Ventricular Tachycardia and Myocardial Fibrosis Diagnosed After Treatment with Pembrolizumab and Ipilimumab

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Introduction
Immunotherapy plays a significant role in the treatment of malignant melanoma. The FDA approved ipilimumab in 2011, an anti-CTLA-4-antibody. In 2014, pembrolizumab, an anti-PD-1 blocking antibody agent was approved for treating patients with refractory disease. Despite known benefits of these therapies, many immune-related adverse events have been reported with up to 64% of patients treated with ipilimumab having severe complications.

We report a unique case of a potentially fatal cardiac complication related to CTLA-4/PD-1 blocking agents – life threatening ventricular arrhythmia secondary to cardiac fibrosis. This side effect has not previously appeared in literature. A single case of myocardial fibrosis related to ipilimumab was briefly mentioned in literature, but no cases appeared in relation to pembrolizumab.

Case Presentation
Patient is a 41 years old female with history of metastatic polyloid choroidal melanoma diagnosed in 2005 who presented in 12/2014 for evaluation of palpitations associated with dyspnea and lightheadedness. Her treatment consisted of ipilimumab from 08/2013 through 08/2014, subsequently switched to pembrolizumab secondary to disease progression.

Cardiac workup was notable for an elevated troponin I level and no electrolytes abnormalities. Polymorphic and bidirectional ventricular tachycardia was evident on initial EKG. Echocardiogram and coronary angiogram did not reveal systolic dysfunction or ischemic heart disease. Cardiac MRI was negative for metastatic disease and acute myocarditis, but showed moderate diffuse myocardial fibrosis in a non-ischemic pattern. Etiology of fibrosis was attributed to treatment with checkpoint inhibitors.

Conclusion
Cardiac complications of immunomodulator therapy have not been readily reported. With the increasing prevalence of malignant melanoma and the advancement of these therapies, it is important to be aware of potential complications like cardiac fibrosis which can serve as a nidus for life-threatening cardiac arrhythmias. Identifying these complications is
necessary to appropriately treat patients with LifeVest and ICD to prevent detrimental outcomes.