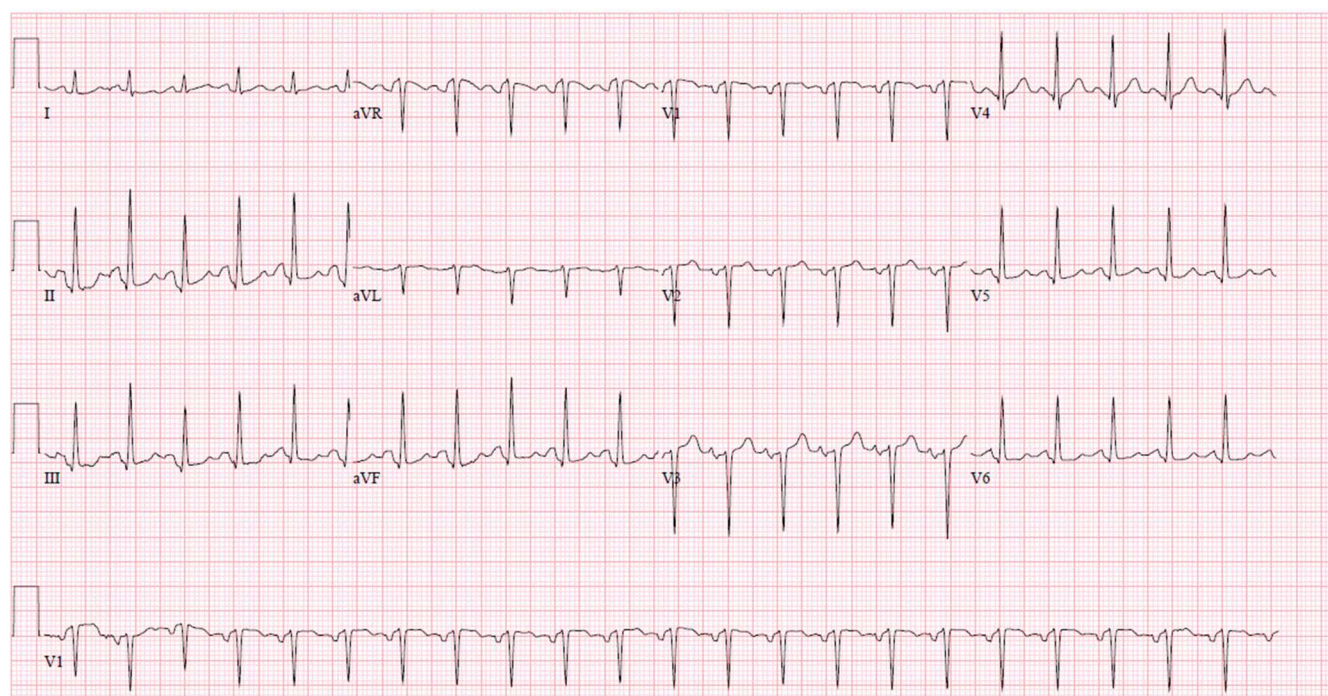


FIGURE 1. Electrocardiogram showing sinus tachycardia.



FIGURE 2. Chest X-ray showing mild hyperinflation consistent with asthma.

Serial checks of theophylline showed a drop until it became less than 2.5 $\mu\text{g}/\text{mL}$. The patient's symptoms resolved, and she was discharged on inhalers for asthma and theophylline was discontinued.

Theophylline clearance can be increased by smoking, phenobarbital, or xanthine-free diet. However, it can be decreased by cirrhosis, heart failure, and macrolides.³ Some studies in children with asthma have shown increased half-life of theophylline and decreased clearance with respiratory viral infections and even with influenza vaccination.⁴ Virus-induced interferon production leading to Cytochrome P inhibition has been proposed as the possible mechanism for this interaction.⁵ Here, we report a first case of theophylline toxicity (level above 30 $\mu\text{g}/\text{mL}$ with consistent signs and

symptoms) due to influenza A in an adult with asthma. Also, we conclude that patients on theophylline should be carefully monitored for toxicity during viral influenza infection, especially in the presence of suggestive signs and symptoms of toxicity (Figures 1, 2).

Zubair Khan, MD

Mohammad Saud Khan, MD

Department of Internal Medicine
University of Toledo Medical Center
Toledo, OH

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Informed consent was obtained from the legal representative of the patient included in the case report.

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