Pembrolizumab Associated Cardiomyopathy in the Setting of Severe Thrombocytopenia: A Diagnostic and Therapeutic Dilemma

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Background

Immune checkpoint inhibitors (ICIs) represent a novel form of cancer immunotherapy which has revolutionized the management of numerous malignancies. The programmed death ligand-1 (PDL-1) inhibitor pembrolizumab is an example of an ICI that has shown survival benefits in patients with Non-Small Cell Lung Cancer (NSCLS). Although relatively safer than conventional chemotherapies, rare and potentially fatal side effects can occur, specifically cardiotoxicity in the form of autoimmune myocarditis and stress induced cardiomyopathy. Due to the rarity of these side effects, there remains a lack of guidelines regarding diagnostic workup and therapies available.

Case Presentation

A 55-year-old female with a 35 pack-year smoking history and stage IVa NSCLC presented with shortness of breath and chest pain. She had received three cycles with carboplatin, paclitaxel and pembrolizumab prior to presentation. She was acutely hypoxic requiring intubation. Imaging revealed multifocal pneumonia and she was started on broad spectrum antibiotics. Labs were significant for troponin-I levels of <0.01 ng/mL and then 0.63 ng/mL six hours later. Basic natriuretic peptide was 193 pg/mL, infectious work up including influenza A/B and COVID-19 PCR were negative.

Case Presentation

She underwent a TTE which revealed a newly reduced left ventricular ejection fraction of less than 20% with global hypokinesis. Thyroid function testing was normal and regadenoson stress testing showed no evidence of inducible ischemia. At this point, the differentials considered included stress induced cardiomyopathy and autoimmune myocarditis. However, further invasive work up including cardiac catherization and endomyocardial biopsy were hindered due to severe chemotherapy related thrombocytopenia (nadir of 23,000) that was non-responsive to appropriate platelet transfusions.

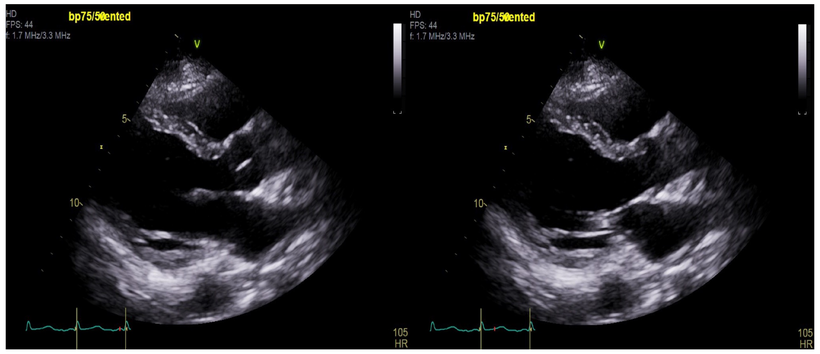

Figure 1. Transthoracic echocardiogram (TTE), parasternal view, showing mildly enlarged left ventricle with severely reduced systolic function, estimated EF <20%.

Due to concern for pembrolizumab induced myocarditis, the patient was empirically treated with 1.2 mg/kg of IV methylprednisolone daily. Patient was extubated within 72 hours of presentation with marked clinical improvement and was eventually discharged with a prednisone taper, suspension of ICIs and follow up with cardiology and oncology.

Conclusions

Treatment of ICI-induced cardiomyopathy begins with removal of the offending agent and in cases of immune-mediated myocarditis, corticosteroids remain a well demonstrated first line treatment. In our case, our patient was unable to undergo endomyocardial biopsy due to her severe thrombocytopenia and elevated bleeding risk. She was empirically treated with corticosteroids due to the relatively high morbidity and mortality that this disease process carries. ICI-induced cardiomyopathy in the form of autoimmune myocarditis and stress induced cardiomyopathy remain rare clinical entities. This rarity combined with the relative novel use of ICIs has led to a paucity of available evidence and therefore established guidelines regarding diagnostic workup and therapeutic options.

References

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