CASE REPORT

Phenytoin as an effective treatment for polymorphic ventricular tachycardia due to QT prolongation in a patient with multiple drug intolerances

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SUMMARY

We present a case of a 69-year-old woman presenting with polymorphic ventricular tachycardia caused by QT prolongation. Owing to known intolerances to a majority of antiarrhythmic medications, one remaining option was to initiate phenytoin. Phenytoin's narrow therapeutic window, multiple drug interactions and side effect profile make it an infrequently used antiarrhythmic. It is, however, a potent antiarrhythmic agent, which may be useful in treatment of ventricular tachycardia, especially in patients with multiple drug intolerances.

BACKGROUND

Phenytoin is a class IB antiarrhythmic agent that has been successfully utilised for over half a century for treatment of ventricular arrhythmias. Over the recent years it has been supplanted by newer, more effective and less toxic agents. It remains, however, a potent agent, which may be potentially useful in selected patients with antiarrhythmic intolerant and refractory arrhythmias.

CASE PRESENTATION

We present a case of a 69-year-old woman with a history of a non-ischaemic cardiomyopathy (NICM) and persistent atrial fibrillation, status post a hybrid maze/catheter-based endocardial ablation procedure performed several months prior to this hospitalisation. She has also undergone prior cardiac resynchronisation therapy for her NICM. Following her hybrid ablation surgery, she experienced recurrent runs of sustained polymorphic ventricular tachycardia (VT) with syncope (figure 1). Her baseline QTc on ECG was prolonged at 480 ms (figure 2). There were no electrolyte imbalances or QT prolonging medications responsible for her polymorphic VT. Left heart catheterisation prior to her hybrid procedure revealed non-obstructive coronary disease. Her polymorphic VT was believed secondary to QT prolongation.

In the past, she was found to be intolerant of many antiarrhythmic medications used for treatment of her atrial fibrillation. β -Adrenergic blockers and calcium-channel blockers were ineffective in controlling her arrhythmia and rate of ventricular response. Dronedarone failed to control her atrial fibrillation. Amiodarone had caused rash requiring treatment with prednisone. Sotalol and dofetilide resulted in QT prolongation.

TREATMENT

Lidocaine was initiated, but had to be stopped due to reported 'excruciating pain' around the intravenous injection site. Treatment with mexiletine was attempted, but caused excessive gastrointestinal side effects.

Owing to her multiple intolerances of antiarrhythmic agents, one remaining option was to initiate phenytoin. With the assistance of a clinical pharmacologist, the patient was intravenously loaded with phenytoin and her arrhythmia resolved.

OUTCOME AND FOLLOW-UP

The patient continued to do well on oral phenytoin maintenance on follow-up several months later.

DISCUSSION

In our patient, the polymorphic VT was likely secondary to QT prolongation. Polymorphic VT or torsades de pointes is a recognised phenomenon in the setting of QT prolongation.¹ Increased QT interval is reflective of prolonged repolarisation, which is associated with early afterdepolarisations (EADs). Mechanisms of EADs include activation of inward depolarising currents, L-type calcium channels or sodium-calcium exchange current (Incx). EAD amplitude may exceed the voltage threshold for depolarisation and cause premature ventricular contractions and ventricular arrhythmia with changing axis and QRS morphology, characteristically described as torsades de pointes. Treatment of polymorphic VT usually includes removal of those medications that may prolong the QT interval, corrections of electrolyte abnormalities and pacing or isoproterenol infusion in cases associated with bradycardia.¹ In our patient, correction of identifiable causes did not resolve QT prolongation and arrhythmia. Known intolerances of antiarrhythmic medications have significantly limited our therapeutic options. Fortunately, her arrhythmia has resolved with phenytoin.

Phenytoin is a hydantoin derivative, most commonly used as an anticonvulsant drug to treat seizures (status epilepticus, post-traumatic, alcohol related, eclampsia/preeclampsia, tumours, cerebrovascular related, febrile). It affects sodium, potassium and calcium ion channels by blocking repetitive firing of neurons and maintaining sodium channels in the inactivated state at therapeutic concentrations.² Owing to its effects on ion channels and receptors on the myocardial cell membrane, phenytoin has also been used as an antiarrhythmic drug.

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HR 98

PVC 17

Figure 1 Telemetry strip showing polymorphic ventricular tachycardia.

As a class IB drug, phenytoin primarily shortens action potentials and inhibits rapid inward sodium currents. The typical dose for phenytoin is 200–400 mg once a day, with a target plasma level of 40–70 $\mu\text{mol/L}$. Phenytoin is 98% metabolised in an inactive metabolite 5-hydroxyphenyl phenyl hydantoin. The elimination half-life is 16–24 h, with the major route of elimination being hepatic. Phenytoin has a 50–70% oral bioavailability and 90% protein binding.³ Phenytoin can be administered intravenously or orally.²

Phenytoin has been used in treatment of torsades de pointes.^{4,5} It reduces the rate of calcium-dependent depolarisation in the plateau phase of the cardiac action potential and increases the

refractory period.⁴ This prevents EADs, thus inhibiting ventricular ectopy and halting a potential tachyarrhythmia,⁵ which is the most likely reason for arrhythmia resolution in our patient. Phenytoin's anticholinergic effects may have beneficial effects in preventing bradycardia.⁵

Phenytoin's narrow therapeutic window, multiple drug interactions and side effect profile (vertigo and nystagmus early, and confusion and lethargy at higher concentrations) make it a rarely used antiarrhythmic. It is, however, a potent antiarrhythmic agent, which may be useful in treatment of VT, especially in patients with multiple drug intolerances.

Figure 2 Baseline ECG with prolonged QT.

Learning points

- ▶ Phenytoin is a hydantoin derivative, most commonly used as an anticonvulsant drug to treat seizures.
- ▶ Phenytoin's antiarrhythmic properties are due to effects on sodium and calcium channels in cardiac myocyte and Purkinje cell membranes.
- ▶ Phenytoin's narrow therapeutic window, multiple drug interactions and side effect profile make it a rarely used antiarrhythmic. It is, however, a potent antiarrhythmic agent that may be useful in treatment of ventricular tachycardia, especially in patients with multiple drug intolerances.

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