Diltiazem/metoprolol-tartrate/pembrolizumab

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Cardiotoxicity and thrombocytopenia : case report

A 73-year-old man developed cardiotoxicity and thrombocytopenia during immunosuppressant treatment with pembrolizumab. Additionally, he exhibited a lack of efficacy during treatment with diltiazem and metoprolol tartrate [*not all routes and dosages stated*].

The man, who had a history of hyperlipidaemia, hypertension, tobacco use, stage IV adenocarcinoma of the lung, coronary artery disease status after stent placement in all three main coronary arteries in 2013, and paroxysmal atrial fibrillation (AF) on apixaban, was hospitalised after a fall. He underwent cyberknife radiation therapy after being diagnosed with right upper lobe lung cancer a year ago. He was later diagnosed with brain metastases and had a solitary brain lesion treated with cyberknife radiation, followed by pembrolizumab. He experienced lightheadedness and had an incidence of syncope a week later, and presented to the emergency department with a heart rate HR of 120 beats per minute. An ECG revealed atrial fibrillation (AF) with a fast ventricular response. His treatment was started with a diltiazem drip and 50mg of oral metoprolol tartrate. Additionally, he continued treatment with apixaban. Subsequently, he developed a worsening of AF and experienced hypotension [lack of efficacy of metoprolol tartrate and diltiazem]. Additionally, he underwent transesophageal echocardiography. Although a normal sinus rhythm was established, he experienced an early recurrence of AF. He was initiated on satolol, and while his heart rate was stable, he suffered from respiratory distress, necessitating oxygen supplementation with a FiO_2 of 40%. His hypotension worsened during the next five days, diltiazem was stopped. A decrease in the platelet count was also noted. His thrombocytopenia was linked to pembrolizumab, despite the fact that he had not received any heparin and showed no indications of infection. He then received treatment with methylprednisolone, and his thrombocytopenia improved over the next few days. His respiratory condition gradually improved, and he was tapered off nasal cannula oxygen supplementation after two failed efforts at cardioversion to restore normal sinus rhythm. An echocardiography was performed on days 7–11 of hospitalisation, which demonstrated soft tissue density inside the pericardial area. Following that, a computed tomography scan revealed a significant quantity of epicardial fat and lipomatous enlargement of the interatrial septum, prompting concerns about myocarditis. His erythrocyte sedimentation rate and his C-reactive protein were abnormally high. Eventually, he was diagnosed with Pneumocystis jirovecii pneumonia. His treatment was initiated with atovaquone. A cardiac MRI reported elevated signal intensity in the apical myocardium as well as midwall late gadolinium enhancement, including the apical septum and lateral wall, indicating a myocardial inflammatory process.

The man's treatment was started with prednisone-based steroids, which resulted in myocardial inflammation resolution on an outpatient repeat cardiac MRI following discharge. He had not received his second pembrolizumab dose due to myocarditis and cardiac arrhythmias (both tachycardia and bradycardia). On day 15 of hospitalisation, he was discharged and referred to a subacute rehabilitation centre (in AF) with medication, including metoprolol tartrate 12.5mg twice daily and amiodarone. During subacute rehabilitation, he was diagnosed with a COVID-19 infection and again admitted. He received off-label treatment with convalescent-anti-SARS-CoV-2-plasma [convalescent plasma]. Additionally, he received concurrent treatment with remdesivir and unspecified steroids. His atovaquone therapy for P. jirovecii pneumonia was repeated. His heart rate alternated between sinus bradycardia and sinus tachycardia during the readmission. Eventually, he was diagnosed with sick sinus syndrome and received a pacemaker. He continued to follow-up on his metastatic adenocarcinoma treatment. Finally, a diagnosis of cardiotoxicity was made secondary to pembrolizumab.

Kichloo A, et al. Pembrolizumab-Induced Myocarditis Leading to Persistent Atrial Arrhythmias and a Cascade of Complications: A Therapeutic Dilemma. American Journal of Therapeutics 28: E606-E608, No. 5, 28 Oct 2021. Available from: URL: http://doi.org/10.1097/MJT.0000000000001287 803617506