

Name: @NAME@
DOB: @DOB@

Date issued:

EMERGENCY LETTER

TANGO2 Deficiency Disorder (TANGO2-Related Metabolic Encephalopathy and Arrhythmias)

[ADD NAME] is a [ADD AGE] year old [ADD GENDER] with TANGO2 Deficiency Disorder. During times of fasting and metabolic stress such as illness, fever/infections or periods of decreased eating or prolonged fasting, [ADD NAME] can develop a metabolic crisis with or without cardiac crisis.

Definitions:

Metabolic Crises: Episodic events triggered by metabolic stress associated with elevated CK (rhabdomyolysis) and prolonged QTc on ECG. A type 1 Brugada pattern on ECG may also be seen (see image below). Severe hypoglycemia may occur in some patients. Symptoms include new or worsening of baseline symptoms. These include weakness, difficulty holding the head up (head lag), body tilting, abnormal movements, difficulty with walking or balance (falling over/ataxia), muscle pain, slurred speech, drooling, disconjugate gaze/exotropia, seizures and lethargy/somnolence.

Cardiac Crises: Cardiac crises occur only during metabolic crisis and entail the development of arrhythmias (premature ventricular contractions (PVC), ventricular tachycardia (VT), torsade de pointes) or systolic dysfunction/cardiomyopathy (ie new heart failure). Both arrhythmias and cardiac dysfunction resolve once the metabolic crisis resolves.

The following are ACUTE complications that can occur during metabolic/cardiac crisis:

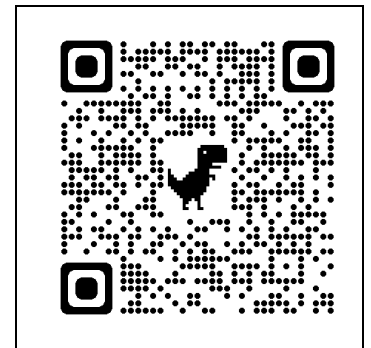
- **LIFE THREATENING severe cardiac arrhythmias and cardiac dysfunction. Sudden death has been reported due to fatal ventricular arrhythmias and cardiac arrest. In addition, cardiac dysfunction can evolve and develop during the crisis even if systolic function is normal at admission.**
- The hallmark signs of metabolic crisis include rhabdomyolysis with elevated CK. Patients also tend to have elevated AST or ALT. Hypoglycemia can also be seen but is not always present. Treatment with intravenous fluids/glucose may stabilize the acute process but does not prevent cardiac crisis and arrest.
- The ECG will almost uniformly show evidence of QTc prolongation. A simultaneous type 1 Brugada pattern (shown below) can also be seen. The Brugada pattern is often intermittent and can come and go; hence close observation for its presence is warranted as it may indicate increased risk for cardiac arrest.

****EMS: – Assess for hypoglycemia, cardiac rhythm and begin treatment immediately if patient is in crisis. If safe for the patient, please transport patient to a hospital which is equipped to care for this rare genetic condition, or nearest tertiary care hospital.**

EMERGENCY ROOM PHYSICIAN:

[ADD NAME] should be triaged as soon as possible upon arrival to the Emergency Room even if the patient does not appear to be ill, because hypoglycemia and life-threatening arrhythmias can progress rapidly.

1. Initial Labs: STAT fingerstick glucose, CK level, AST/ALT, lactate, venous blood gas, chemistry panel (Chem 10) with glucose.
2. Rhythm monitoring/ECG: Immediately place the patient on continuous rhythm monitoring and obtain a 12 lead ECG. If the patient has a prolonged QTc (>450msec) or type 1 Brugada pattern, admit and obtain an echocardiogram to assess function. Any PVCs or VT warrants immediate medical attention and transfer to the intensive care unit.
3. After sending labwork, carefully assess the patient's ability for nutritional intake. If full oral intake is not possible, a nasogastric tube or TPN should be considered. Initiate IV fluids (D10 with added age-appropriate electrolytes) at 1x maintenance rate. If the patient is in crisis, consider addition of IV multivitamins to the IV fluids (see full recommendations via QR code) until feeds can be initiated.
4. Due to high risk or mortality for patients in crises and need to prevent progression to cardiac crises, we recommend reviewing full details for management available in GeneReviews (<https://www.ncbi.nlm.nih.gov/books/NBK476443/>) during TANGO2 related crises. You can also access this by scanning the following QR code:



We also recommend contacting your local expert in TANGO2 Disorder and calling or paging your genetics/metabolic service to inform them of the ER or hospital admission. A page to the cardiology/electrophysiology service is also warranted for all admissions. If local expertise is not available, you may request peer-to-peer assistance by emailing the TANGO2 medical team (tango2.research@bcm.edu) although email is not checked after-hours and response time may vary.

Recognizing Brugada Pattern

A type 1 Brugada Type pattern example (on standard 12 lead ECG) demonstrates anterior (V1 and V2) ST elevation with T wave inversion:

