Case Report

Leukemic synovitis as a presentation of myelomonocytic blast crisis of chronic myeloid leukemia

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ABSTRACT

We describe a patient with a 2-month history of right shoulder monoarthritis and fever as the presenting symptoms of a subsequent diagnosis of chronic myeloid leukemia in blast crisis. Imaging studies showed changes consistent with leukemic infiltration of the soft tissues around the right shoulder joint and the proximal humerus. Immunophenotypic and morphologic analysis of the large number of cells obtained from the synovial fluid confirmed the shoulder synovitis to be an extramedullary manifestation of myelomonocytic blast crisis of chronic myeloid leukemia. The patient was not a candidate for aggressive chemotherapy treatment because of her poor overall condition, and she had no compatible donor for allogenic bone marrow transplantation. Her painful arthropathy was refractory to standard pain management but she achieved excellent pain relief with palliative radiation therapy. We conclude that the involvement of extramedullary sites by chronic myeloid leukemia blast cells can predate hematological blast crisis in some of chronic myeloid leukemia cases. Also, painful leukemic synovitis can be managed by low dose radiotherapy in a candidate who is refractory to chemotherapy and other medical therapy.

Keywords: Leukemic arthritis, chronic myeloid leukemia, myelomonocytic blast crisis, flow cytometry, radiation therapy.

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The musculoskeletal manifestations of leukemia include symmetric or migratory polyarthritis. Large joints are more commonly affected than small joints, and the arthritis is often periarticular and severe.[1,2] Leukemic arthritis has been reported in adults with acute and chronic leukemia and in the myeloid and lymphoid phenotypes, with estimated overall prevalence of 4%-13%.[3] Synovial biopsy may provide a definite diagnosis of leukemic arthritis,[1] but due to the focal nature of the leukemic infiltrate, the biopsy may be misleading, while the immunocytologic analysis of joint fluid may facilitate early diagnosis of leukemic arthritis.[4] We describe a young woman with shoulder monoarthritis as the presenting symptom of a subsequent diagnosis of chronic myeloid leukemia (CML) in blast crisis. The diagnostic immunophenotypic and morphologic features of the blast crisis seen in this case were initially confirmed and established from the studies performed on the cells, obtained from the synovial fluid aspiration.

Case Report. A 27-year-old woman presented to a local hospital in May 1999 with a 2-month history of progressive right shoulder pain and swelling associated with fever. Her initial blood count showed white blood count (WBC) of 100 x 10^9/L, and her bone marrow biopsy was diagnostic of CML, for which treatment with hydroxyurea plus

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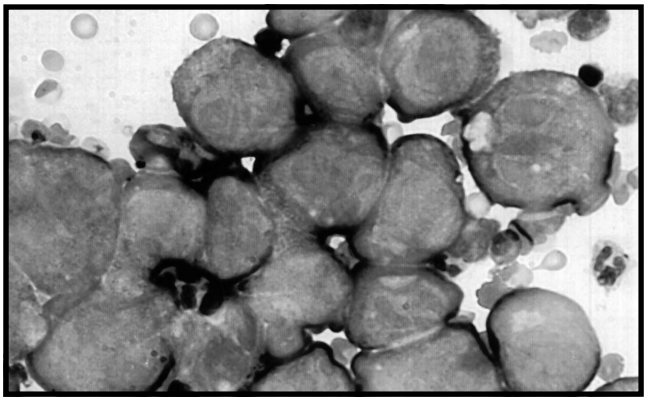

Figure 1 - Synovial fluid microscopy showing very large primitive cells with open chromatin and prominent nucleoli.

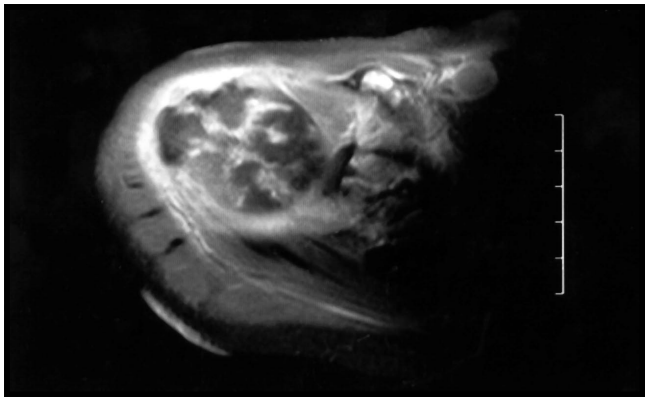

Figure 3 - Magnetic resonance imaging of the right shoulder showing high signal intensity leukemic infiltration of the proximal humerus, synovium, and soft tissue around the jount associated with joint effusion.

allopurinol was initiated. The leukocyte count dropped slowly, but overall, the patients condition remained the same with persistent right shoulder pain and fever. In June 1999 the patient was seen in our hospital with worsening of her right shoulder pain. In addition, she reported a new onset of left shoulder and bilateral hip and knee pain. There was no history of morning stiffness or small joint pain. The physical examination of the right shoulder showed swelling, hotness, and extremely painful movement of both abduction and external rotation. Her hips were tender with painful restriction of the abduction and the internal rotation. Laboratory studies revealed WBC of 35 x 10^9/L. The peripheral blood film showed neutrophil leukocytosis with marked left shift and rare blasts. Arthrocentesis of the right shoulder yielded a cloudy synovial fluid with a WBC of 1700 x 10^6/L. The WBC differential showed 36% polymorphs, 9% lymphocytes and 55% malignant cells (very large cells with open chromatin and prominent nucleoli) (Figure 1). Flow cytometry showed these cells to be positive for Cluster of Definition (CD) CD_{33}, CD_{25}, and cytoplasmic myeloperoxidase, which was consistent with a myelomonocytic origin. Synovial fluid culture and crystals were negative. Bone marrow aspirate and biopsy studies were compatible with CML in transformation with the same morphology and immunophenotype. Bone marrow aspirate cytogenetics confirmed the presence of Philadelphia chromosome with additional karyotype abnormalities. The x-ray of the right shoulder showed multiple radiolucent areas in the proximal humerus with erosion of the medial aspect of the head and neck (Figure 2). Magnetic resonance imaging of the right shoulder showed significant patchy tumor infiltration of the fatty marrow of the proximal humerus, the synovium and the soft tissues around the joint (Figure 3). The diagnosis of leukemic arthritis was made, and the patient was continued on hydroxyurea in addition to oral prednisone (30 mg/day) and naproxen without improvement of the joint pains. As the patient had no compatible donor for allogenic bone marrow transplantation and she was not felt to be a candidate for aggressive chemotherapy treatment due to her poor overall condition and rapid deterioration of her disease, she was provided with supportive care and low dose (<1000 cGy) palliative radiation therapy to the right shoulder and both hips, with excellent pain relief, and was sent back to her referring institution.

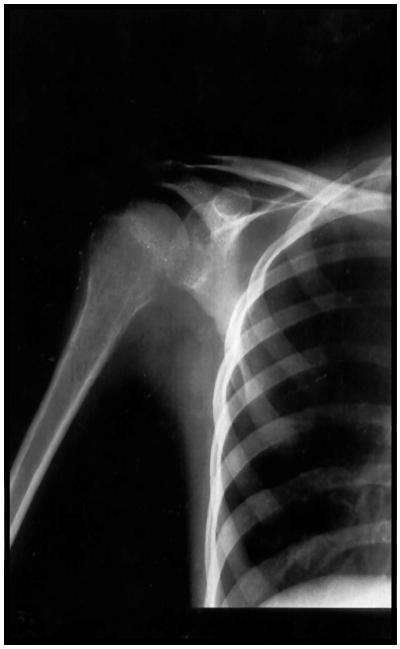

Figure 2 - X-ray of the right shoulder showing multiple radiolucent areas in the proximal humerus with erosion of the medial aspects of the head and neck.

Discussion. Leukemic arthritis is a known manifestation of both acute and chronic leukemia, and is seen more frequently in children and occurs more commonly in acute than in chronic leukemia.[1,5,6] The overall prevalence of leukemic arthritis in adults is estimated to be 4%-13%.[2,3] The etiology of leukemic arthritis is diverse and has been attributed to leukemic synovial infiltration, hemorrhage into the joint or crystal-induced synovitis.[1,2,5] Leukemic synovitis with leukemic infiltration or direct invasion of the synovial tissue occurs mostly in patients with widespread disease and is generally associated with poor prognosis.[7,8] Leukemic arthritis may occur at any time during the course of the leukemia and can be the presenting manifestation. Among the various reports and case series, leukemic arthritis predated the diagnosis of different leukemias in 47% of the cases.[3,9] Chronic myeloid leukemia patients usually present in the chronic phase, which usually evolves after several years of stable course into the acute type of leukemia known as blast crisis.[10] Occasional CML patients present in an accelerated phase or blast crisis, presumably after being in an asymptomatic chronic phase for several years.[10,11] Blast crisis of CML is most commonly of myeloid phenotype (and its subtypes) and less frequently of lymphoid or other phenotype.[12,13] Involvement of extramedullary sites by CML blast cells is usually not seen in the chronic phase of CML and is considered as a sign of disease acceleration or blast crisis.[14] This infrequently may predate hematological blast crisis (bone marrow and peripheral blood) in some patients. Other patients may present with blast crisis involving the bone marrow and extramedullary sites at the same time, as seen on our patient, but presentation with hematologic blast crisis is the most common clinical presentation of CML disease progression.[10,11,13,14] Acute myeloid leukemia with monocytic and myelomonocytic phenotype has a tendency to involve extramedullary sites and soft tissues and it would be expected that the same dosage applies for CML blast crisis of myelomonocytic type as was observed in our patient.[15,16] Joint fluids have been studied infrequently in patients with leukemia and arthritis.[1,8,17,18] Both inflammatory and non-inflammatory synovial effusions, with widely varying leukocyte counts, have been reported. Leukemic cells have only rarely been detected in these effusions.[4,5,7] Examination of cells from the synovium and synovial fluid by immunocytology and immunophenotyping, or both, by flow cytometry have helped to identify cases of leukemic synovitis in several reports, as in our patient.[4,12,19] Our patient had a large number of malignant blast cells in the synovial fluid, and these cells were of the same morphology and immunophenotype (myelomonocytic) as the cells in the bone marrow. Among the different available imaging studies, MRI appears to be an extremely useful diagnostic tool in suspected cases of leukemic arthritis, as it provides information with regards to the joint capsule, periarticular soft tissue and is being increasingly used to assess the degree of bone marrow involvement by hematologic neoplasms.[20] Leukemic arthritis usually responds to chemotherapy for the underlying leukemia,[3] however, as was observed in the case reported here, low dose radiotherapy of painful leukemic arthropathy provides excellent and prompt pain relief in patients that are not candidates for, or who are refractory to chemotherapy, or any other treatment.

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