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Relationship between Immune Checkpoint Inhibitors and Myocarditis

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Abstract

Immune checkpoint inhibitors (ICIs) induce anti-cancer immunity. Several reports have indicated that treatment with ICIs is involved in myocarditis. In this Editorial, the relationship between ICIs and myocarditis is reviewed. The ICIs include ipilimumab, which is an anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) antibody, and nivolumab, pembrolizumab, and cemiplimab, which are anti-programmed cell death protein 1 (PD-1) antibodies, and avelumab, atezolizumab, and durvalumab, which are anti-programmed cell death-ligand 1 (PD-L1) antibodies. Myocarditis, defined as inflammation of the muscular walls of the heart, is induced by several infectious diseases and molecules. The investigation into ICI-related myocarditis is ongoing.

Keywords

Cancer; Cancer treatment; Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4); Immune checkpoint inhibitor; Myocarditis; Programmed cell death protein 1 (PD-1)

Immune checkpoint inhibitors (ICIs) in cancer treatment and myocarditis

Immune checkpoint inhibitors (ICIs) have been approved for cancer treatment and it was reported to have some cases of ICI-related cardiotoxicity [1]. There are some sporadic cases of ICI-associated myocarditis [2]. ICI-induced myocarditis in cancer patients has been reported [3]. ICI-related myocarditis is associated with a high reported mortality [4]. A comprehensive review of ICI therapy and myocarditis has found that ICI therapy-related myocarditis occurs at an average age of 68 years, and the characteristics of the patients include higher incidence in men and pretreatment cardiac history of hypertension [5]. Especially, ICI therapy with nivolumab, an anti-programmed death protein 1 (PD-1) monoclonal antibody, had mortality in 51.9% [5].

Preclinical experiments revealed that heterozygous loss of cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) gene in *Pdcd1* (encoding PD-1)-knockout mice demonstrated cardiac immune infiltration, and abatacept, a recombinant CTLA4-immunoglobulin fusion, rescued the fatal myocarditis in the *Ctla4^{+/-} Pdcd1^{-/-}* mice [6]. A study of cardiovascular magnetic resonance in ICI-related myocarditis demonstrated that late gadolinium enhancement was present in less than 50% of patients examined [7]. Investigation of the mechanism behind ICI-induced myocarditis needs to be continued in terms of the molecular pathway and infection-induced immunity perspectives.

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