

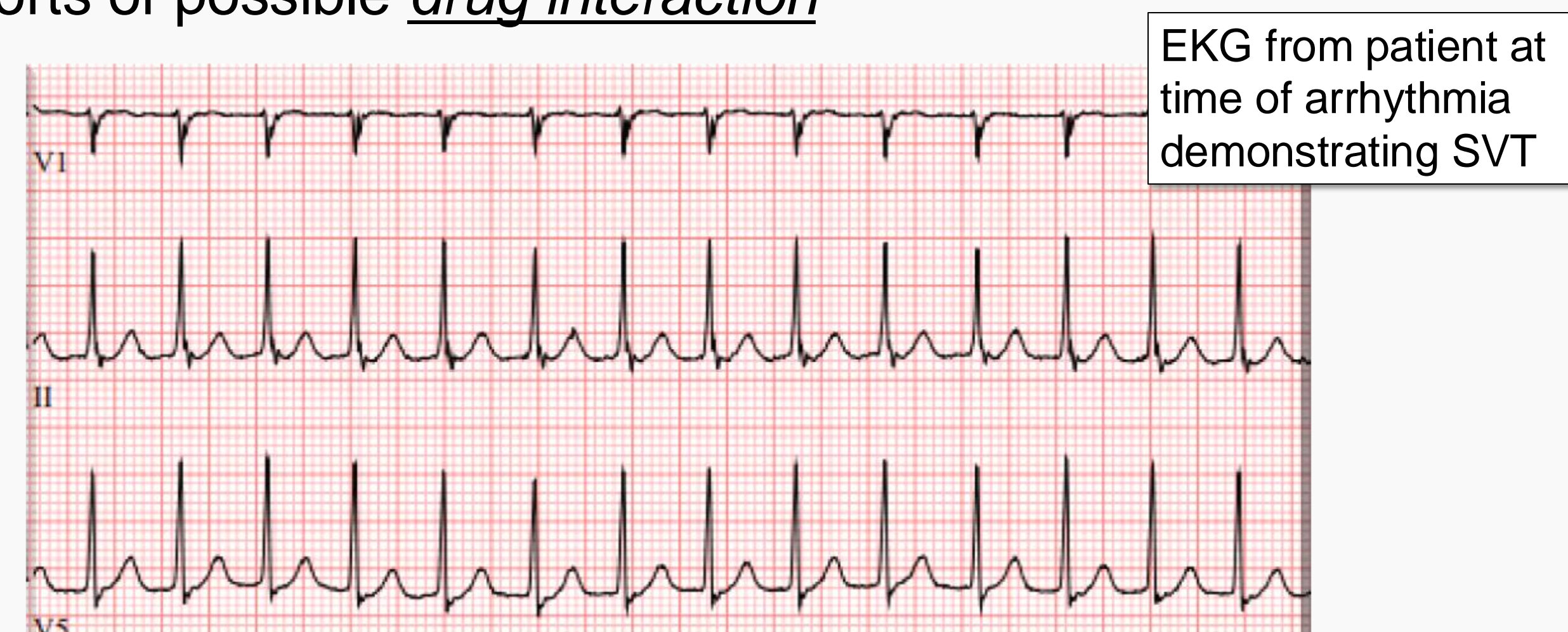
Concurrent Clozapine and Amiodarone Treatment

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Consult Question

- 66-year-old female patient on internal medicine service develops *supraventricular tachycardia (SVT)* (HR: 150-170s), primary team wants to initiate *amiodarone*
- Psychiatry consulted for guidance regarding her *clozapine* maintenance medication (400 mg/day) due to literature reports of possible *drug interaction*



Background

- Cardiovascular disease is a leading cause of death for patients with schizophrenia
- Amiodarone routinely used for atrial and ventricular arrhythmias
- Interaction between clozapine and amiodarone through hepatic cytochrome P450 isoenzyme (CYP) system
- Amiodarone inhibits several CYP enzymes involved in clozapine metabolism, including CYP1A2, 3A4, and 2D6; therefore, amiodarone may raise serum levels of clozapine
- Limited guidance on concurrent usage despite increased risk of clozapine toxicity
 - Previous literature: reports of significant increases in clozapine levels after amiodarone co-administration and worsening of clozapine side effects, research limited by lack of longitudinal clozapine serum levels
- Both medications may prolong QTc, posing risk of Torsades de Pointes

Consult Recommendations

- Recommended reducing clozapine dose from 400 mg/day to 300 mg/day to prevent toxicity
- Serial clozapine and amiodarone serum levels collected every other morning during admission
- EKGs to track QTc interval

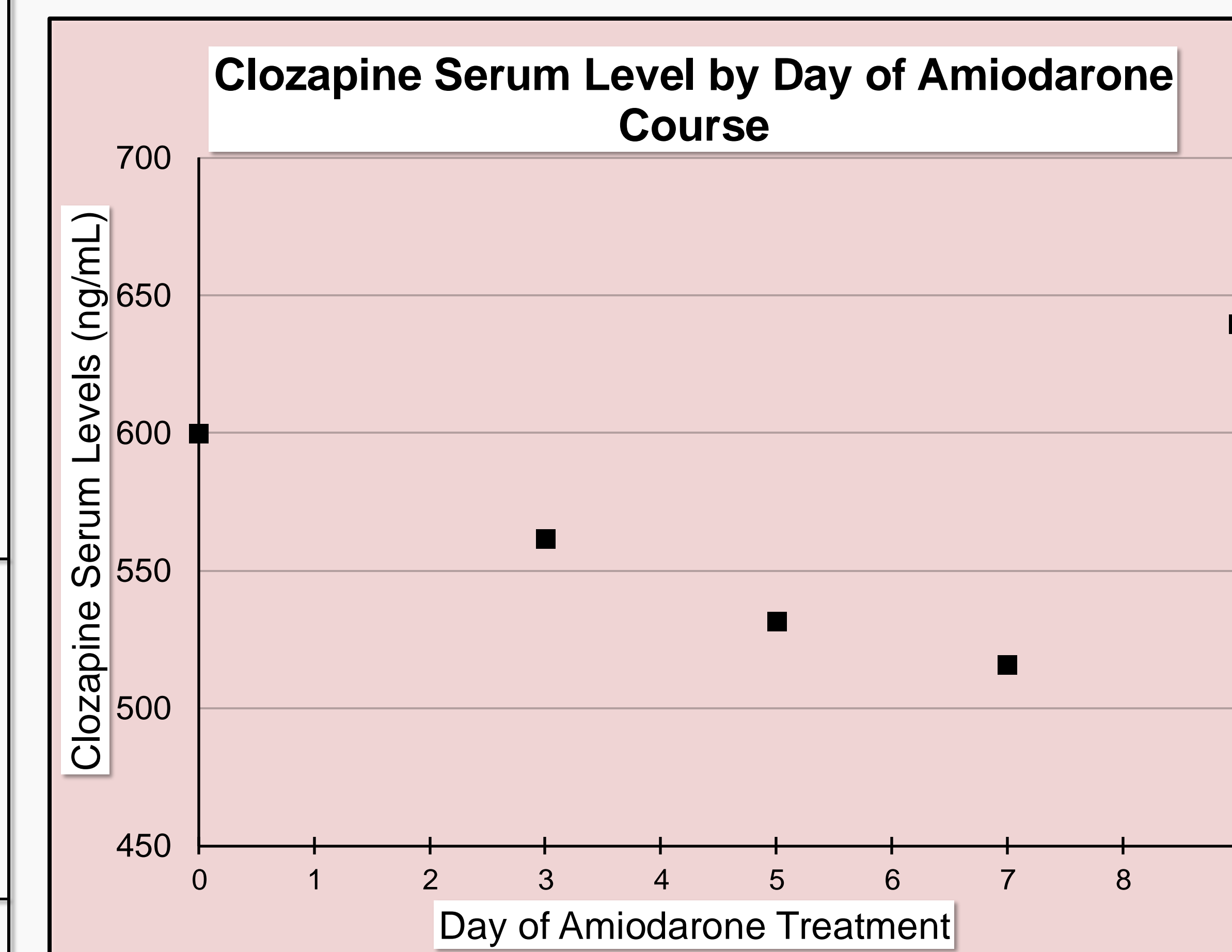
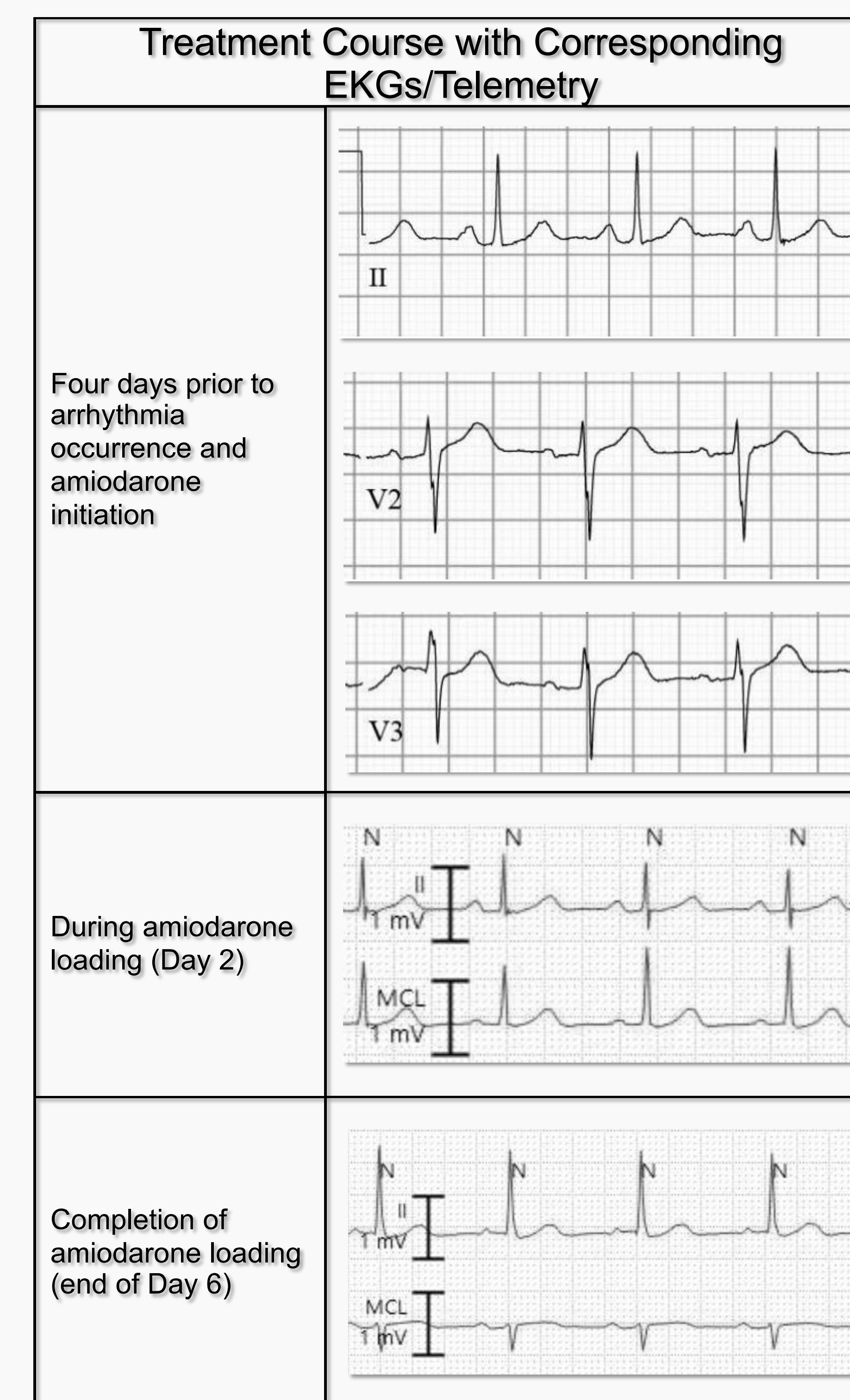
Results

- Day 1 of amiodarone, SVT converted to normal sinus rhythm and maintained
- Serum clozapine levels remained therapeutic during amiodarone loading
- Day 9, elevated clozapine serum level despite amiodarone at lower maintenance dose
- No reported side effects during loading or maintenance dosing
- Discharged to facility, recommended checking clozapine serum levels and QTc every two weeks, adjust clozapine dose as indicated
- Patient declined clozapine monitoring following discharge, facility switched to olanzapine, resulted in significant psychiatric decompensation

Clozapine Serum Levels, Amiodarone Serum Levels, and QTc During Treatment Course

Day of Amiodarone Treatment	Clozapine Total Daily Dose	Clozapine Serum Level (TR: 350-600)	Amiodarone Total Daily Dose	Amiodarone Serum Level (TR: 0.5-2.0)	QTc Interval (Framingham correction, 7 AM daily)
Day 0	400 mg	600 ng/mL	-	-	-
Day 1	400 mg	-	400 mg	-	-
Day 2	400 mg	-	1200 mg	-	414 ms
Day 3	300 mg	562 ng/mL	1200 mg	-	414 ms
Day 4	300 mg	-	1200 mg	-	424 ms
Day 5	300 mg	532 ng/mL	1200 mg	1.2 mcg/mL	387 ms
Day 6	300 mg	-	1200 mg	-	407 ms
Day 7	300 mg	516 ng/mL	200 mg	1.4 mcg/mL	-
Day 8	300 mg	-	200 mg	-	-
Day 9	300 mg	640 ng/mL	200 mg	0.5 mcg/mL	-

TR = therapeutic range, determined by electronic medical record reference values.



Discussion

- Oral amiodarone was successfully loaded by reducing clozapine dose in anticipation of impaired metabolism
- Clozapine serum levels remained in the therapeutic range throughout loading
- Increase in clozapine levels on day 9 (maintenance dose of amiodarone), resulted after patient had been discharged, no side effects reported
 - Possible explanations: time for plasma amiodarone concentrations to reach steady state (approximately 4–6 weeks) and/or variability in clozapine serum levels
- Serial clozapine levels and QTc intervals are helpful to guide treatment and monitor interaction
- Relying on amiodarone serum levels or a single point clozapine level would not have fully characterized interaction
- Temporary need for serial monitoring creates additional barrier to psychiatric treatment with clozapine, possibly contributed to discontinuation of clozapine and decompensation
- Lack of post-discharge follow-up data is limitation

Conclusions

- Possible to achieve safe amiodarone loading by preemptively reducing the clozapine dose
- Advise monitoring of clozapine serum levels and EKGs longitudinally
- Do not rely only on single point clozapine serum level or fluctuating amiodarone serum levels to predict interaction
- Longitudinal monitoring helpful but creates additional barriers to clozapine treatment

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Disclosures

Following submission of poster, case report published (see first citation above). Conference organizers notified and granted permission to present. Otherwise, none of the authors have any relevant relationships to disclose.