



CASE REPORT

# Serious Complex of Arrhythmias Post-Combinations of Clarithromycin and Theophylline with Marijuana Smoking in Underlying WPW Syndrome and Malignant Repolarization Pattern

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**Abstract**

**Rationale:** Drug-inducing adverse reactions are sometimes critical and fatal. Interactions of drug combinations are often an unexpected and unavoidable diagnostic challenge. Both clarithromycin and theophylline may have inevitable bad events. Recreational use of marijuana has reported serious cardiovascular adverse effects. Wolff-Parkinson-White (WPW) syndrome is a congenital cardiac preexcitation syndrome due to abnormal cardiac electrical conduction through an accessory pathway that can cause life-threatening arrhythmias. Discrimination of the benign form from the malignant one of early repolarization is a diagnostic cornerstone. Malignant early repolarization may be associated with cardiac arrest and idiopathic ventricular fibrillation. **Patient concerns:** A young-aged, single, student, Egyptian male, heavy smoker patient was admitted to the intensive care unit with complex serious arrhythmias post-combinations of clarithromycin and theophylline with marijuana cigarette smoking. **Diagnosis:** Complex serious arrhythmias post-combinations of clarithromycin and theophylline, with marijuana smoking in underlying WPW syndrome and malignant repolarization pattern. **Interventions:** Electrocardiography, chest, oxygenation, CT and echocardiography. **Outcomes:** A dramatic clinical and electrocardiographic improvement post-O<sub>2</sub> inhalation had happened. **Lessons:** Combinations of theophylline and clarithromycin with marijuana cigarette smoking may carry severe and dangerous arrhythmic insults. Right quick clinical and electrocardiographic diagnosis is sometimes decisive and pivotal. Drug dealing with diseases like Wolff-Parkinson-White syndrome and malignant repolarization patterns should be highly cautious.

**Keywords:** Wolff-Parkinson-White syndrome, Repolarization pattern, Arrhythmia, Left bundle branch block, Atrial fibrillation, Drug interaction, Theophylline, Clarithromycin, Marijuana

## Abbreviations

AF: Atrial fibrillation  
CBC: Complete blood count  
ECG: Electrocardiography  
ICU: Intensive care unit  
IV: Intravenous  
LBBB: Left bundle branch block  
O<sub>2</sub>: Oxygen  
SGOT: Serum glutamic-oxaloacetic transaminase  
SGPT: Serum glutamic-pyruvic transaminase  
SHD: Structural heart disease  
VR: Ventricular rate  
VT: Ventricular tachycardia  
WPW syndrome; Wolff-Parkinson-White syndrome

## Introduction

Drug interaction is a change in a drug's effect inside the body if the drug is taken together with another drug. The net effects of drug-drug interaction will decrease or increase the action of either or both drugs or cause adverse effects. An interaction between two or more drugs causes the total effect of the drugs to be greater than the sum of the individual effects of each drug. A synergistic effect can be beneficial or harmful [1]. Clarithromycin is a commonly prescribed macrolide antibiotic and alternative to penicillin in allergic states [2]. There is evidence association between clarithromycin use and cardiovascular outcomes [3]. Myocardial infarction (MI), QT prolongation, serious ventricular tachyarrhythmias (TdP, PVT, and MVT), stroke, and sudden cardiac death were reported with clarithromycin [2-4]. Theophylline is a methylxanthine derivative and is commonly prescribed for moderate to severe asthma [5]. Its usage has diminished dramatically over the last couple of decades due to its frequently adverse effects [6]. Theophylline intoxication is potentially life-threatening, mainly due to severe variable arrhythmias (such as sinus tachycardia, VT, AF, PVCs, PACs, and PSVT), QRS widening, QTc prolongation, hypotension, convulsions, cardiac arrest, and SCD [5-7]. The delta 9-tetrahydrocannabinol (THC), Cannabinoids (CB), and cannabidiol (CBD) are the three major active ingredients in marijuana (cannabis). CB is mainly responsible for the pathophysiological effects of cannabis [8]. The effects of these compounds are mediated through the endocannabinoid system via CB receptors which are widely spread throughout the body. Current evidence and case reports suggest a transient relationship between marijuana use with major cardiovascular events such as acute coronary syndromes (e.g. MI), arrhythmias (e.g. AF and VT), cardiomyopathies, stroke, vasculopathy, and cardiac arrest [8,9]. The impact of marijuana on high-risk cardiovascular outcomes is less understood [8]. Wolff-Parkinson-White (WPW) syndrome is a congenital cardiac preexcitation syndrome that can cause life-threatening arrhythmias due to the presence of an accessory pathway. Electrocardiographic (ECG) hallmarks of WPW syndrome are a short PR interval, wide QRS-complex, and delta wave [10]. Patients with WPW syndrome may develop tachyarrhythmia, chest pain, dyspnea, dizziness, syncope, and sudden cardiac death [10]. Catheter ablation is the preferable therapy in asymptomatic patients [10]. Medical therapy is

available for patients who are not a candidate for catheter or surgical ablation or who do not wish to pursue this therapies [10]. In 2015, ACC/AHA/HRS guidelines; flecainide, and propafenone are considered plausible for WPW syndrome without structural heart disease (SHD). But dofetilide and sotalolol are reasonable options for SHD [11]. Discrimination of the benign form from the malignant one of early repolarization is a diagnostic cornerstone [12]. Malignant early repolarization may be associated with cardiac arrest and idiopathic ventricular fibrillation [12].

## Case presentation

A 24-year-old single male Egyptian student, heavy smoker patient was presented to the intensive care unit (ICU) with palpitations, non-specific acute chest pain, and dizziness for about 4 hours. Peripheral paresthesia and circumoral numbness were associated symptoms. The chest physician recently prescribed a theophylline anhydrous tablet (300mg), clarithromycin tablet (250mg), and marijuana cigarette smoking (one cigarette). The above tablets were prescribed by a chest physician for upper respiratory infection in the outpatient clinic. Informed consent was taken. Upon general physical examination; generally, the patient was sweaty and distressed, with an irregular pulse rate (HR) of 140bpm, blood pressure (BP) of 140/80mmHg, respiratory rate (RR) of 23bpm, a temperature of 37°C, and pulse oximeter of oxygen (O<sub>2</sub>) saturation of 94%. He seemed thin and long. Tests for latent tetany were positive. Otherwise, with tachypnea, there are no reported local chest signs. There are no more relevant clinical data on the clinical examination. The patient was admitted to the ICU with multiple serious rhythms. All the above medications were stopped. The initial ECG was done on the initial presentation showing multiple transient runs of ventricular tachycardia (VT), partial WPW syndrome, malignant repolarization pattern, sporadic PVCs, and atrial fibro-flutter (of VR; 137) (**Figures 1A**). Initially, he was treated with O<sub>2</sub> inhalation (100%, by nasal cannula, 5L/min) for about 30 minutes. Serial ECG tracings were done. The second ECG tracing was done within 30 minutes of O<sub>2</sub> inhalation showing there is still evidence of WPW syndrome in I, aVL, and V4-6, T-wave inversion in aVL lead, and QRS fragmentation in aVF lead with evidence of LAD of NSR (of VR 94) (**Figures 1B**). The troponin test was negative (less than 0.01 ng/dl). The initial complete blood count (CBC) showed lymphocytosis (55.4%). SGPT, SGOT, serum albumen, serum creatinine, blood urea, CRP, RBS, plasma sodium, and serum potassium were within normal limits. Ionized calcium was slightly low (0.86mmol/L). ABG showed respiratory alkalosis. The initial complete blood count (CBC) within 12 hours of the initial CBC showed normalization of lymphocytes count (44.7%). Echocardiography was done on the same day of the ICU admission showing normal EF (71%), (**Figure 2A**). Chest CT was normal (**Figure 2B**). Complex serious arrhythmias post-combinations of theophylline and clarithromycin, with marijuana cigarette smoking in underlying WPW-syndrome and malignant repolarization pattern, was **the most probable diagnosis**. Within 24 hours of the above management, the patient finally showed nearly clinical and heart rate improvement. Otherwise, the O<sub>2</sub> inhalation, no more added therapies. The patient was discharged within 48 hours of admission and continues bisoprolol tablets



Figure 1: ECG tracing-1A & 1B

(5mg, OD) and calcium with vitamin D preparation for two weeks. Planning for future electrophysiological studies with catheter ablation and intracardiac defibrillator implantation was advised.

**Figure 1: ECG tracing-1A** was done on the initial presentation showing multiple runs of VT (lime and red arrows) with AF (light blue arrows) (of VR; 138). There are isolated PVCs (golden arrows), delta waves in V4-6 (dark blue arrows) with ST-segment elevation with J-point in II, III (golden arrows) I, AVL, and V4-6 leads (golden arrows). There are QRS fragmentation in III, and aVR leads (yellow arrows), T-wave inversion in III and aVF leads (pink arrows), saw-toothed appearance of atrial flutter in Lead II

(brown arrows), evidence of a normal axis (rose arrows), **ECG tracing 1B** was done within 30 minutes of O<sub>2</sub> inhalation showing

there is still evidence of WPW syndrome in I, aVL, and V4-6 (orange arrows), T-wave inversion in aVL lead (pink arrows) and QRS fragmentation in aVF lead (lime arrows) with evidence of LAD (green arrows) of NSR (of VR 94).

**Discussion**

**Overview:**

A young-aged, single, student, Egyptian male, heavy smoker patient was admitted to the ICU with complex serious

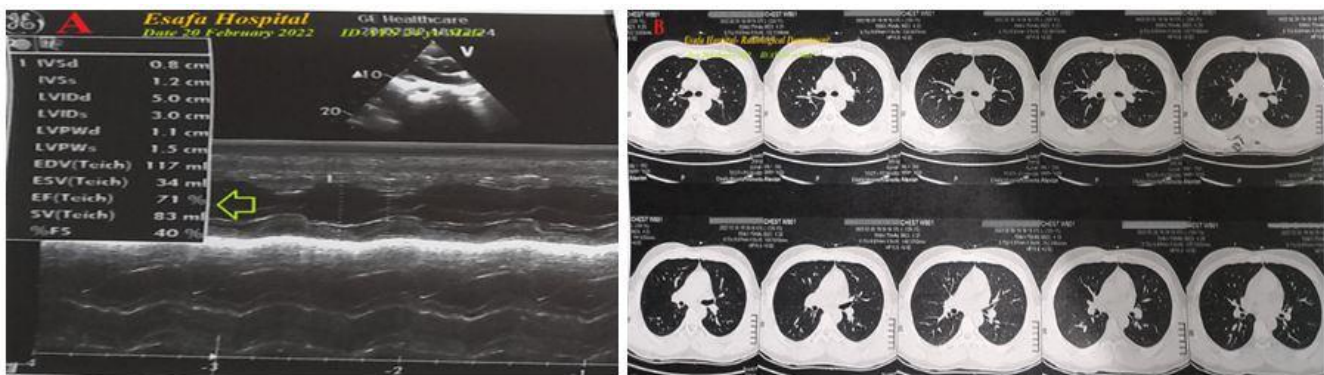


Figure 2: 2A. Echocardiography was done on the day of the ICU admission and showed no abnormalities detected with normal EF (71%) (lime arrows). 2B. Chest CT on the day of the ICU admission showed no abnormalities detected.

arrhythmias post-drug combinations of theophylline and clarithromycin with marijuana cigarette smoking.

**The primary objective** for my case study was the presence of multiple runs of VT, WPW syndrome, malignant repolarization pattern, sporadic PVCs, and atrial fibro-flutter in a patient who was admitted to the ICU.

- **The secondary objective** for my case study was the **question**; how did you manage the case?
- There was no history of cardiovascular and chest diseases.
- Undoubtedly, to a variable degree, all theophylline [5-7] and clarithromycin [2-4] with marijuana [8-9] are arrhythmogenic.
- The ECG evidence of multiple runs of VT, WPW syndrome, malignant repolarization pattern, sporadic PVCs, and atrial fibro-flutter on using combinations of theophylline, clarithromycin, and marijuana.
- Peak serum levels of theophylline can occur from 30 to 120 minutes for immediate-release formulations. Sustained-release formulations have peak levels between 6 and 10 hours [7]. Theophylline has a narrow therapeutic index with profound cardiotoxicity [6]. Toxic effects are often seen above 20 µg/mL plasma concentrations [6]. Toxic doses of theophylline can be as low as 7.5 mg/kg [7]. Toxic effects can be seen within therapeutic levels as well [7]. There may be a slight elevation of theophylline levels during concomitant clarithromycin administration [13]. Arrhythmias and hypotension are the most commonly reported cardiovascular side effects [5].
- The presence of multiple runs of VT, WPW syndrome, malignant repolarization pattern, and atrial fibro-flutter are indicators of the seriousness and the higher risk.
- The urgent cessation of the above predisposing drugs was the most important preventive step. The clinical and ECG dramatic response of the above serious rhythms strengthen the role of O<sub>2</sub> inhalation.
- Potentiating the drug interaction among the both drugs and marijuana is the net result.
- The still presence of WPW syndrome and malignant repolarization pattern post-O<sub>2</sub> inhalation indicates that these are the underlying rhythms.
- Using an implantable cardiac device and catheter ablation is a future suggested therapy.
- Wide-QRS complex tachycardia with LBBB or pre-excitation was the most probable ECG **differential diagnosis** for the current case study.
- I can't **compare** the current case with similar conditions. There are no similar or known cases with the same management for near comparison.
- The absence of follow-up for serum level of theophylline is the only limitation of the current case study.

## Conclusion and Recommendations

- Combinations of theophylline and clarithromycin with marijuana cigarette smoking may carry severe and dangerous arrhythmic insults.
- Right quick clinical and electrocardiographic diagnosis is sometimes decisive and pivotal.

- Drug dealing with diseases like Wolff-Parkinson-White syndrome and malignant repolarization patterns should be highly cautious.

## Conflicts of interest

There are no conflicts of interest.

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## References

1. BNF 78. Typical layout of a monograph and associated medicinal forms. September 2019 – March 2020, pp;xii. Pharmaceutical Press. ISBN: 978 0 85711 351 1.
2. Root AA, Wong AY, Ghebremichael-Weldeslassie Y, et al. Evaluation of the risk of cardiovascular events with clarithromycin using both propensity score and self-controlled study designs. *BJCP*. 2016 Aug;82(2):512-521. DOI: 10.1111/bcp.12983. PMID: 27090996; PMCID: PMC4972168.
3. Wong AY, Root A, Douglas IJ, Chui CS, Chan EW, Ghebremichael-Weldeslassie Y, et al. Cardiovascular outcomes associated with use of clarithromycin: population based study. *BMJ*. 2016 Jan 14;352:h6926. DOI: 10.1136/bmj.h6926. PMID: 26768836.
4. Lyer G, Caleb Alexander GC. Cardiovascular risks associated with clarithromycin, Editorials. *BMJ*. 2016;352:i23. DOI: <https://doi.org/10.1136/bmj.i23>
5. Greene SC, Halmer T, Carey JM, Rissmiller BJ, Musick MA. Theophylline toxicity: An old poisoning for a new generation of physicians. *Turk J Emerg Med*. 2018 Jan 5;18(1):37-39. doi: 10.1016/j.tjem.2017.12.006. PMID: 29942882; PMCID: PMC6009804.
6. Aggelopoulou E, Tzortzis S, Tsiourantani F, Agrios I, Lazaridis K. Atrial Fibrillation and Shock: Unmasking Theophylline Toxicity. *Med Princ Pract*. 2018;27(4):387-391. doi: 10.1159/000490145. Epub 2018 Jun 22. PMID: 29936503; PMCID: PMC6170900.
7. Journey JD, Bentley TP. Theophylline Toxicity. [Updated 2022 Jun 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK532962/>
8. Latif Z, Garg N. The Impact of Marijuana on the Cardiovascular System: A Review of the Most Common Cardiovascular Events Associated with Marijuana Use. *J Clin Med*. 2020 Jun 19;9(6):1925. doi: 10.3390/jcm9061925. PMID: 32575540; PMCID: PMC7355963.
9. Rezkalla S, Kloner RA. Cardiovascular effects of marijuana. *Trends Cardiovasc Med*. 2019 Oct;29(7):403-

407. doi: 10.1016/j.tcm.2018.11.004. Epub 2018 Nov 10. PMID: 30447899.
10. Chhabra L, Goyal A, Benham MD. Wolff Parkinson White Syndrome. [Updated 2021 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK554437/>
  11. Page RL, Joglar JA, Caldwell MA, Calkins H, Conti JB, Deal BJ, et al. Evidence Review Committee Chair. 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2016 Apr 5;133(14):e506-74. DOI: 10.1161/CIR.0000000000000311. Epub 2015 Sep 23. Erratum in: *Circulation*. 2016 Sep 13;134(11):e234-5. PMID: 26399663.
  12. Rosso R, Viskin S. Benign Versus Malignant Early Repolarization Patterns. In: El-Sherif, N. (eds) *Cardiac Repolarization*. Springer, Cham. 2020, pp 277–283. ISBN: 978-3-030-22671-8. DOI: [https://doi.org/10.1007/978-3-030-22672-5\\_16](https://doi.org/10.1007/978-3-030-22672-5_16).
  13. Wood M. The tolerance and toxicity of clarithromycin. *J Hosp Infect*. 1991;19: 39-46. Available from; [https://doi.org/10.1016/0195-6701\(91\)90216-U](https://doi.org/10.1016/0195-6701(91)90216-U)

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