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【 EDITORIAL 】

A Lack of Biomarkers for Cardiac Complications of Immune Checkpoint Inhibitor Therapy

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Immune checkpoint inhibitors (ICIs) as modern cancer treatments have demonstrated significant clinical benefit for various malignancies. However, these agents may induce a wide spectrum of immune-related adverse events (irAEs) by enhancing immune responses in non-target organs, including the cardiovascular system (1-3). Cardiac irAEs can be life-threating, but their mechanism and biomarkers remain unclear. In the case series from Tsuruda et al. (4), the authors reported serum concentrations of several cytokines, such as interleukin (IL)-6, IL-8, and granulocyte macrophage colony-stimulating factor, in three cancer patients with cardiac complications after ICI treatment at different stages in their clinical course. They reported that IL-8 was the predominant cytokine in the three patients of this report, and the data suggested that this might reflect the severity of cardiac complications after ICI therapy (4). However, the conclusions from this case series were very limited due to the data being reported for only three patients and the lack of data on the cytokine levels before ICI therapy. Further investigations are necessary to assess the association between cytokine levels and the pathology of cardiac irAEs. IL-8, also known as neutrophil chemotactic factor, is produced by many normal cells, including monocytes, macrophages, and endothelial cells, as well as by several types of malignant cells and tumor stromal cells (5). Recently, IL-8 has gained attention as a biomarker for monitoring and predicting clinical benefit from ICI therapy (6). Sanmamed et al. reported that changes in serum IL-8 levels were associated with the response to ICI treatment, and its levels were able to distinguish a response in cancer patients presenting with pseudo-progression (7). In addition to IL-8, several cytokines, chemokines, and other molecules are expected to be useful as biomarkers predicting the response to ICI therapy (5, 8). However, there are few reports of biomarkers for the prediction or early detection of irAEs, and no reports have described such markers for cardiac irAEs (8). ICI-related myocarditis has drawn the most attention, since it may result in life-threatening heart failure, advanced conduction disturbances, or ventricular arrhythmias, sometimes with a fulminant course (1, 3). Despite being the most clinically significant complication, studies of cardiac irAEs are less-advanced than those for other irAEs mainly due to their low incidence (0.04-1.14%) (9). Large-scale multicenter studies are needed to identify biomarkers that predict cardiac irAEs for the safe use of ICIs.

The authors state that they have no Conflict of Interest (COI).

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