Methadone Inducing Serotonin Syndrome and Torsade's de Pointes: A Case Report

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Introduction

Torsade's de Pointes is a polymorphic variation of ventricular tachycardia precipitated by prolonged Qtc. It is commonly seen with wave like alterations in the amplitude of the QRS complexes on an ECG[7]. Serotonin syndrome is a constellation of symptoms associated with elevated serotonin levels, including elevated temperatures, myoclonus/ hyperreflexia, encephalopathy, and diaphoresis [1,2]. Although different entities, both Torsade's de Pointes and Serotonin Syndrome are individually known and feared potential consequences of Methadone usage. We present a case of a 33-year-old female with a past medical history of polysubstance abuse on methadone and congenital prolonged Qtc who was found to have serotonin syndrome and ultimately developed Torsade's de pointes.

Clinical Presentation

- 33-year-old female; pmhx significant for supraventricular tachycardia, Congenital Long QT syndrome, Depression, and Intravenous drug use currently on methadone. Home medications: Gabapentin, Mirtazapine, Prazosin, Propranolol, Sertraline, and Topiramate.
- Patient was brought in by EMS after her partner called for concerns of a potential drug overdose at home. Patient received her last dose of methadone one day prior to admission, at a dose of 297 mg.

Emergency Department

Physical Exam: AAOx0; Encephalopathic, nonverbal, diaphoretic. Notable trismus. with rigidity of all her extremities. Patient tachycardic with no murmurs appreciated. Multiple wounds were present on bilateral upper and lower extremities, compartments soft.

UA	+ protein, 1+ glucose, 2+ blood, 1+ leukocyte esterase, with 7 WBC and 121 squamous epithelial cells and culture (+) for lactobacillus species
UDS	(+) Benzodiazepines, (+) Fentanyl, (+) Methadone
ECG	Prolonged Qtc 518
Labs	Elevated Creatinine kinase, hypophosphatemia, elevated lactate, slight increase in AST,ALT, Alk Phos

Patient was administered a total of 360 mg of ketamine, 2g of Magnesium, 8 mg of Versed, and 1 L Normal saline.

Admission

- Patient developed inducible clonus in all four extremities with recurrent episodes of rigidity. Patient was started on versed infusion with aggressive IV fluid administration
- Patient had non-sustained episode of Torsade's de pointes that resolved without intervention (Image 1). The following morning patient noted to have several more episodes (Image 2-4). Patient was given a total of 8 gm IV magnesium.
- Cardiology was consulted, and patient was started on Mexiletine. EPS was consulted, and recommended LIFEVEST until wounds have healed. If patient can abstain from further IV drug use, would consider pursuing subcutaneous ICD
- Patient left the hospital against medical advice due to withdrawal symptoms

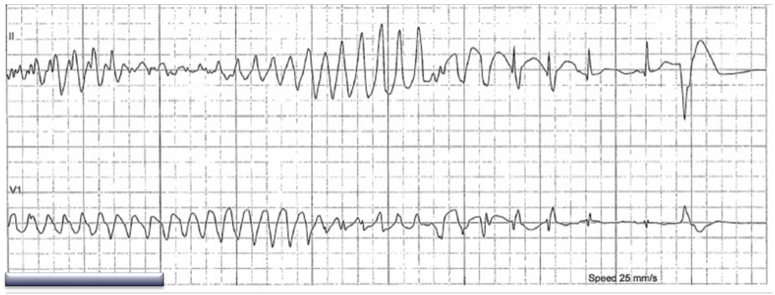

Image 1: October 12th, 21:15

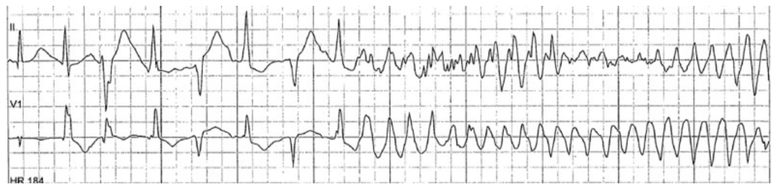

Image 2: October 13th, 7:10

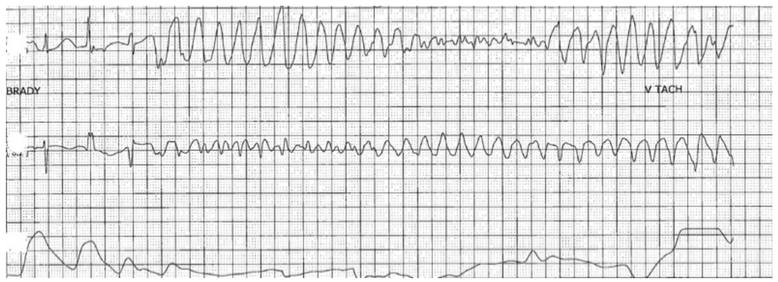

Image 3: October 13th, 10:57:48

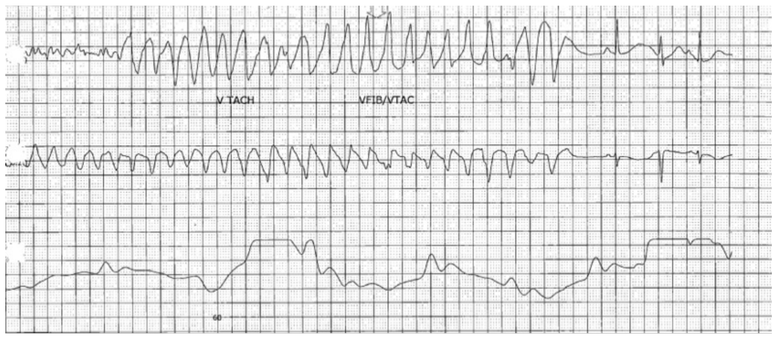

Image 4: October 13th, 10:57:54

Conclusion

Prior to patient leaving against medical advice, patient was continued on her home propranolol with instructions to continue to hold QTc prolongation agents. Due to patients current IV drug use with open wounds, patient was high risk for any invasive procedures which is why LIFEVEST was recommended for the time being.

Of note, after patient was treated with magnesium, patient had no further episodes of Torsade's de pointes while she was hospitalized. Patients home methadone was held during her entire hospitalization, as well as other Qtc prolonging agents.

Patient was encouraged to follow up with wound care, along with her primary care provider as well as EPS for further monitoring and management of her prolonged QTc, as well as for an alternative to her methadone treatment.

Discussion

Methadone has a black box warning for causing Qtc prolongation, as well as torsade's de pointes. This patient had known congenital prolonged Qtc and was on a high dose of maintenance methadone, which put her at risk for developing such complications [4,7].

With regards to serotonin syndrome, methadone inhibits SERT, resulting in an increase amount of serotonin available in the synaptic cleft as well as in the plasma[2]. This patient was concurrently taking a SSRI medication, sertraline, which not only can increase the amount of serum methadone ,but also increases the risk of developing a serotonin syndrome since sertraline also inhibits reuptake of serotonin [3,4].

This case is important because it highlights a high-risk patient who developed the feared complications of methadone. Although methadone has FDA warnings regarding torsade's de pointe's and Qtc prolongation, it remains important to continue to monitor patients as well as review other medications they are taking to try and avoid adverse effects.

While there are studies regarding the potential complications of methadone, there seems to be limited information regarding alternatives for other opioid use treatment options for patients at high risk for developing such feared complications.

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