CASE REPORT

# Polymorphic Ventricular Tachycardia (PMVT) Secondary to a Combination of Azithromycin and Fluoxetine in a Case of Acute Pancreatitis

**Ashish Gangasani[1], Kavitha R. Donthireddy[2]**

[1]Oakwood Hospital and Medical Center, Dearborn, Michigan Country, United States
[2]Department of Medicine, The Ohio State University, Columbus, Ohio

Corresponding author: Dr. Ashish Gangasani Email: agangasani@hotmail.com
Published: 01 February 2012
Ibnosina J Med BS 2012,4(1):28-31
Received: 03 February 2011
Accepted: 13 May 2011
This article is available from: http://www.ijmbs.org


**Abstract**
Polymorphic ventricular tachycardia (PMVT) is characterized by QRS complexes of changing amplitude that appear to twist around the isoelectric line. Torsades de Pointes (Tdp) is a variant of PMVT in which there is prolongation of QTc interval (generally exceeding 500 milliseconds). A number of medications have been noted to prolong the QTc interval. We describe a clinical case in which the culprits are Azithromycin and Fluoxetine. Azithromycin has been regarded as a "safer" macrolide when it comes to proarrhythmia as compared to erythromycin or clarithromycin. However, in certain clinical circumstances like combination drug usage, unique clinical features like underlying pancreatitis in this particular patient, some of the medications that are deemed low risk can certainly be more proarrhythmic. It is therefore important to review the clinical and pharmaceutical profiles of every patient before choosing which medications to prescribe.

**Key Words:** Polymorphic Ventricular Tachycardia, QTc interval, Azithromycin, Fluoxetine.

## Introduction

Polymorphic ventricular tachycardia (PMVT) is characterized by an ECG with QRS complexes of changing amplitude that appear to twist around the isoelectric line. Torsades de Pointes (Tdp) is a variant of PMVT in which there is prolongation of QTc interval (generally exceeding 500 milliseconds). A number of medications have been noted to prolong the QTc interval.

## Case Report

We report the case of a 51-year-old male admitted to the hospital with complaints of acute epigastric pain along with nausea and vomiting for one day. He reported consuming excessive amounts of alcohol prior to this admission. He had a past history of recurrent pancreatitis secondary to

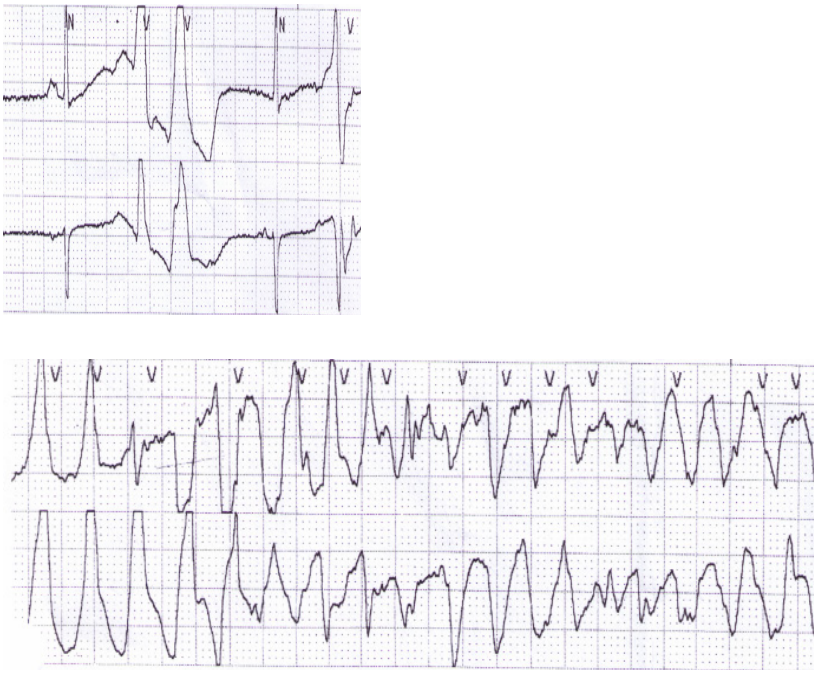

**Figure 1.** Two selected ECG tracings illustrating the prolonged QT interval along with multiform PVCs triggering PMVT

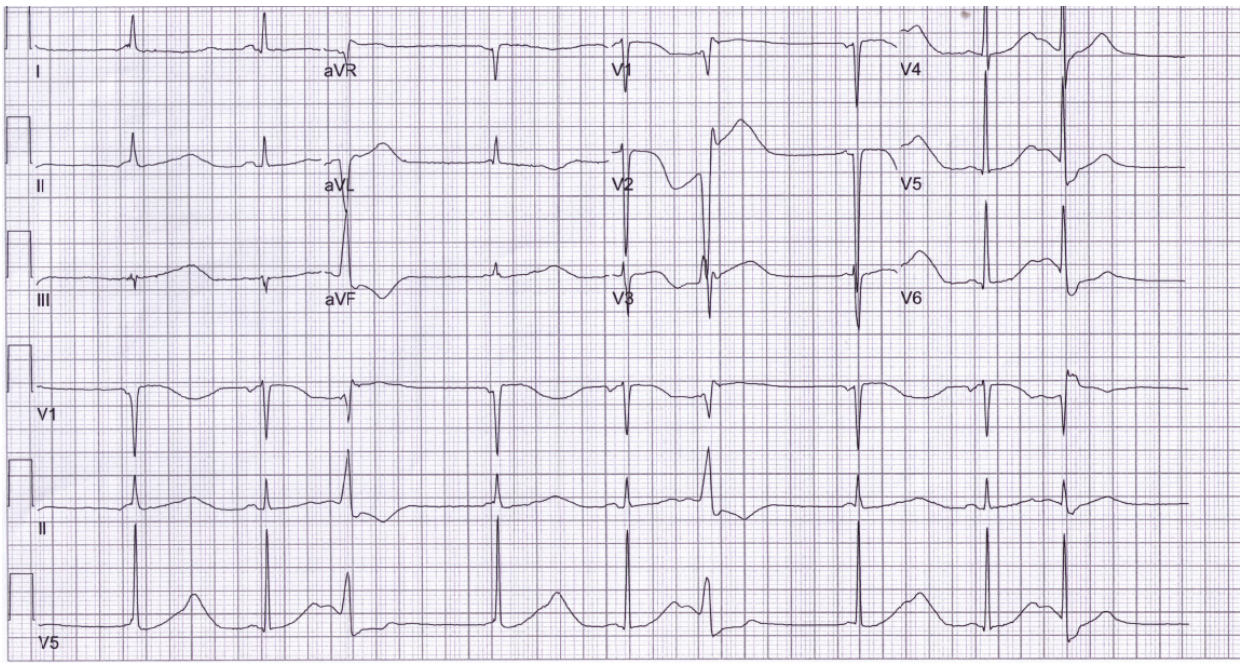


**Figure 2.** A 12 lead ECG showing extremely prolonged QT interval with PVCs

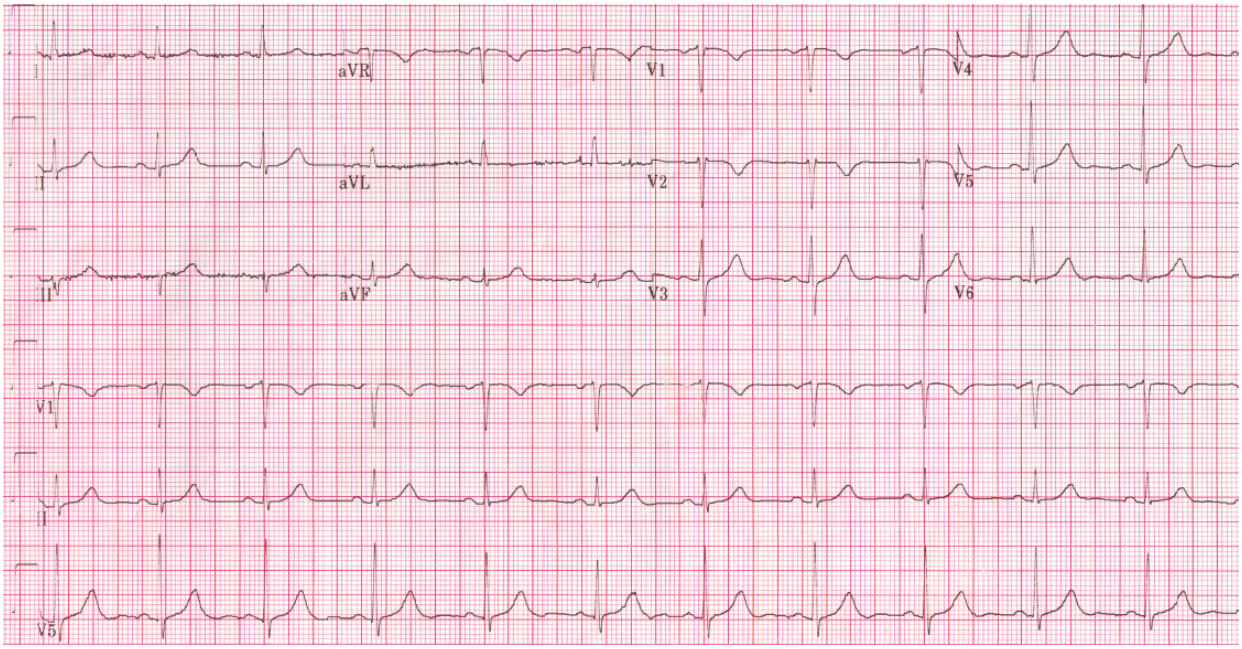


**Figure 3.** A 12 lead ECG showing complete normalization of QT interval after several days.

alcohol consumption. He also had a history of depression for which he was prescribed Fluoxetine. He was on no other medications at the time of the hospitalization. His family history was insignificant. Pertinent lab work at the time of admission demonstrated significant hypokalemia (serum potassium of 2.9 mmoles/L) and also mild hypomagnesemia (serum magnesium of 1.8 mg/dl) There was evidence of pancreatitis with modest elevation of serum amylase (312 U/L, normal being 28-100 U/L) and serum lipase (93 IU/L, normal being 22-53 IU/L). Liver function tests were normal. Total bilirubin was 1.1 mg/dl, ALT was 31 units/litre and AST was 24 units/L. His ECG at the time of admission showed sinus rhythm and a normal QTc interval. Fluoxetine at 20 mg QD was continued in the hospital. He was treated with IV fluids and his electrolytes were supplemented with near normalization within a couple of days. During the hospital stay, he developed fever and bronchitis for which he received intravenous Azithromycin (500 mg IV once daily). Two days later, he had an episode of polymorphic ventricular tachycardia secondary to excessive QT prolongation (up to 800 milliseconds) from which he was successfully resuscitated (Figure 2 ). At the time of his cardiac arrest, his serum electrolyte levels were within normal limits. Serum potassium was 4 millimoles /L, serum magnesium was 2 mg/dl, and serum calcium was 8.6 mg/dl. Thyroid function tests were also within normal limits. He had normal serum electrolytes for a couple of days before the arrest. He did not receive any other medications (like antipsychotics) that could have contributed to QTc prolongation. No non-pharmaceutical causes like grape juice could be implicated. He was sent for a cardiac catheterization that revealed normal left ventricular systolic function and his coronaries were normal. A 2-D echo did not reveal any left ventricular hypertrophy. His ECG showed no new onset bundle branch block pattern. Over the course of several days after this event, his QTc interval eventually normalized (Figure 3).

**Discussion**

Polymorphic ventricular tachycardia or Torsades de Pointes is usually preceded by prolongation of the QT interval. Usually the PMVT is preceded by a variable period of bigeminal rhythm and triggered by one or two premature ventricular beats coupled to the prolonged QT segment of the preceding basic beat. As is evident in Figure 1, it is not uncommon to have a trigeminal pattern preceding the onset of PMVT. After a review of the available literature, it is possible that the polymorphic ventricular tachycardia (PMVT) in this case could be the result of some of the medications he was taking at the time of the event. The likely culprits are Azithromycin and Fluoxetine. Pancreatitis and alcohol intake also contributed to the problem.

There have been case reports of both Fluoxetine- and

Azithromycin-induced PMVT in the past (1,2). Although to the best of our knowledge, there has not been a report of both the medications being administered when the clinical event occurred. Azithromycin belongs to the Macrolide class of antibiotics. The metabolism of Azithromycin has not been studied in patients with alcohol use. Biliary excretion as an unchanged drug is a major route of elimination in the normal population ( per package insert).

In experimental models, Azithromycin has shown prolongation of QT interval and monophasic action potential duration (3). However, unlike erythromycin and clarithromycin, which have the same effect, it did not result in a predisposition to early after-depolarizations and the triggering of TdP. This can explain the reduced tendency to develop TdP with Azithromycin. It may not, however, completely eliminate the possibility.

Most of the reported cases of PMVT secondary to prolonged QTc interval with Azithromycin involved the intravenous use of this drug in a hospital setting. It is unclear if oral use poses less of a predisposition. Certainly, cases in a hospital setting due to the dramatic presentation have a much higher visibility. The timing of PMVT after Azithromycin seems variable. Review of cases in the literature suggests a latency period anywhere from a few hours to several days.

There have been extremely rare reports of Fluoxetine-related TdP in the literature (2). Fluoxetine is metabolized by the Cytochrome P450 system in the liver. Alcohol intake and poor nutritional status can certainly compromise this and potentially exacerbate any of the rarer toxicities of Fluoxetine. There has also been at least one case report of TdP (4) in a case of acute pancreatitis. Transient ECG changes of T wave alterations, ST segment depressions, intraventricular conduction delays, and rarely QT prolongation have been reported in cases of acute pancreatitis. In a number of instances and certainly as depicted by this case, QT prolongation leading to TdP is multifactorial. Therefore, whenever possible, careful monitoring in high risk situations is advisable.

It is certainly good clinical practice to review and adjust the doses of medications to accommodate for any compromise in liver or renal function to minimize the potential fatal toxicity of QTc prolongation especially among those drugs that are proven to demonstrate this. This particular patient did not have serious biochemical compromise of his liver or renal function. However, a combination of medications, particularly in a patient who is predisposed, can have devastating consequences. The predisposition here can stem from multiple causes including the effect of pancreatitis on ECG, and rarely the QTc interval as detailed above. Another interesting possibility is the reduced repolarization reserve in this patient due to possible lower testosterone levels due to alcohol use (5). In this particular patient, it is important to avoid future use of the culprit medications. He has also been counseled to avoid alcohol consumption. There are a number of medications that can cause QTc prolongation (www.azcert.org ). It is usually possible to avoid medications that have a high tendency to cause QTc prolongation in any predisposed patient as long as careful consideration is given to the problem. A collaborative effort between physicians and pharmacists is important to identify such medications and potential drug interactions in predisposed patients.

**References**


1. Huang BH , Wu CH, Hsia CP, Yin Chen C. Azithromycin – Induced Torsade De Pointes, PACE. 2007;30:1579-82.
2. Wilting I , Smals OM, Holwerda NJ, Meyboom RH, De Bruin ML, Egberts TCG. QTc Prolongation and Torsade De Pointes in an elderly woman taking fluoxetine, American Journal of Psychiatry. 2006;163:325.
3. Milberg P, Eckardt L,Bruns H,Biertz J,Ramtin S, Reinsch N et al. Divergent proarrhythmic potential of macrolide antibiotics despite similar QT prolongation, JPET. 2002;303:218-25.
4. Mofrad PS, Rashid H, Tracy CM. New onset QT prolongation and TdP accompanied by Left Ventricular dysfunction secondary to acute pancreatitis. PACE. 2003;26:1765-8.
5. van Noord C, Dörr M, Sturkenboom MC, Straus SM, Reffelmann T, Felix SB, et al. The association of serum testosterone levels and ventricular repolarization. Eur J Epidemiol. 2010;25:21-8.