



May I Introduce You To My Patient? Cardiology 1

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A RARE CASE OF IPILIMUMAB/NIVOLUMAB-INDUCED MYOCARDITIS COMPLICATED BY HIGH GRADE ATRIOVENTRICULAR BLOCK IN A PATIENT WITH METASTATIC RENAL CELL CANCER

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Background: Immune checkpoint inhibitors (ICIs) such as Ipilimumab and Nivolumab have revolutionized the field of cancer therapy. These monoclonal antibodies help to reinforce antitumor immunity, resulting in robust activation of the immune system which promotes tumor cell death. T-cell-targeted immunomodulators are now widely used in the treatment of about 50 cancer types, including metastatic Renal Cell Carcinoma (RCC). However, immune responses by ICIs, especially when used in combination, may lead to systemic immune-related adverse events (irAEs), such as inflammatory and non-inflammatory cardiotoxicity.

Case Presentation: A 70-years old woman without previous cardiovascular events, affected by RCC metastasized to lungs, was admitted to our intensive care unit for the onset of worsening fatigue and dyspnea after a second cycle of ICI-based combination therapy (Ipilimumab plus Nivolumab). The 12-lead ECG showed a third-degree atrioventricular block (AVB) with junctional escape rhythm and negative T-waves in inferior and lateral leads. The laboratory examinations revealed increased values of troponine I, myoglobin, C-reactive-protein and NT-pro-BNP. The transthoracic echocardiography was within the normal range. A temporary cardiac pacing was provided and an acute coronary syndrome was ruled out by coronary angiography. High doses of intravenous methylprednisolone were initiated for the suspicion of ICIs-related myocarditis. Moreover, due to the persistence of the conduction disorders in the following days, a leadless atrioventricular pacemaker (PM) was implanted. During the in-hospital follow up no complications occurred, and the patients was discharged at home in good clinical condition. The therapy with ICIs was not resumed during the follow up.

Discussion: ICIs have improved the clinical outcome for several malignancies, although they may cause a wide spectrum of severe irAEs. ICI-related myocarditis is a rare but potentially life-threatening event with a high mortality without an early recognition. A strict monitoring involving cardiologists and oncologists should be advisable in patients treated with these innovative drugs, for a prompt identification and treatment of irAEs. In presence of these serious adverse events, the discontinuation of the immunotherapy with or without the administration of glucocorticoids should be considered. The development of persistent conduction alterations is infrequent and may require the implantation of a permanent PM.

