Introduction

- Friedreich's ataxia was first described in 1863 by German physician Nikolaus Friedreich.
- Although a relatively rare disease, it is the most common form of hereditary ataxia, affecting approximately 1 in every 50,000 people.
- Friedreich's ataxia is an autosomal recessive disease caused by a trinucleotide repeat of GAA in the FXN gene on Chromosome 9, which codes for the mitochondrial protein frataxin. This expansion causes gene silencing and decreased production of frataxin.
- Frataxin incorporates iron cofactors into iron sulfur clusters which form enzymes involved in electron transfer and mitochondrial ATP production, which decreases when frataxin levels are low.
- Cells with low frataxin have lower mitochondrial ATP production, decreased cellular energy, and development of toxic free radicals which cause oxidative damage to DNA in nerve cells, pancreatic beta cells, and cardiac myocytes.
- This leads to ataxia, diabetes mellitus, and cardiac complications including hypertrophic cardiomyopathy, myocardial fibrosis, and heart failure, all of which contribute to cardiac disease being the most common cause of death in FA.
- Interestingly, about 1 in 90 Americans of European ancestry is a carrier of an abnormal FXN gene.

Case Presentation

- A 31-year-old female with FA and cardiomyopathy presented to the ED with palpitations, dyspnea, myalgias, diaphoresis, and anxiety after taking a Canadian weight-loss supplement for 7 days.
- She denied chest pain. Poison control determined the active ingredient to be 2,4-dinitrophenol.
- Vitals: BP 142/100, HR 120, temp 98.2F.
- Physical exam: tachycardia, skin erythema, and anxious mood.
- EKG: Sinus tachycardia and lateral T wave inversions.
- Troponin: 2,369 (initial) -> 4,580 (peak).

Decision Making

- Despite the elevated troponin, Cardiology advised against typical NSTEMI treatment with IV Heparin given the low likelihood of plaque rupture induced ischemic event (Type 1 MI).
- The likely cause of presentation was demand ischemia (Type 2 MI), this is supported by her lack of chest pain, mild troponin elevation, and echocardiogram without ischemic changes.
- She was given supportive care, cardiac monitoring, Aspirin 324mg, Metoprolol, and Acetaminophen, and had relief of symptoms after a few days.

Discussion

- Given that patients with FA can have an elevated baseline troponin and already have mitochondrial dysfunction given low frataxin levels, the 2,4-dinitrophenol would impact her fragile cardiomyocytes further as the medication uncouples mitochondrial phosphorylation leading to increased metabolic rate, cellular hyperthermia, and can precipitate cellular death.
- With this mechanism of action, it is not surprising the patient developed a type II NSTEMI with higher-than-expected troponin.

References

2) Figure 1 accessed August 8th from https://en.wikipedia.org/wiki/Oxidative_phosphorylation
6) Figure 4 accessed August 8th. https://www.sigmaaldrich.com/us/en/product/aldrich/d198501