Cyclosporin A in the treatment of idiopathic recurrent pericarditis: a case report

Lessio S, Laveder F, Marcolongo R, Rigoli A, Tona F

Homepage:

www.kup.at/jcbc

Online Data Base Search for Authors and Keywords
Cyclosporin A in the treatment of idiopathic recurrent pericarditis: a case report

S. Lessio, F. Tona, A. Rigoli, F. Lavender, R. Marcolongo

The aetiology of idiopathic recurrent pericarditis is still unknown, but there is evidence of an immune-mediated pathogenesis. While there is general agreement on non-steroidal anti-inflammatory drugs as initial treatment for the disease, the use of steroids or immunosuppressive agents still remains controversial; these drugs are usually reserved for selected or resistant cases, before considering surgical management.

We describe a 44 years old man who presented recurrent pericarditis and familial non-immune-mediated thrombocytopenia, who obtained a stable remission following a five months treatment with cyclosporin A. The drug was administered alone because of the patient’s poor tolerance for corticosteroids and the risk of myelosuppression related to cytotoxic immunosuppressive drugs. Before cyclosporin A therapy, he suffered three consecutive recurrences over a period of four months despite prolonged treatment with non-steroidal anti-inflammatory drugs and/or prednisone. In the two years following cyclosporin A discontinuation, the patient did not experience any further recurrence of the disease.

In the patient described here, cyclosporin A alone appeared effective in preventing the recurrences of pericarditis. This evidence supports the hypothesis that idiopathic recurrent pericarditis may have an immune-mediated pathogenesis and suggests further study on the role of immunosuppressive agents in the management of the disease. J Clin Basic Cardiol 1999; 2: 130–1.

Key words: Pericarditis, cyclosporin, immunosuppressive agents

Primary acute pericarditis is usually a self-limiting disease with a good prognosis [1]. Nevertheless, chest pain and fever, along with or without pericardial effusion and typical ECG signs may recur in 15–30 % of patients over a period of months or years. Treatment of recurrences is often difficult and surgical management may be necessary; furthermore, rare complications have been reported, including pericardial tamponade, haemopericardium and myocarditis [2].

Although the aetiology of idiopathic recurrent pericarditis (IRP) remains unknown, an immune pathogenesis is presumed [2–3]. Despite this assumption, the use of immunosuppressive drugs in the treatment of the disease remains controversial because of the limited number of clinical studies [2]. While there is general agreement regarding the use of non-steroidal anti-inflammatory drugs (NSAIDs) as initial therapy, steroids or other immunosuppressive agents are usually reserved for selected, resistant cases.

We describe a patient with IRP refractory to NSAIDs and prednisone, who was successfully treated with cyclosporin A (CsA) as single therapy.

Case report

A 44 year old man was admitted to our hospital in May 1996, because of recurrent pericarditis. He had a history of penicillin allergy and familial non-immune-mediated thrombocytopenia. In January 1996 he was first admitted to another hospital because of the gradual onset of chest pain following a flu-like episode. On that occasion laboratory tests gave the following results: leukocytes 21.64 x 10⁹/L (82.1 % neutrophils); platelets 27.0 x 10⁹/L; erythrocytes sedimentation rate (ESR) 34 mm/h; C reactive protein (CRP) 0.013 mmol/L (13 mg/dL); fibrinogen 9.91 g/L (normal range 2.0–4.0 g/L); serum IgG 19.0 g/L (normal range 8.0–15.0 g/L); IgM 3.72 g/L (normal range 0.45–1.5 g/L); IgA 5.90 g/L (normal range 1.0–4.90 g/L); serum circulating immunocomplex (CICs) and RA-test were negative. Antinuclear, anti-DNA, antimitochondria, anti-smooth muscle, anti-gastric parietal cells, antimicrosome, antithryoglobulin, antcardiolipin antibodies, VDRL and cryoglobulins were negative. Peripheral blood lymphocyte phenotype was normal. Hepatitis B and C serology was negative. Other routine tests were negative or normal.

Electrocardiogram showed sinus tachycardia (110/min), and diffuse ST-segment elevation; cardiomegaly was found at chest X-ray and the echocardiography revealed a pericardial effusion of about 400 mL. The diagnosis of acute pericarditis was made and a therapy with aspirin (3 g/day) was started.

At first, the patient obtained a rapid benefit, but when, after 2 weeks, the drug was tapered, fever, chest pain and laboratory signs of inflammation, along with ECG and echographic evidence of pericardial effusion recurred. The symptoms immediately disappeared when treatment with prednisone (0.6 mg/Kg/day for 6 days, then gradually reduced) was undertaken. Nevertheless, after 4 weeks, when prednisone was tapered to 0.3 mg/Kg/day, the patient suffered from a second recurrence, which was treated again with prednisone, 1 mg/Kg/day. After one week, the patient developed steroid-related psychiatric symptoms (mania) and so prednisone was gradually reduced to 0.1 mg/Kg/day within 2 months, when he suffered from a third pericarditis recurrence.

The patient was then referred to our hospital. Pericardial fluid sampling and pericardial biopsy were not performed because of the bleeding risk due to thrombocytopenia; secondary causes of pericarditis had been previously excluded and the diagnosis of idiopathic recurrent pericarditis was confirmed.

Because of the inefficacy of NSAIDs, the poor tolerance to high dose prednisone and the thrombocytopenia, which contraindicated cytotoxic drugs, after informed consent, CsA single therapy was started. To minimize side effects, the patient...
received a low-dose regimen (3 mg/kg/day, in two divided doses, using the new oral formulation Sandimmun Neoral®), avoided the NSAIDs association and performed a careful laboratory follow-up.

Following the first month of treatment, inflammatory indexes, electrocardiogram, chest X-ray and echocardiography returned steadily normal. Thereafter, CsA alone was maintained for four months, then stopped. During the treatment and a follow-up period of two years after CsA discontinuation, the patient has been completely free from recurrences and did not show any symptom or sign of CsA toxicity. At present, the patient condition remains stable, without any treatment.

Discussion

In the patient discussed here, immunosuppressive therapy with CsA was associated with the complete and stable remission from every sign or symptom of pericardial inflammation. Because of the close temporal relationship with CsA therapy, the normalisation of inflammatory indexes and the resolution of the clinical picture that occurred coincidentally with immunosuppression, a spontaneous remission appears unlikely.

Some evidence seems to suggest the possible immune pathogenesis of IRP, which has been also associated with hypersensitivity diseases [1–3]. It has been proposed that recurrences may be the result of auto-aggression mediated by cytotoxic T-lymphocytes and natural killer (NK) cells [3]. This mechanism seems to take place in rheumatoid pericarditis, where the presence of CD8+ T-lymphocytes has been demonstrated in the pericardial inflammatory infiltration [4]. In IRP, indeed, a prominent lymphocytic infiltration has been reported and immunological studies provide evidence of T-lymphocyte autosensitization against cardiac antigens [5]. However, pericardial inflammation and its recurrences could be also sustained by an antibody-mediated reaction (type II and immunocomplex deposition).

In this view, a treatment with NSAIDs or low dose/short-term steroid, which at first could be effective in controlling pericardial inflammation, may prove inadequate to maintain a long-term inhibition of local immune responses taking place during IRP. The lasting resolution of pericardial inflammation observed in our patient after a prolonged treatment with CsA supports this hypothesis. Unlike the cytotoxic agents, such as azathioprine or cyclophosphamide, CsA does not kill immune effectors, but selectively inhibits the activation and the proliferation of T cells, helper T-lymphocytes being the most important target. The molecular mechanism of action of CsA, which interferes with IL-2 synthesis, has been elucidated [6]. In the absence of T-cell help, the generation of both cytotoxic T-lymphocytes and T-cell-dependent antibody responses is inhibited. Thus, a prolonged CsA treatment could effectively inhibit and eventually eradicate T cell-mediated immune responses taking place in IRP.

Therefore, immunosuppressive agents, which antagonise both pericardial inflammation and local immune responses, may be the treatment of choice in most cases of IRP.

In two prospective clinical trials, treatment with colchicine proved to be effective in preventing the recurrences in most cases of IRP [7–8], since its anti-inflammatory effect is due to the inhibition of neutrophils degranulation, colchicine could be active also when it is sustained by circulating immune-complex deposition.

At present, we don’t know exactly which is the best treatment for IRP. However, before considering surgical management, it seems reasonable to evaluate the possibility of immunosuppressive treatment. Recently, the efficacy of long-term immunosuppression with methylprednisolone pulse therapy [9], azathioprine [10], cyclophosphamide and high dose prednisone [11] has been reported in IRP. CsA and other new immunosuppressives, such as FK-506, rapamycin and mycophenolate mofetil, due to their cost and toxicity, should be reserved for patients with proved steroid resistance or intolerance or when cytotoxic drugs are contraindicated.

CsA has already proved effective in the treatment of pericarditis related to rheumatoid arthritis or other autoimmune diseases [6], but, to the best of our knowledge, this is the first report describing the successful use of CsA in a patient with recurrent pericarditis not related to a connective tissue disease. Thus, we suggest a further study of the pericardial immune responses and the effect of immunosuppressive agents in the selected subgroup of patients with resistant IRP.

References

Mitteilungen aus der Redaktion

Besuchen Sie unsere
zeitschriftenübergreifende Datenbank

✔ Bilddatenbank ✔ Artikelldatenbank ✔ Fallberichte

Haftungsausschluss
Die in unseren Webseiten publizierten Informationen richten sich ausschließlich an geprüfte
und autorisierte medizinische Berufsgruppen und entbinden nicht von der ärztlichen Sorgfaltspflicht sowie von einer ausführlichen Patientenaufklärung über therapeutische Optionen
und deren Wirkungen bzw. Nebenwirkungen. Die entsprechenden Angaben werden von den
Autoren mit der größten Sorgfalt recherchiert und zusammengestellt. Die angegebenen Do-
sierungen sind im Einzelfall anhand der Fachinformationen zu überprüfen. Weder die Autoren,
noch die tragenden Gesellschaften noch der Verlag übernehmen irgendwelche Haftungsan-
sprüche.

Bitte beachten Sie auch diese Seiten:

Impressum Disclaimers & Copyright Datenschutzerklärung

e-Journal-Abo
Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.
Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.
Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der markt-
üblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

✔ Bestellung e-Journal-Abo