**Observatio**

**INTRODUCTION**

Sipuleucel-T (Provenge) is an autologous active cellular immunotherapy containing blood mononuclear cells activated by a recombinant prostatic acid phosphatase (PAP) epitope to granulocyte-macrophage colony-stimulating factor (GM-CSF) that is indicated in castration-resistant prostate cancer1. Thromboembolic and myocardial infarction events have been reported with sipuleucel-T however are very rare (0.01%). We describe a case of suspected sipuleucel-T related cardiomyopathy and provide insight into its possible immune-related mechanisms.

**CASE PRESENTATION**

A 64 year old Caucasian male presented to the emergency department with progressive weakness for several days and orthopnea. He denied chest pain, lightheadedness/dizziness, syncope, dyspnea on exertion, lower extremity edema, unintentional weight gain, nausea, vomiting.

**Physical Exam:**
- Cardiovascular: JVP at clavicle at 45° angle, irregularly irregular rate and rhythm, no murmurs/gallops/ectopics
- Lungs: clear to auscultation bilaterally, no wheezes/brasses/honchi
- Extremities: no lower extremity edema

**Past Medical History:**
- Stage IV castration-resistant prostate adenocarcinoma
  - Xandr (enzalutamide) – 11/12/2018 to present
  - Tarotire (docetaxel) – 11/20/2018 to 02/07/2019
  - Lupron (leuprolide) – 01/03/2019 to present
  - Xgeva (denosumab) – 05/23/2019 to present
  - Provenge (sipuleucel-T) – 06/10/2019 to 07/22/2019
- Non-ischemic cardiomyopathy (EF of 32% in 06/2019)
- Hypertension, well controlled

**Past Surgical History:** transurethral resection of the prostate

**Past Social History:** never smoker or illicit drug use

**Medications:**
- Carvedilol 3.125 mg BID
- Lisinopril 20 mg QD
- Furazolidone 40 mg BID
- Leuprolide Q6 months
- Denosumab Q4 weeks

**Laboratory Results:**
- WBC: 7.41k/uL
- Hgb: 11.6 g/dL
- Hct: 35.6 %
- Creatinine: 1.04 mg/dL
- Leukocyte Q8 months: Pt: 200 k/uL
- Denosumab Q4 weeks: BUN: 19 mg/dL
- Cr: 1.03 mg/dL

**DISCUSSION**

- Sipuleucel-T cardiotoxicity is rare with post-marketing analyses demonstrating 0.01% risk of thrombotic events and myocardial infarction2.
- Cardiomyopathy observed in our patient may have been a result of an increased immune response secondary to sipuleucel-T as evidenced by chronic inflammation predominant in CD4+ and CD8+ T cells. This may have caused a similar effect seen in autoimmune myocarditis3 or increased propensity for viral myocarditis4 leading to cardiomyopathy.
- Limitations to this study include lack of myocardial biopsy and viral testing during the sentinel event in June 2019 and lack of baseline echocardiogram prior to sipuleucel-T.
- In summary, close monitoring of cardiotoxicity in patients receiving immunotherapy is warranted and additional studies are needed to evaluate its pathophysiology.

**REFERENCES**
4. Rhee SI. Journal of Clinical Immunology 2006;26:73–7

**Figure 1:** Echocardiogram at A) baseline, B) June 2019 and C) October 2019

**Figure 2:** Cardiac MRI. The LGE covers the basal inferolateral wall of the left ventricle demonstrated with gadolinium contrast and EF of 32%. Evidence of LGE with a mottled red wall pattern in the basal septum and basal inferior segment (non-ischemic pattern representing myocardial edema or interstitial fibrosis).

**Figure 3:** 99mTc-PYP scan for cardiac amyloidosis. Semiquantitative visual scoring showed grade 1 mild uptake activity in the region of the heart with quantitative analyses showing a HCL ratio of 1.2. This was indicative of an equivocal study with no definitive suggestion for presence of ATTR cardiac amyloidosis.