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Brief Report

Methotrexate in recurrent postpericardiotomy syndrome

Nili Zucker, Aviva Levitas, Eli Zalzstein

Pediatric Cardiology Unit, Division of Pediatrics, Soroka University Medical Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel

Abstract The postpericardiotomy syndrome occurs in up to one-third of children undergoing cardiac surgery. Its treatment includes anti-inflammatory agents, diuresis, and drainage of effusions. Administration of steroids can have a dramatic effect, but is limited by adverse effects. Usually the syndrome lasts weeks only, and persistence beyond six months is exceptional. We describe a rare case of chronic postpericardiotomy syndrome, with recurrent pericardial effusions and steroid dependency, that was treated successfully with a low weekly dose of methotrexate.

Keywords: Pericardial disease; steroid dependency; postsurgical complication

The postpericardiotomy syndrome occurs in up to one-third of children undergoing cardiac surgery.[1] The symptoms include fever, malaise, chest pain, irritability, diminished appetite and, occasionally, arthralgia. These clinical features are commonly accompanied by the development of pericardial effusions, and at times pleural effusions. Pericardial tamponade, although uncommon, has been reported.[2]

The etiology of the syndrome is unclear. Engle et al.[1] postulated a viral pathogenesis, and demonstrated a significant increase in titers of antibodies to a number of viral agents. An immunologic mechanism has also been proposed, with a high titer of anti-cardiac antibodies identified in affected patients. Thus, Maisch et al.[3] demonstrated specific anti-sarcolemmal and anti-fibrillatory antibodies in the serums of over nine-tenths of patients with the post-pericardiotomy syndrome.

Treatment includes administration of anti-inflammatory agents, diuresis, and drainage of symptomatic effusions. Nonsteroidal anti-inflammatory agents, such as aspirin, indomethacin and ibufen, have been used widely. Colchicine has also been reported to be effective for the treatment of recurrent effusions. Administration of steroids can have a dramatic, positive effect, but their use is limited by the risk of immunosuppression and other known adverse effects.[4]

We describe here a unique case of chronic postpericardiotomy syndrome, in which the patient became dependent on steroids, but was treated successfully with a low weekly dose of methotrexate. To our knowledge, there is no previous report of the use of methotrexate for the treatment of recurrent pericardial effusion due to the postpericardiotomy syndrome.

Case report

A 10-year-old boy underwent surgical closure of an atrial septal defect within the oval fossa. After a delay of 45 days from surgery, he complained of chest pain and fever. An echocardiogram revealed a pericardial effusion of moderate severity. Treatment was initiated with aspirin at a dose of 70 mg/kg/day. One week later, the patient was free of symptoms, but a follow-up echocardiogram demonstrated the persistence of a large pericardial effusion. Aspirin was discontinued, and treatment with prednisone was started at a dose of 2 mg/kg/day. On follow-up examination, the pericardial effusion diminished, so the dose of prednisone was tapered over a 3-week period to cessation. When the prednisone was stopped, however, chest pain returned, and the pericardial effusion recurred. Another course of steroid therapy was begun, and tapered over a period of 4 weeks with

Correspondence to: Nili Zucker MD, Pediatric Cardiology Unit, Soroka University Medical Center, P.O. Box 151, Beer-Sheva, 84105, Israel. Tel: 972-8-6403050; Fax: 972-8-6400665; E-mail: niliz@bgumail.bgu.ac.il

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similar results, including recurrence of the symptoms and reappearance of the pericardial effusion when the therapy ended. Combination therapy with first prednisone and aspirin, then prednisone and indomethacin, followed by prednisone and rofecoxib, and subsequently prednisone, aspirin, and colchicine at a dose of 30 mg/day for 3 months, led to the same result when the steroid was discontinued. After 25 months following surgery, the patient remained dependent on the steroid, requiring 10 mg on alternate days. Methotrexate was started at a low dose of 10 mg/week, after initiating therapy at 5 mg/week. After 3 months of this treatment, the steroid as again tapered, and on this occasion could be stopped without evidence of relapse. There were no adverse effects. The patient continued to receive weekly treatment with methotrexate for another three months. Ten months after treatment was discontinued, there was no clinical or echocardiographic evidence of recurrence.

Discussion

The etiology and pathogenesis of the postpericardiotomy syndrome remain unclear. Several authors have noted a seasonal variation in its incidence, and have suggested that a new or reactivated viral infection could be a factor. In a large clinical series of children reported in 1980, Engle and colleagues[1] implicated an autoimmune process, concomitant with a viral infection, as a possible etiology for postpericardiotomy syndrome. A fourfold rise in viral antibody titer was found in over two-thirds of those with clinical evidence of the syndrome, compared with only one-twentieth in those without clinical evidence of pericardial involvement. A recent study using serology, polymerase chain reaction, and viral cultures,[5] however, has failed to confirm a viral etiology. Another study[6] demonstrated an association between the postpericardiotomy syndrome and circulating anti-cardiac antibodies, with the formation of immune complexes during exposure of the cardiac antigen at surgery. Maisch et al.[3] investigated the subtypes of specific autoantibodies and showed that over nine-tenths of their patients with postpericardiotomy syndrome had antibodies to myocardium and skeletal muscle, including anti-sarcolemmal and anti-fibrillary antibodies. In light of the types of immunoglobulin, and the timing of their appearance in the serum, the authors suggested that the anti-fibrillary antibodies were related to a primary immune response, while the anti-sarcolemmal antibodies reflected a secondary response. Surgery and trauma were the hypothesized causes of the myocardial injury, which led to the release of the myocardial antigens.[3]

Various anti-inflammatory agents have provided symptomatic improvement in patients with the syndrome. Salicylates at anti-inflammatory doses are often given to children and adults.[2] In a double-blind, placebo-controlled study of 149 patients with the syndrome, ibufen and indomethacin relieved symptoms and shortened the duration of illness.[7]

Steroids are often recommended for patients with more severe symptoms and large pericardial effusions.[2] In one double-blind study,[8] patients with severe postpericardiotomy syndrome received either salicylates or steroids. Those receiving prednisone had earlier resolution of clinical symptoms and findings. The titer of anti-cardiac antibodies was not affected in those treated with salicylates, but these antibodies disappeared from the serum earlier than expected in patients treated with prednisone. In another double-blind placebo-controlled trial of steroids in children,[4] significant relief of symptoms was noted after a week of treatment. Caution is required with administration of steroids, however, because of their immunosuppressive effect and the well recognized tendency for relapse to occur when treatment is stopped.

Methotrexate, an immunosuppressant antagonist of folic acid, has an anti-inflammatory effect when given in low doses, and facilitates reduction of the dosage of steroids among patients with severe chronic asthma, severe psoriasis, and rheumatoid arthritis.[9] It has also been used successfully in the treatment of pericardial effusion in a patient with rheumatoid arthritis.[10] In our patient, who became dependent on steroids, use of methotrexate enabled us to reduce and eventually stop the medication with steroids. To the best of our knowledge, our case is unique, both in its duration and the reaction of the patient to medication. The use of methotrexate, therefore, warrants attention in cases of prolonged recurrent pericarditis where a patient develops dependency on steroids.

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