

## A case of rheumatic fever with multiple recurrences of carditis

İbrahim İlker Çetin, Yunus Emre Bıkmaz, Birgül Varan, Kürşad Tokel

Department of Pediatrics, Başkent University Hospital, Ankara, Turkey

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Rheumatic fever is still one of the major public health problems in developing countries. Recurrences have been reported during continuous regular prophylaxis. Here, we describe a 13-year-old girl who had four apparent recurrences of carditis while on a regimen of intramuscular benzathine penicillin G (BPG) every three weeks. The interesting and special features of this case were the presence of frequent recurrences of carditis with no evidence of arthritis despite regular BPG injections every three weeks, the requirement of long-term corticosteroid therapy due to these recurrences, and the shortness of time periods between attacks after withdrawal of steroid therapy. In this case, the administration of supraphysiologic doses of glucocorticoids caused iatrogenic Cushing syndrome with decreased bone mineral density and bilateral avascular tibial necrosis mimicking the symptoms of arthritis. Thus, this is a rare case. In similar cases with recurrences of either arthritis or carditis, instead of long-term corticosteroid therapy, we suggest a regimen of BPG prophylaxis every two weeks rather than every three weeks or monthly BPG injections because of the superiority of the every two weeks schedule in the adequate control of rheumatic fever recurrences, as shown in some previous studies.

*Key words:* rheumatic fever, carditis, multiple recurrences, prophylaxis.

Rheumatic fever is an inflammatory disease that follows infection with certain strains of group A beta-hemolytic streptococci (GABHS). Rheumatic fever is an endemic disease in developing countries. Despite a dramatic fall in the incidence, it remains the major cause of morbidity and mortality from acquired heart disease in developing countries. Acute carditis with the subsequent development of rheumatic heart disease is the most serious consequence of rheumatic fever, as it is the only one that can cause serious disability<sup>1</sup>. Recurrences in patients receiving regular secondary prophylaxis are not unusual; however, frequent recurrence of carditis in a patient is very rare<sup>2</sup>.

We report a patient with symptoms, signs and laboratory evidence of multiple recurrences of carditis despite benzathine penicillin G (BPG) injections every three weeks.

### Case Report

A 13-year-old girl was referred to our hospital for mitral valve replacement because of rheumatic valvular disease. Her past history

revealed that she had been admitted to a local hospital with complaints of fever, fatigue, palpitation and swelling of face and feet three years ago. On the basis of a systolic murmur of IV/VI grade, heard at the 5<sup>th</sup> intercostal space on the left sternal border reflecting to the axilla, an increased titer of antistreptolysin O (ASO), and an increased level of C-reactive protein (CRP) together with fever, she had been diagnosed as rheumatic carditis. Telecardiogram had shown increased cardiothoracic index. Echocardiography had revealed moderate mitral regurgitation, left atrial and left ventricular dilatation and minimal pericardial effusion. The patient had been started on regular injections of BPG every three weeks for prophylaxis. Despite regular BPG administrations with adherence to the recommended regimen as stated by the family members, she had had four recurrent episodes of carditis. Each episode had been documented as either worsening of congestive heart failure despite anti-congestive medications or with involvement of valves not previously affected, together with a new GABHS infection (Table I). There had been no other

Table I. Acute Phase Reactants and ASO Titer at the Initial Attack and During Recurrences

Time interval	ASO	CRP	ESR
Initial attack	517	26	30
16 weeks later	665	103	90
57 weeks later	358	122	40
17 weeks later	692	19	82
18 weeks later	248	106	45

ASO: Antistreptolysin O (IU/ml). CRP: C-reactive protein (mg/L). ESR: Erythrocyte sedimentation rate (mm/h).

major criteria of rheumatic fever. For each episode, she had been treated with steroids for four weeks (prednisolone for 2 weeks at a dose of 2 mg/kg/day followed by tapered dose for 2 weeks). Recurrences had been seen 16 to 57 weeks later following corticosteroid withdrawal and between episodes, acute phase reactants and ASO titers had been demonstrated as normal (Table II).

Table II. Duration of Therapy and Time of Recurrence After Withdrawal of Therapy

Time interval	Duration of steroid therapy
Initial attack	No steroid
16 weeks later	4 weeks
57 weeks later	4 weeks
17 weeks later	4 weeks
18 weeks later	4 weeks

\*Time interval indicates the interval between withdrawal of therapy and recurrence.

When we saw the patient in our clinic during the last attack, she was on the second week of steroid treatment. On physical examination, her weight was 48 kg (50<sup>th</sup> percentile) and height 135 cm (<3<sup>rd</sup> percentile), pulse rate 124 bpm, blood pressure 100/70 mmHg, and respiratory rate 26 pm. She had cushingoid appearance with moon face, buffalo hump, truncal obesity and purplish striae on the hips, abdomen and thighs. There was no organomegaly. The cardiac examination revealed a pansystolic murmur at the left sternal border.

In laboratory studies, hemoglobin was 11.3 g/dl, white blood cell count 11,000/mm<sup>3</sup>, CRP 106 mg/L (0-10), ASO 71 IU/ml (0-200), and serum electrolytes, SGOT, SGPT, blood urea nitrogen (BUN), and creatinine were normal. The electrocardiography demonstrated p-mitrale, left atrial dilatation and left axis deviation. Cardiothoracic index was 0.65 on telecardiogram. Echocardiography revealed thickened mitral valve leaflets with incomplete

coaptation and severe mitral regurgitation, a mild tricuspid regurgitation, minimal aortic regurgitation, and left atrial and left ventricular dilatation. The patient was operated for mitral valve replacement with preoperative and postoperative additional doses of steroid to prevent acute adrenal crisis. After surgery, the dose of steroid was tapered gradually. Surprisingly, swelling and pain on the left knee were noticed four days after corticosteroid withdrawal. Because of the symptoms arising just after the withdrawal of steroid therapy, we suspected the possibility of connective tissue diseases. Her serum levels of complements C3 and C4 were normal, antinuclear antibody (ANA), antidouble-stranded DNA (anti-dsDNA), and perinuclear and cytoplasmic antibodies to nuclear cytoplasmic antigens (p-ANCA, c-ANCA) were negative. Radiography and computerized tomography revealed bilateral avascular tibial necrosis. Determination of bone mineral density showed osteoporosis.

## Discussion

Rheumatic heart disease remains the most common form of acquired heart disease in all age groups in many developing countries. Recurrences are most likely to be seen in patients who have had one attack of rheumatic fever, and the clinical features of the recurrences tend to mimic those of the initial attack. Although the Jones criteria are fulfilled by most of the patients with recurrences of rheumatic fever, in some patients this may not be valid.

Recurrence rate (RR) of rheumatic fever has been reported in several previous reports. In 1964 Feinstein et al.<sup>3</sup> found two recurrences in 156 patients with a RR of 0.04 per patient per year. In 1982, Sanyal et al.<sup>4</sup> reported a RR of 0.006 per patient per year in 65 patients. In 1992, Majeed et al.<sup>5</sup> found two recurrences in 64 patients with a RR of 0.003 per patient per year. In the present study, four recurrences developed in one patient within three years.

The prognosis of rheumatic fever depends on the clinical manifestations present at the time of the initial episode and the presence of recurrences. There is a positive correlation between the risk of residual heart disease and the severity of the initial cardiac involvement. Patients with carditis during the initial episode are more likely to have carditis with recurrences and the

risk of permanent heart damage increases with each recurrence<sup>5,6</sup>. Recurrent attacks following reinfection of the upper respiratory tract with GABHS are not surprising in patients who have had rheumatic fever. Therefore, long-term continuous chemoprophylaxis is inevitable in these patients<sup>7</sup>.

Arthritis is the major manifestation of recurrences of rheumatic fever<sup>8</sup>. In this report, the features of unusual presentation of the case were the presence of frequent recurrences of carditis, resulting in severe rheumatic heart disease and finally mitral valve replacement despite continuous regular BPG injections every three weeks; the requirement of long-term corticosteroid therapy due to these recurrences; and the shortness of the time period after stopping steroid therapy to a new attack. In this case, carditis was the major and only manifestation.

During her stay in our hospital, the patient had pain and swelling on the left knee, for which she was further investigated for the possibility of connective tissue diseases that can present with both arthritis and carditis. Cardiac involvement can occur in all connective tissue diseases<sup>9</sup>, but it is most common in systemic lupus erythematosus. Pericarditis without tamponade is the usual presenting feature. The characteristic atypical verrucous endocarditis (Libman-Sacks) can cause valve regurgitation. In juvenile rheumatoid arthritis, cardiac abnormalities usually occur in the acute systemic form of the disease with pericarditis, myocarditis and occasionally mitral regurgitation. Echocardiography may demonstrate a pericardial effusion in children with no clinical signs of heart disease. Cardiac failure is an uncommon complication but can be fatal. Connective tissue diseases were investigated, but none of them was detected in the patient. In our case, the administration of supraphysiologic doses of glucocorticoids caused iatrogenic Cushing syndrome with clinical features including moon face, buffalo hump, purplish striae, truncal obesity, decreased muscle mass, fatigue, increased bruisability, short stature and decreased bone mineral density. Radiography and computerized tomography revealed bilateral avascular tibial necrosis secondary to steroid therapy. A question of whether the recurrences of rheumatic fever should be best left untreated has arisen in consequence of such serious complications of steroid therapy.

In several previous reports, it was determined that the recurrences of rheumatic fever can be prevented with BPG prophylaxis every two or three weeks rather than monthly BPG injections<sup>10,11</sup>. Ginsburg et al.<sup>11</sup> had shown that BPG in the recommended doses may not provide adequate serum penicillin activity to prevent reinfection with GABHS in some patients beginning as early as 18 days after the injection. The results of the study of Kassem et al.<sup>10</sup> had shown the superiority of the every two weeks schedule in the adequate control of rheumatic fever recurrences. We suggest that this schedule should be implemented for prophylaxis of rheumatic fever in a selected patient group with at least one recurrence of the disease.

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