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Editorial

Who Can Stop This Fire?

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▸ See the article "Thalidomide and a Dipeptidyl Peptidase 4 Inhibitor in a Rat Model of Experimental Autoimmune Myocarditis" in volume 53 on page 795.

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Myocarditis is an inflammatory condition characterized by inflammatory cell infiltration and cardiomyocyte injury such as degeneration and necrosis of adjacent cardiomyocytes showing a broad spectrum of clinical pictures and course.[1] The etiology of myocarditis varies including infection (viral, bacterial, or other organisms), drugs, toxic substances, and autoimmunity.[2][3] While viral infections are commonly attributed as the leading cause of myocarditis, autoimmune myocarditis also constitutes a significant portion of its etiology. In cases of non-infectious autoimmune myocarditis, immunosuppressive or immunomodulatory treatments like corticosteroids have demonstrated efficacy. Recent guidelines and scientific statements recommend the use of corticosteroids in immune-mediated fulminant myocarditis, eosinophilic myocarditis, giant cell myocarditis autoimmune cardiomyopathies like cardiac sarcoidosis when viral infection is not evident.[4] However, for patients unable to tolerate corticosteroids, alternative immunosuppressive therapies like methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide, pentoxifylline, and thalidomide can be considered, although their clinical use remains limited due to inconsistent outcomes and the risk of various side effects, including infections.[5]

In their study, Kim et al.[6] investigated the efficacy of thalidomide and a dipeptidyl peptidase (DPP) 4 inhibitor in a rat model of experimental autoimmune myocarditis (EAM). Thalidomide, known for its anti-tumor necrosis factor properties, exhibits immunomodulatory effects in various rheumatic and hematologic disorders. The DPP4 inhibitor, on the other hand, is primarily used for lowering glucose levels by inhibiting DPP4, which reduces the activity of incretin peptides like glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide, contributing to the attenuation of insulin secretion. Given the evidence of anti-inflammatory actions associated with these drugs, there was a reasonable expectation that they might mitigate myocardial damage during autoimmune myocarditis. However, the study yielded disappointing results. In the EAM rat model, neither thalidomide nor the DPP4 inhibitor demonstrated a reduction in myocardial inflammation and fibrosis, as determined through cellular, immunologic, echocardiographic, and histologic evaluations.

When conducting experiments related to myocarditis, it is essential to carefully consider the complexity of the inflammatory processes involved. Even though autoimmune myocarditis was induced through the same immunization process, the level of inflammatory reaction

Data Sharing Statement
The data generated in this study is available from the corresponding author upon reasonable request.

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may vary among individual subjects, necessitating different mechanisms or strengths of immunomodulation.[7] It should be noted that there were fatalities among the rats in the immunomodulatory treatment groups during the study, including one in the cyclosporine group in the 3-week experiment, one in the thalidomide group, and 2 in the DPP4 inhibitor group in the 6-week experiment.[6] Drugs that can alter the immune processes may compromise the body's ability to defend against concurrent infections or directly cause toxic responses in vital organs, leading to fatal outcomes.[8][9] Therefore, every treatment approach should be tailored to the individual's circumstances, particularly when dealing with potentially harmful drugs for serious conditions like myocarditis.[5] Thus far, corticosteroids remain the most widely used immunosuppressants in cases of non-infectious myocarditis due to their broad action on inflammatory processes and relatively lower incidence of side effects. Finding optimal fire extinguisher to put out fire caused by inflammatory process in myocardium requires precise and rapid target detection along with appropriate dosing and timing. Further translational research incorporating artificial intelligence may uncover new possibilities for effectively treating myocarditis.

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