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**EMERGING THERAPY FOR CORTICOSTEROID-DEPENDENT
AND COLCHICINE-RESISTANT PERICARDITIS: INTERLEUKIN-1 ANTAGONISTS**

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Pericarditis remains a challenging clinical entity, particularly in cases refractory to standard therapies such as corticosteroids and colchicine. Corticosteroid-dependent and colchicine-resistant pericarditis are associated with recurrent episodes, prolonged disease course and increased risk of complications. Recent advances in immunomodulatory treatments have highlighted the pivotal role of interleukin-1 (IL-1) in the inflammatory pathways underlying pericardial disease.

IL-1 is a cytokine with proinflammatory properties that regulates the nod-like receptor pyrin domain 3 (NLRP3), a component of the inflammasome signaling pathway, which promotes the production of systemic inflammatory mediators such as cyclooxygenase and prostaglandins. Pyrin is a cytoplasmic protein predominantly found in neutrophils and monocytes/macrophages.

Anakinra is a recombinant, nonglycosylated human interleukin-1 receptor antagonist that competes with and blocks the actions of IL-1 α and IL-1 β , thereby decreasing their systemic inflammatory effects. Riloncept is a dimeric fusion protein composed of parts of the IL-1 receptor and the IL-1 receptor accessory protein fused to the Fc region of IgG1. It acts as an interleukin-1 inhibitor.

A recent systematic review and meta-analysis of two randomized controlled trials and five observational studies, involving a total of 397 patients with corticosteroid-dependent and colchicine-resistant recurrent pericarditis – primarily of idiopathic origin (87%) – demonstrated that treatment with anti-IL-1 agents (anakinra or riloncept) significantly reduced the recurrence rate of pericarditis compared to placebo and standard therapy, without causing severe adverse events. These findings emphasize the role of the IL-1 pathway as a key mediator of systemic inflammation in pericarditis.

Another observational study indicated that anti-IL-1 therapies might reverse pericardial constriction, with complete resolution observed in 5 out of 8 patients (60%). In this study, 39 patients (74% with idiopathic etiology) were evaluated, with a baseline recurrence rate of 2.79 flares per patient-year and a median disease duration of 12 months. During follow-up, pericarditis recurred in 8 patients. After administering anakinra at 100 mg/day, five patients experienced complete resolution of pericardial constriction within a median of 1.2 months. The remaining three patients developed chronic pericarditis, necessitating pericardiectomy within a median of 2.8 months.

We also analyzed a double-blind, placebo-controlled, randomized trial designed to evaluate the efficacy and safety of interleukin-1 antagonists in patients with colchicine-resistant and corticosteroid-dependent pericarditis. The study involved 21 consecutive patients recruited from three Italian referral centers. All participants had recurrent pericarditis with at least three previous episodes, elevated C-reactive protein levels, resistance to colchicine, and dependence on corticosteroids. Anakinra was administered at a dose of 2 mg/kg daily, up to 100 mg, for 2 months. Patients who achieved remission of pericarditis were then randomized to either continue anakinra or switch to placebo for 6 months. Additionally, a prospective cohort study included patients receiving 100 mg of anakinra once daily subcutaneously, all the patients were monitored for 6 months. Eleven patients were randomized to anakinra, and 10 to placebo. Recurrent pericarditis developed in 9 of 10 patients in the placebo group, compared to only 2 of 11 in the anakinra group. The study also demonstrated that anakinra enabled corticosteroid withdrawal in all treated patients. Furthermore, treatment with anakinra facilitated tapering or discontinuation of corticosteroids without any subsequent recurrences of acute pericarditis.

The review of the above mentioned studies showed that interleukin-1 antagonists are effective in corticosteroid-dependant and colchicine-resistant recurrent pericarditis and if initiated early can alleviate the troublesome complications such as constrictive pericarditis.