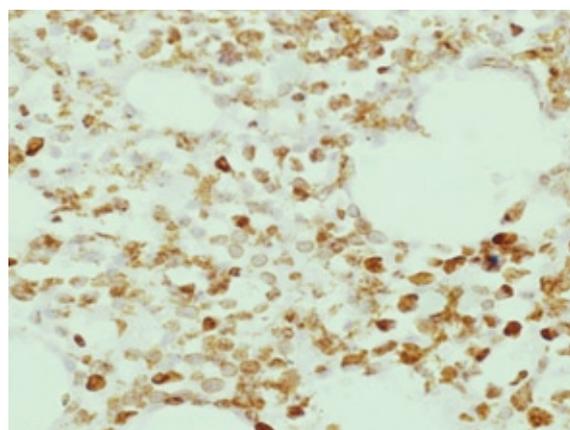
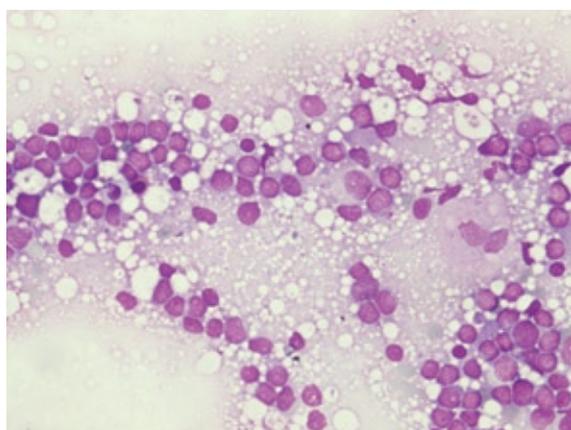


**ACUTE UNDIFFERENTIATED LEUKAEMIA IN AN ADULT PRESENTING AS ARTHRITIS**

Dear Sir,

Skeletal manifestations of acute leukaemia (bone or back pain, arthritis or radiographical abnormalities of skeleton) are well described in children<sup>(1)</sup>. Arthritis as the first manifestation of acute leukaemia is however extremely uncommon in adults<sup>(2)</sup>. We present an unusual case of a 35-year-old man who had acute-onset additive, symmetrical, inflammatory polyarthritis involving the knee, ankle, wrist, metacarpophalangeal and elbow joints and progressive dyspnoea on exertion of ten weeks' duration. He was in Steinbrocker functional class III. There was no history of fever, cough, orthopnoea, paroxysmal nocturnal dyspnoea, oral ulcers, oedema, oliguria, skin rash or nodule, and bleeding diathesis. He had seen a general practitioner where investigations showed a haemoglobin level of 8 g/dL, total leukocyte count 8,000/mm<sup>3</sup> (neutrophils 75%, lymphocytes 22%, monocytes 2%, eosinophils 1% with no blasts). He was started on non-steroidal anti-inflammatory drugs along with haematinics but there was no relief.

Examination revealed tachycardia, tachypnoea, pallor, and active synovitis of both metacarpophalangeal, wrist, and elbow joints. The rest of the general and systemic examination was unremarkable. Investigations revealed a haemoglobin level of 6.5 g/dL, corrected reticulocyte count 1%, mean corpuscular volume 80 fL, total leukocyte count 12,000/mm<sup>3</sup> with 93% blasts and platelets 20,000/mm<sup>3</sup>, erythrocyte sedimentation rate of 64 mm for the first hour and C-reactive protein 2.6 mg/dL (normal <0.6 mg/dL). Renal and liver function tests were normal. Serum uric acid was normal (5.6 mg/dL). Blood, urine and throat cultures were sterile. Stool for occult blood on three consecutive days was negative and upper gastrointestinal endoscopy did not reveal any abnormality. Serology for rheumatoid factor, antinuclear antibody and antineutrophil cytoplasmic antibody was negative. Radiograph of the chest was normal while that of the hands showed soft tissue swelling at the wrists. There was no erosion or juxta-articular osteopenia. Radiographs of the knee, ankle and elbow were normal. Joint aspiration was not done because of thrombocytopenia. Bone marrow examination showed 93% blasts with positivity for both myeloperoxidase stain and terminal deoxynucleotidyl transferase stain (80% of the cells) (Fig. 1a). Flow cytometry from the peripheral blood showed cluster of differentiation CD 7 +ve and CD 19 -ve blasts (Fig. 1b). A diagnosis of acute undifferentiated leukaemia (M0) was made and the patient was referred for further management.



**Fig. 1** (a) Bone marrow aspirate shows sheets of immature cells (May-Grunwald-Giemsa,  $\times 40$ ); (b) Cells shows CD7 immunostain positivity (May-Grunwald-Giemsa,  $\times 40$ ).

Arthritis can occur at any time during the course of acute leukaemia. Very rarely, arthritis is the initial manifestation of acute leukemia in adults<sup>(3)</sup>. Gur et al reported such a presentation in eight out of 139 patients of adult acute leukaemia over a ten-year period<sup>(4)</sup>. It may lead to delay in diagnosis and therapy<sup>(5)</sup>, and any delay in therapy is associated with poor prognosis. In the index case, the initial full blood count showed only anaemia but in the hospital, there was no diagnostic difficulty as the first haematological report showed blasts in the peripheral blood. Similarly, relapse of acute leukaemia may mimic arthritis<sup>(6)</sup>. The most common clinical presentation of leukaemic arthritis is additive or migratory asymmetrical oligoarticular large joint arthritis. The joints most commonly involved are the knee, followed by the ankle, wrist, elbow, shoulder and hip. Onset of arthritis may be sudden or insidious, and parallel the course of acute leukaemia<sup>(7)</sup>.

The exact cause of arthritis in acute leukaemia is not clear. However, various postulated mechanisms include: infiltration of synovium by the leukaemic cells, haemorrhage into the joint, hyperuricaemia, synovial

reaction to periosteal or capsular infiltration, immune complex-induced synovitis and septic arthritis. Synovial infiltration appears to be the predominant mechanism<sup>(3,5)</sup>. This has been well documented in a few case series and case reports<sup>(7-10)</sup>, and further supported by the fact that clinical features of synovitis respond to chemotherapy and improvement of joint pain is the first sign of a clinical response to chemotherapy. Moreover, in series by Thomas et al's series, none of the patients with haematological response had persistent joint pain and upon recurrence of leukaemia, the location and character of joint pain was similar to each patient's initial symptoms<sup>(2)</sup>. In one report, excessive expression of interleukin-1 $\beta$  and tumour necrosis factor  $\beta$  was demonstrated in the synovium of a patient with destructive arthritis due to leukaemic infiltrate of B-cell chronic lymphocytic leukaemia<sup>(10)</sup>.

In 1994, Evans et al reviewed leukaemic arthritis in 29 adults from 1986 to 1994, and had reported that joint pains out of proportion to the degree of inflammation, arthritis refractory to anti-inflammatory drugs, back pain with nocturnal exacerbation, and unexplained weight loss may suggest a possibility of underlying leukaemia<sup>(7)</sup>. In other studies, early significant osteopenia or lytic bone lesions<sup>(4)</sup>, presence of out-of-proportion anaemia, leukopenia or leukocytosis and thrombocytopenia<sup>(2)</sup> or atypical cells in peripheral smear<sup>(4-11)</sup> are clues to possibility of malignancy in a case of arthritis and must be searched for. Our case clinically mimicked rheumatoid arthritis. However, out-of-proportion anaemia occurring simultaneously with onset of arthritis was the red flag and clue to the underlying leukaemia.

Yours sincerely,

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