Introduction
In cardiac transplant medicine, an elevated troponin may be a sign of organ rejection. This may prompt invasive testing and increased immunosuppression with significant risks and side effects. This series of events stems from a positive troponin, which can sometimes be falsely elevated.

Learning Objectives
- To recognize the implications of a positive troponin in a heart transplant patient
- To learn how heterophilic antibodies interfere with immunoassays
- To learn other causes of interference in the troponin assay

Case Presentation

History
- A 23 year old man presented with chest pain to an outside ER where his first troponin was <0.01 ng/ml and he was transferred to our institution for further evaluation
- Five years prior he had undergone orthotopic heart transplantation for catecholamine mediated polymorphic ventricular tachycardia
- Post-transplant he displayed maladaptive behavior with intermittent compliance to immunosuppressive therapy and frequent presentations to Emergency Rooms (ER) with syncope and chest pain. Evaluations did not identify any cause for these recurrent symptoms.

Medications
- Mycophenolate 360 mg BID
- Tacrolimus 3.5 mg BID
- Carvedilol 3.125 mg BID
- Aspirin 81 mg daily
- Trimethoprim/Sulfamethoxazole 160/800 mg M, W, F

Past Medical History
- Catecholamine Mediated Polyformic Ventricular Tachycardia
- Orthotopic Heart Transplantation (with daclizumab induction)
- Asthma
- Polysubstance Abuse
- Mood Disorder, NOS

Family History
- Non-contributory

Social History
- Smokes 0.5-1 packs every day for 5 years
- Occasional alcohol use
- Intermittent use of marijuana and methamphetamine after transplantation

Physical Exam
Blood pressure: 112/50 mmHg; Heart Rate: 70/min
General: No acute distress.
Cardiac exam: Regular rate and rhythm, S1 and S2
Lung exam: Clear to auscultation bilaterally
Extremities: No edema or cyanosis

Investigational Studies

Graph displaying mean troponin value measured during different presentations to our hospital.

Clinical Course

- 11/11: Initial troponin 22.9 ng/ml, patient underwent cardiac catheterization and endomyocardial biopsy and tacrolimus level measured. Augmentation of immunosuppression deferred after discussion with transplant center.
- 12/11: Repeat endomyocardial biopsy at transplant institution
- 1/2/12: Elevated troponin, steroid burst of prednisone 60 mg started
- 3/2/12: Troponin higher than measurable, repeat cardiac catheterization and endomyocardial biopsy performed and second steroid burst started
- 5/2/12: Troponin measured 40 ng/ml, suspicion of assay interference and sample sent for testing with a heterophilic antibody blocking reagent, which measured troponin at 0.06 ng/ml then 0.04 ng/ml
- Transfered to UC Davis. Troponin measured 1.4 ng/ml. Sample sent to first hospital for measurement. No troponin detected confirming interference.

Discussion

- Elevated cardiac troponin in a heart transplant recipient may be from:
  - Ischemia
  - Rejection with injury of vasculature and ischemia
  - Rejection with injury to myocardium
- Troponin is measured by an immunoassay
  - Immunoassays commonly use a “two-site sandwich”
  - A “capture” antibody binds troponin floating in serum
  - A “signal” antibody is added and binds the captured troponin to signal the presence of troponin
  - The intensity of light emitted correlates with the amount of troponin present
- Immunoassays are prone to various forms of interference
  - Multiple different substances and conditions have been shown to cause false positive troponins (see Table)
  - It is estimated between 0.4 and 3.1% of troponin measurements are false positives
- A heterophilic antibody describes a type of antibody that displays weak and non-specific binding, often with broad reactivity
  - Sometimes they display stronger targeted binding, often in individuals previously exposed to a specific antigen
- Provoking factors that can induce a heterophilic antibody include:
  - Clinical therapeutics
  - Blood transfusions
  - Vaccinations
  - Exposure to animals
  - Ingestions
- The patient had Daclizumab, a humanized mouse anti-interleukin-2-receptor antibody, at time of transplantation potentially inducing heterophilic antibodies
- This case highlights the need to consider laboratory interference when other clinical parameters do not support laboratory results

Heterophilic Antibodies
- Alkaline Phosphatase
- Inadequate Washing
- Ectromelin
- Infection with Legionella

Table
Conditions and substances that can interfere with troponin assay and cause a false positive.

References
- McCormick S, Halaska JD, Hoekstra GL, Kamm M, Ho KK. Clinical prevalence and ramifications of false-negative cardiac troponin I elevations from the Amiott AxSYM Analysis. Am J Cardiol. May 1 2003;93(9):1125-1127.