with moderate pericardial effusion. Doppler examination revealed a dip-plateau aspect of the pulmonary regurgitation flow. Cardiac magnetic resonance imaging (MRI) revealed inflammation of the pericardium with circumferential pericardial effusion, increased thickness and high signal intensity of both visceral and parietal layers of the pericardium due to the enhancement 10 min after gadolinium injection (Fig. 1). We started anti-inflammatory therapy with three intravenous boluses (500 mg each) of methyl-prednisolone. No improvement was noted after 1 week. In an attempt to avoid surgical epicardiectomy, we decided to try antagonization of TNF-α/C11 with subcutaneous etanercept, 25 mg twice weekly. After 1 week, oedema and ascites had completely disappeared. Cardiac Doppler revealed that the dip-plateau aspect had resolved. Pericardial extravasation had decreased from 14 to 5 mm. The patient was discharged from hospital 10 days after the start of anti-TNF-α therapy. Six months later, no right ventricular signs or oedema have recurred. The MRI revealed that the pericardium was still abnormally thick, but it was now mobile throughout the cardiac cycle and did not enhance after contrast administration (Fig. 1).

Pericarditis occurs in 30–50% of rheumatoid arthritis patients, but only 1–3% were symptomatic in a set of patients assessed before 1990 [2]. Analysis of pericardial fluid commonly reveals inflammation with neutrophils [2]. Corticotherapy is usually curative but does not prevent recurrences or complications, and disease-modifying drugs are not efficient in rheumatoid pericarditis [2]. Complications of pericarditis, such as cardiac tamponade or constriction, are very rare in rheumatoid arthritis: 200 cases have been reported in the literature [3]. In rheumatoid pericardial constriction, steroids are totally inefficient and epicardiectomy is the only effective treatment described so far [3].

In our case, the first two episodes of pericarditis were complicated by cardiac tamponade. Surgical pericardial drainage preceded intensification of steroid therapy, which was successful on both occasions, with complete regression of clinical and echocardiographic abnormalities within 1 week. During the third
episode within 4 months, constrictive pericarditis was diagnosed using echocardiography and Doppler, which showed signs typical enough to avoid cardiac catheterization [4]. Corticosteroid therapy, the aim of which was to reduce pericardial inflammation and effusion, was totally inefficient despite very high doses of methylprednisolone [5]. We decided to try anti-TNF-α therapy because the patient was quite reluctant to undergo a third surgical intervention and because anti-TNF therapy is the reference treatment for rheumatoid arthritis [6]. Dramatic clinical echocardiographic improvement followed rapidly: the dip-plateau disappeared within 1 week, and pericardial effusion completely resolved within 1 month. As pericardial inflammation involved the entire circumference, as shown by MRI, it is likely that the fibrosis was not yet fixed [7].

This report strongly suggests that anti-TNF-α therapy is effective in cases of constrictive pericarditis complicating rheumatoid arthritis, with established resistance to more conventional disease-modifying drugs. We conclude that etanercept therapy seems to be highly effective in inflammatory and constrictive pericarditis complicating rheumatoid arthritis, and should be considered as an alternative to surgery.

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Letters to the Editor

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Periodic fever as a presenting sign of childhood acute lymphoblastic leukaemia

Sir. Periodic fever in childhood is usually due to genetic autoinflammatory diseases but may be the presenting sign of more serious illness. We describe a girl with acute lymphoblastic leukaemia (ALL), presenting with periodic fever.

The patient, an East-Asian girl, had been healthy until the age of 11 yr when she started to experience episodes of 6–10 days of musculoskeletal pain and fever of 39–40°C, occurring about once a month. Over time, the pain during these attacks worsened. Its localization varied from chest, shoulders and elbows to the sacro-iliac region and hips and sometimes the abdomen. Non-steroidal anti-inflammatory drugs (NSAIDs) reduced the pain. Between episodes she was completely well. She had not recently travelled abroad. The family history was negative for periodic fever.

Physical examination between attacks was initially normal, but later revealed painful limitation of movement in hips, shoulders and elbows, without frank arthritis.

During the fever episodes the patient was anaemic (haemoglobin 6.0–8.7 mg/dl). Peripheral blood repeatedly showed normal platelet, white cell and differential counts and no blasts. The erythrocyte sedimentation rate (ESR, 53–140 mm/h) and C-reactive protein (CRP, 52–152 mg/l) were raised. Between episodes the CRP was below 5 mg/l. Analysis of the anaemia revealed a heterozygous beta-thalassemia.

There were no localizing signs of infection and the tuberculin test was negative. X-rays of chest, abdomen, lumbar spine and pelvis, ultrasound of the abdomen and hips and magnetic resonance imaging (MRI) of the lumbar spine were all normal.

The genes MEVF (familial Mediterranean fever), TNFRSF1A (TNF receptor associated periodic syndrome, TRAPS) and CIAS1 (Muckle–Wells syndrome) were analysed. All exons and intron–exon boundaries were sequenced and were found to be normal. Serum immunoglobulin D (IgD, 51 IU/ml) and urinary mevalonic acid excretion (hyper IgD periodic fever syndrome) were also normal.

Fifteen months after the first symptoms, the girl presented with extreme pallor, 39°C fever, respiratory distress and pain in the back, legs and arms. On examination she had tachycardia (150/min), low blood pressure (115/50 mmHg), a -systolic murmur over the base of the heart and crackles over the right dorso-basal lung area. Blood tests showed a raised lactic dehydrogenase (LDH, 1227 U/l) and ESR (>140 mm/h), severe anaemia (haemoglobin 2.9 mg/dl) and thrombocytopenia (29 x 10^9/l). The white cell count was normal (5.8 x 10^9/l), but now showed peripheral blast cells (3.03 x 10^9/l).

A bone marrow aspirate contained 89% blasts with a pre-B-cell immunophenotype, confirming a diagnosis of ALL. Cerebrospinal fluid was normal and a chest X-ray showed no widened mediastinum or lymph nodes. Liver and spleen were enlarged on ultrasound.

Induction chemotherapy according to the DCOG ALL-9 protocol was started and soon the fever and pain disappeared. Both leukaemia and fever have remained in complete remission for 12 months now.

The cause of episodic high-grade fever and musculoskeletal pain in this patient had remained elusive for over a year. A hereditary periodic fever syndrome was suspected [1], but could not be confirmed. Moreover, the episodes were unusual in that bone pain and profound anaemia were prominent. The fever pattern was not typical for Pel–Ebsenstein fever, which typically lasts 1–2 weeks, separated by afebrile periods of similar duration [2]. We initially ascribed the anaemia to the combination of chronic inflammation and beta-thalassemia minor.

Fever is a common sign of leukaemia [3, 4], but periodic fever as a prodrome is rare. One report describes chronic relapsing fever in an adult over a 15-month period, before leukaemia (not otherwise specified) was diagnosed [5]. Two cases of relapsing fever preceding acute myelogenous leukaemia have been reported [6]. One, a 26-yr-old male, had a 6.5 month history of bone pain, progressive anaemia, neutropenia and episodic fever before a third blood smear showed leukaemia. The other, a 28-yr-old male, had suffered intermittent fever and migratory pain around the joints for