

INTRODUCTION

A subset of schizoaffective disorder is the bipolar type. Clozapine has shown efficacy in treating acute mania and in overall mood stabilisation¹. However, on rare occasions, the use of clozapine has been associated with cardiotoxicity.

CLINICAL CASE

A 31-year-old man known to have schizoaffective disorder, bipolar type and cannabis dependence was brought to our hospital by law enforcement because of delusional thoughts and aggressive behavior. He was admitted to our psychiatry floor due to psychotic relapse.

The patient was placed on clozapine 12.5mg orally twice daily. Clozapine was uptitrated by 12.5mg per dose every two days up to a maximum of 100mg twice daily on Day 10, which was maintained thereafter. On Day 16 he had a Tmax of 39.3C, associated with malaise, generalised myalgia and pleuritic-type chest pain. BP 106/50 mmHg, heart rate 113 beats per minute. Physical exam revealed a regular and rapid pulse, S1 and S2, without rubs, murmurs or gallops. No jugular venous distension. His lungs were clear to auscultation. He was transferred to the medical floor.

Blood culture revealed no growth. Influenza A and B antigens, Streptococcus Group A Antigen, SARS CoV-2, HIV antibody/antigen were all negative. CXR revealed no acute disease findings.

Due to the absence of EKG abnormalities and the troponin elevation being less than would be expected in the setting of myocarditis, a transthoracic echocardiogram was ordered. This revealed a decreased LV systolic function, and an EF of 45-45% without regional wall motion abnormalities.

DIAGNOSTIC WORKUP

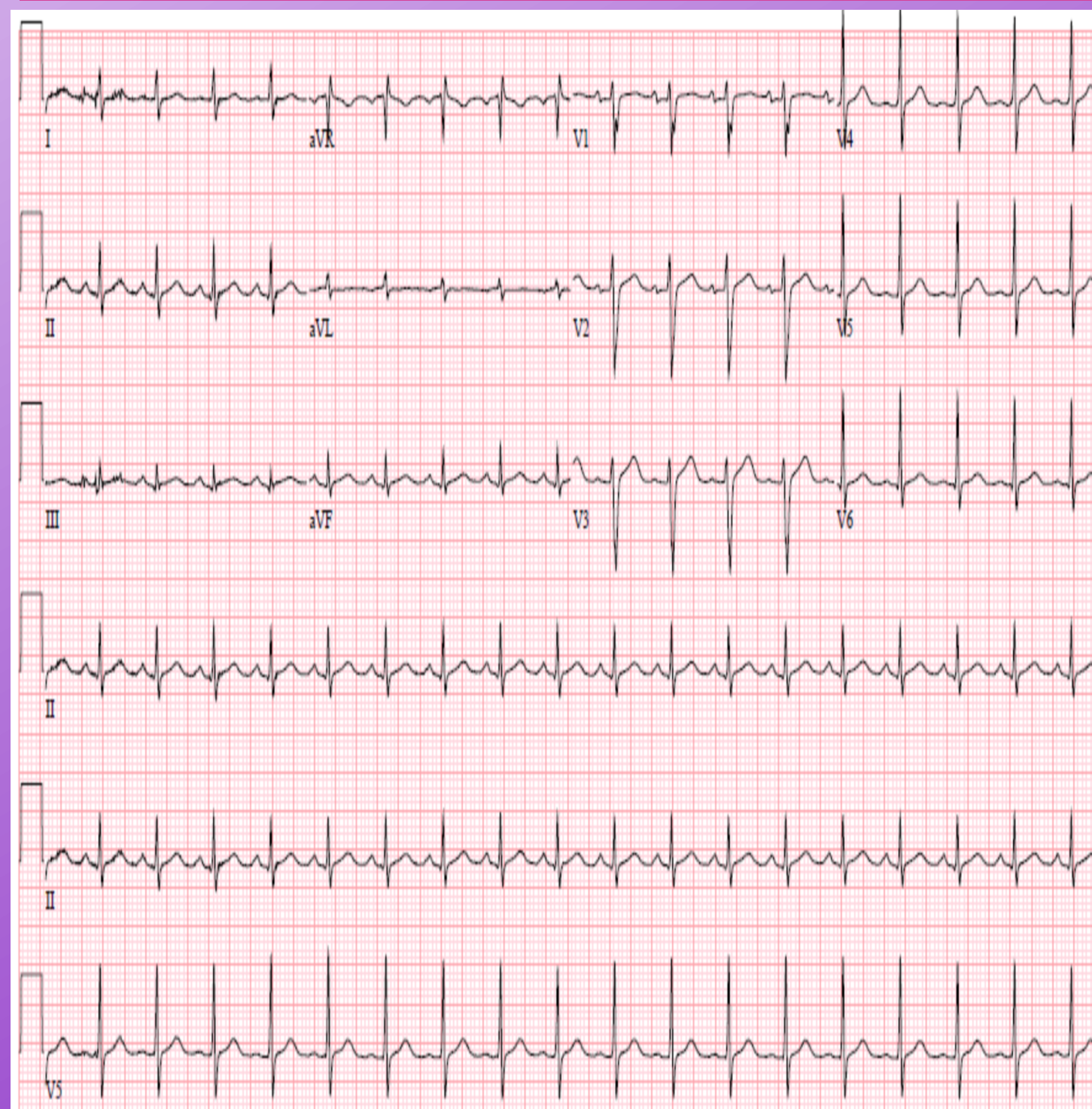


Figure 1. EKG showing sinus tachycardia without ischemic changes

Day of admission	Troponin (ng/mL)	WBC (Thou/uL)	CRP (mg/dL)
1		7.1	
16	0.19	10.5	10.5
18	0.12	8.3	9.0
19	0.07	6.5	5.4

Table 1. Biomarker trending

CLINICAL CASE

Given the absence of any signs of infection, suspicion was raised for clozapine-induced cardiotoxicity (cardiomyopathy/myocarditis). As such the last dose of clozapine 100mg was administered on the night of Day 15 of admission and he was switched to Lithium Carbonate 600mg orally twice daily. Concurrently, he was started on Metoprolol tartrate 12.5mg orally twice daily on Day 16 and monitored via continuous telemetry.

He subsequently became afebrile 36-48 hours after discontinuation of the clozapine. There was resolution of the chest pain, malaise and myalgias, without development of shortness of breath or lower leg swelling. He remained cardiovascularly stable and returned to the Psychiatry Floor for the remainder of his hospitalization.

DISCUSSION

- Clozapine ↑ serum catecholamines → ↑ myocardial oxygen demand both directly and indirectly via direct myocardial stimulation and ↑ cardiac afterload and ↓ myocardial oxygen perfusion. This ↑ serum catecholamines correlates with the degree of myocardial inflammation.
- In one study, the dose at the onset of symptoms and signs was between 50 mg/day and 600 mg/day while the median was 250 mg/day in the 53 cases where patient-specific data was available.² Our patient was on a maximum of 200mg/day at the time of symptom onset.
- Discontinuation of clozapine leads to cardiac functional recovery with a direct correlation in degree of compromised systolic function to degree of recovery. In our patient's case the degree of compromised systolic function was mild and as such we expect a complete recovery.
- The medication management benefits from psychiatry consultation to prevent relapse of an acute psychiatric episode.

TAKE HOME MESSAGE

Early clozapine-induced cardiotoxicity may not be florid myocarditis or cardiomyopathy with heart failure symptoms. Instead symptoms may be vague initially and withdrawal of the drug along with supportive care is crucial. Recognizing early features helps in reducing the associated cardiovascular morbidity and mortality.

REFERENCES

1. Patel RK, Moore AM, Piper S, et al. Clozapine and cardiotoxicity — a guide for psychiatrists written by cardiologists. *Psychiatry Res.* 2019;112491.
2. Bellissima BL, Tingle MD, Cicović A, Alawami M, Kenedi C. A systematic review of clozapine-induced myocarditis. *Int J Cardiol.* 2018 May 15;259:122-129. doi: 10.1016/j.ijcard.2017.12.102. Erratum in: *Int J Cardiol.* 2018 Apr 11;: PMID: 29579587.