Congenital Long QT_c Syndrome

Welcome back Clinical Problem Solvers! This is Gurbani Kaur a third-year medical student and your host for today's Illness Script Episode airing live on Channel "O Pathy" focused on Congenital Long QT_c Syndrome. This episode is brought to you by Cuties Clementines.

Let's start with the juicy details of what the QT represents on the EKG. The QT interval on the EKG represents the duration of ventricular action potential and correlates with the duration of ventricular depolarization and repolarization. In people assigned male at birth, the QT interval is considered prolonged if it is greater than 440 milliseconds. Meanwhile, in people assigned female at birth, the QT interval is considered prolonged if it is greater than 460 milliseconds. This is important as cardiac events, and fatal arrhythmias may occur when the QT interval is prolonged either congenitally or through acquired causes. We're going to focus on congenital causes.

Let's start unpeeling our illness script. First, we consider the pathophysiology or

How? genetically encoded abnormalities in cardiac ion channels cause congenital long QT syndrome. Remember, the QT interval is largely dependent on the duration of the ventricular action potential. Ventricular action potential duration is mostly determined by the influx of positive ions: sodium and calcium causing depolarization, and the efflux of positive ions: potassium causing repolarization through ion channels across cardiomyocyte membranes. Mutations in genes encoding these ion channel proteins cause their malfunction. The three major types of congenital long QT are associated with malfunctions in cardiac potassium and sodium channels. Other less common mutations have been found to affect calcium handling. These impaired ion channels lead to excess retention of positive ions intracellularly. Excess intracellular positivity prolongs the action potential, thereby lengthening the QT interval through delayed repolarization or continued depolarization. Prolongation of the QT interval increases the probability for early afterdepolarizations. Common precipitants of early afterdepolarizations include hypokalemia, hypomagnesemia, hypocalcemia, a variety of medications, increased sympathetic activity promoting bradycardia, exercise, stress, and early arousal. EADs and triggered activity are thought to be the most common initiating mechanism for the ventricular ectopy and polymorphic VT associated with long QT intervals.

Next, let's discuss the epidemiology or risk factors that plant the seeds to indicate **Who?** gets congenital long QT syndrome. The prevalence of this autosomal dominant syndrome is difficult to measure but it is estimated to affect more than 1 in 2,000 people. However, this syndrome shows variable expressivity and incomplete penetrance as low as 10%. In autosomal dominant disorders like long QT syndrome, this means at maximum 10% of individuals with a disease-causing mutation actually manifest it. Variable expressivity means of those who do manifest the syndrome will vary in range and severity of symptoms. Congenital Long QT syndrome is usually diagnosed by the time the patient enters their 30s. Finally, given the autosomal dominant inheritance pattern, the syndrome runs in families.

Okay, now let's get to the core signs and symptoms or **What?** patients may experience. The majority of patients with congenital long QT syndrome are asymptomatic at the time of diagnosis and throughout their lives. However, syncope is the most common symptom usually triggered by physical or emotional stress. Syncope immediately after diving into the water while swimming is highly specific on history for Long QT syndrome 1. Near syncope and seizures are other symptoms of this syndrome. So, it is most often diagnosed by an incidental long QT observed on EKG. Congenital long QT syndrome is a leading cause of sudden cardiac death, but in only 10-15% of cases is sudden cardiac death the first manifestation of the syndrome. This means there's great hope, if you properly diagnose and treat your patient their mortality rate drops from 21% within the first year after initial syncope to less than 1% at 15-year follow-up! Finally, for women with Long QT syndrome, the 9-month postpartum time is associated with a 2.7-fold increased risk of experiencing a cardiac event.

We know Long QT itself is NOT an **Arrhythmia,** but the resultant arrhythmias it can precipitate are what account for the concerning clinical presentations. Torsades de Pointes is a specific form of polymorphic ventricular tachycardia that appears on the EKG as QRS complexes twisting around the isoelectric line. Torsades de Pointes is often self-limiting, producing transient syncope. However, if it degenerates into ventricular fibrillation, sudden cardiac arrest or death can result. Finally, Long QT syndrome can be complicated by AV block, mostly 2:1, and it's mostly associated with long QT syndrome type 1.

Some non-cardiac clinical manifestations of this syndrome include sensorineural hearing loss in Jervell and Lange-Nielsen Syndrome and hypokalemic periodic paralysis which entails periodic episodes of severe extremity weakness or paralysis lasting for hours to days that typically occurs in childhood to adolescence.

Putting all of this together, imagine your patient Miss Cutie Pai is a 15-year-old girl presenting status post one self-limited episode of syncope at swim practice. You are most concerned that she has congenital Long QT syndrome. How would you diagnose, treat, and counsel Miss Pai and her family?

To **diagnose** congenital Long QT syndrome, we'll need to order an EKG on Cutie Pai and her blood relatives, as well as order genetic testing to identify de novo or familial mutation in one of the cardiac ion channels. Remember, on the EKG, we are looking for an abnormally long *corrected* QT interval. The QT interval is defined as the beginning of the Q wave to the end of the T wave. Typically lead II and V5 is the best for measuring QT_c. It is usually the longest in V2 and V3. There are at least four different formulas to help you calculate the corrected QT interval. A common one used is the Bazett formula. This is beyond our scope here, but they can be found on MD Calc.

Treatment and management of Cutie and her family's arrythmia. The central tenet of management is going to be that an ounce of prevention is worth a pound of cure. Patients like Miss Cutie Pai need to avoid QT prolonging medications which include certain antipsychotics

like haloperidol and risperidone, antiarrhythmics like amiodarone and procainamide, antibiotics including macrolides and fluoroquinolones, antidepressants like amitriptyline and citalopram, and other drugs like methadone, to name a few. Further treatment will depend on if your patient is symptomatic versus asymptomatic and which type 1, 2 or 3 of congenital long QT they have. Type 1 patients are most at risk for arrhythmias during sympathetic activation such as physical or emotional stress, so unfortunately Miss Cutie Pai will need to be counseled on discontinuing competitive sports, especially swimming, since 99% of these episodes are associated with swimming in Type 1 patients. Type 2 patients are extremely sensitive to serum potassium levels and thus hypokalemia needs to be avoided through diet or oral supplementation. Since they are also at higher risk for symptoms when aroused from sleep or rest from a sudden noise, it is recommended to remove alarm clocks and phones from their bedroom and to awaken them gently without yelling. Type 3 also known as Romano-Ward is predominantly due to sodium channel mutations and will need to be tested for efficacy of sodium channel blockers like mexiletine or ranolazine as functional heterogeneity accounts for variable response of mutations to these therapies.

All pediatric patients with a congenital EKG confirmed *corrected* Long QT should be started on an appropriate ß-blocker and referred to a pediatric cardiologist for management given the risk for sudden cardiac death.

Regarding ICDs, The American Heart Association's guidelines recommend their use in multiple patient scenarios, so please defer to their policies for a more in-depth overview. ICDs are not needed in most patients.

Finally, we need to educate our patients like Miss Cutie Pai. Often, some patients are incorrectly diagnosed with having had a seizure. That is why an ECG is recommended for those patients who present after their first-ever seizure. For one, it is to possibly diagnose an underlying Long QT syndrome or other arrhythmia but two, it is to ensure that patients do NOT remain on antiepileptic drugs that are sodium channel blockers, which can increase the risk for sudden cardiac death if they have Long QT syndrome.

Thanks for tuning in to Channel O Pathy today. We hope you enjoyed this refreshing illness script ☺!!