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A Case of Leukemia-Associated Arthritis

— Identification of Leukemic Cells in Synovial Fluid by Light Microscopy —

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One case of arthritis complicating leukemia is described in which leukemic cells were identified in synovial fluid by light microscopy. Although arthritis is a well-known manifestation of leukemia with an incidence of 13.5%, the pathogenesis often is unclear, and the direct demonstration of leukemic cells in synovial fluid has been very uncommon. A 16 year-old male patient was admitted due to left elbow joint pain and swelling. Synovial fluid examination revealed blast cells and this finding has directed to a final diagnosis of acute lymphoblastic leukemia.

Key Words: *Acute lymphoblastic leukemia, arthritis, synovial fluid*

INTRODUCTION

In a number of lymphoproliferative diseases including leukemia, osteoarticular complaints has been a presenting manifestation (Buckingham & Rodnan, 1985; Thomas, et al., 1961), especially in children, who may be thought at first to have rheumatic fiver, juvenile rheumation arthritis (Hallidie-Smith & Bywaters, 1958), and later may be confirmed to have hematologic diseases.

Joint manifestations in leumkemia have been attributed to a variety of causes, including leukemic synovial infiltrations, hemorrhage into the joint or periarticular structures, synovial reaction to adjacent bony, periosteal, or capsular lesions, and crystal induced synovitis (Weinberger et al., 1981), and very rarely, several cases with leukemic cells in synovial fluid have been reported (Weinberger et al., 1981; Emkey, 1977; Harden et al., 1984; Soebergen, 1982.)

Recently, we have experienced one case of arthritis complicating leukemia in a 16 year-old boy who complained of left elbow joint pain & swelling in which leukemic cells were identified in synovial fluid by light microscopy and then acute lymphoblastic leukemia was confirmed by peripheral blood and bone marrow examinations.

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CASE REPORT

A 16-year-old male patient came to the Department of Internal Medicine, Seoul National University Hospital with the complaint of the left elbow joint pain and swelling. He was well until 16 months earlier, when he noted a bean-sized nodule in the postauricular area with attendant fever and rhinorrhea. Eight months later, the nodule grew up to thumb-tip size but histologic examination was not remarkable at a local hospital. One month prior to the visit, he noted left tibial pain and 10 days prior to the visit, he noted left elbow joint pain and swelling. The temperature was 37.5°C by mouth, the pulse was 115/min, and the blood pressure was 130/90mmHg. On examination, he appeared well. On the both sides of the neck, multiple movable bean-sized-lymph nodes were palpable. The liver was palpable about 1 finger breadth

below the costal margin but the spleen was not palpable. Both inguinal lymph nodes were palpable but nontender. Pain and swelling on the left elbow joint and right tibial area were noted but no sternal tenderness was elicited. The hemoglobin was 13.5gm/dl. The hematocrit was 39.8%; the white cell count was 6,300/mm^3, with 3% myelocytes, 2% metamyelocytes, 10% band forms, 22% neutrophils, 42% lymphocytes, 3% monocytes, 1% eosinophils, 11% blasts, 6% immature cells. The erythrocyte sedimentation rate was 30mm/hour. An X-ary film of the chest revealed a suspicious right superior mediastinal soft tissue mass density (Fig. 1). X-ray films of the knee and elbow joints revealed no remarkable finding except the delay of epiphyseal closure. The synovial fluid of the left elbow joint contained 760 red blood cells/mm^3, 230 white blood cells/mm^3, with 20% neutrophils, 56% lymphocytes, 10% monocytes, 8% blasts, 6% immature lymphocytes and the mitotic cells were observed occasionally (Fig 2.3). Immature lymphocytes comprised most of the peripheral white blood cells (Fig. 4). Bone marrow was replaced by immature lymphocytes and 92.6% of all the nucleated cells were neoplastic in nature (Fig. 5). T-cell acute lymphoblastic leukemia

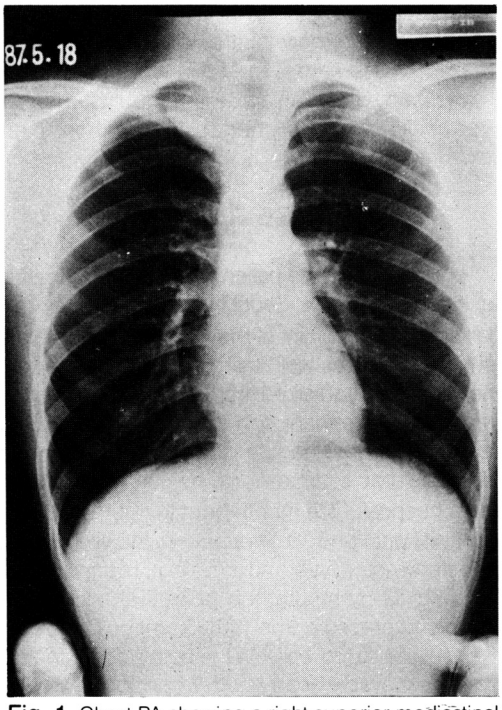

Fig. 1. Chest PA showing a right superior mediastinal mass.

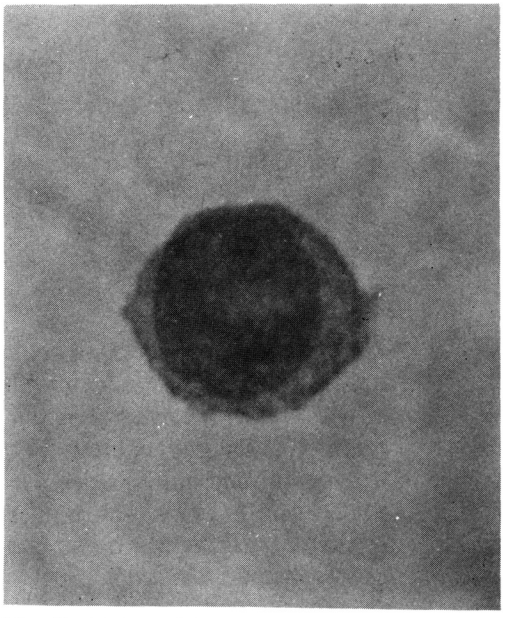

Fig. 2. A blast cell in synovial fluid.

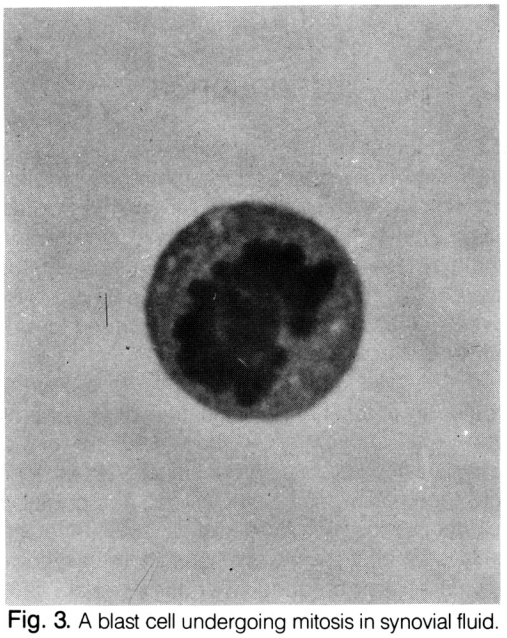

Fig. 3. A blast cell undergoing mitosis in synovial fluid.

was confirmed after the surface marker study. Cryoglobulin, rheumatoid factor and fluorescent antinuclear antibody were all negative.

After the diagnostic procedure, he refused any anticancer chemotherapy due to economic problem and was discharged.

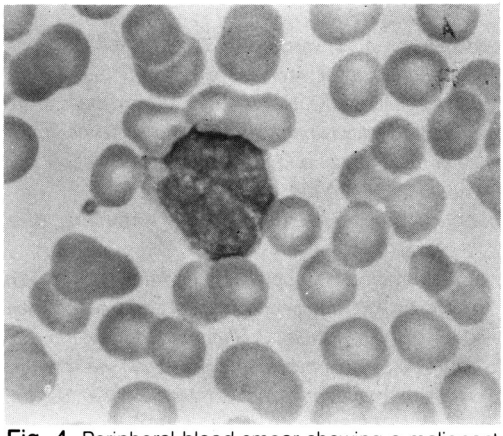

Fig. 4. Peripheral blood smear showing a malignant blast cell.

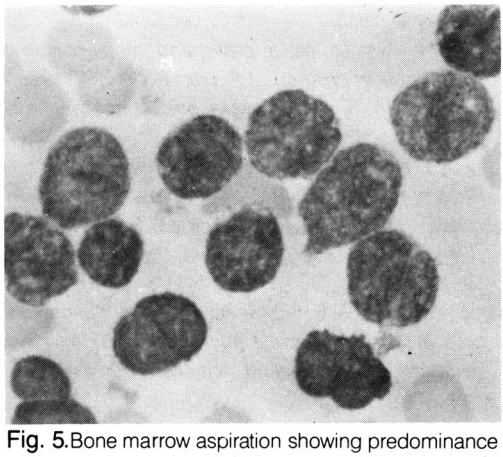

Fig. 5. Bone marrow aspiration showing predominance of blast cells.

DISCUSSION

In a number of hematologic diseases, osteoarticular complaints play an important or even a dominant role and arthritic manifestations accompany leukemia with an incidence of 13.5% (Thomas et al., 1961; Spilberg & Meyer, 1972). These symptoms may be either the result of direct involvement of the bones and joints in the primary disease process or a consequence of secondary metabolic or immunologic disturbances (Luzar & Sharma, 1983).

Arthritis symptoms are observed more frequently in acute leukemia than in chronic leukemia and more often in children than in adults, so they may be though at first ot have rheumatic fever, juvenile rheumatoid arthritis (JRA), or Still's disease (Hallidie-Smith & Bywaters, 1958). Pain and tenderness of the bones may be present, and most patients have polyarticular diseases with prominent involvement of the knees and ankles and, variably, large joint effusions (Buckingham & Rodnan, 1985). Severe bone pain out of proportion to the degree of arthritis has been stressed as a distinguishing feature of leukemia, in addition to the lymph node enlargement and hematologic abnormalities (Schaller, 1972). Rheumatoid factor may be detected in leukemics, and rheumatoid like nodules may occur (Buckingham & Rodnan, 1985) and the presence of LE cells in patients with Hodgkin's disease was reported (Howqua & Mackay, 1963). Also many individuals with established systemic lupus erythematosus or rheumatoid arthritis have developed lymphoma or leukemia (Buckingham & Rodnan, 1985; McCarty, 1982). The joint symptoms are related in some instances to leukemic infiltrations in synovium, subperiosteum, and juxtaarticular portions of the bones (Thomas et al., 1961, Spilberg & Meyer, 1972). In such cases, bone scintigraphy may show increased juxta-articular uptake of radioactivity (Valimaki et al., 1981), but very rarely, they may appear photon-deficient foci or cold lesions (Park et al., 1983). In other cases, one sees no infiltrate in synovium or bone (Weinberger et al., 1981) and disease may be mediated by an immune mechanism (Luzar & Sharma, 1983). Also arthritis in leukemia may be a result of hemorrhage in the joint or periarticular structures, or it may be a result of gout or pseudogout (Buckingham & Rodnan, 1985; Weinberger et al., 1981).

Joint effusions in leukemia have been reported as mildly inflammatory, with avarage cell count of 5,500 to 8,790/mm^3 with predominantly polymorphonuclear leukocytes (Spilberg & Meyer, 1972). Leukemic synovitis has been occasionally noted and when performed, synovial biopsy has demonstrated leukemic infiltration of the synovium, but leukemic cells in the synovial fluid have rarely been reported and 4 cases were known at present. Chronic lymphocytic leukemia of T-cell origin was associated with nodular polyarthritis in a woman with many T cells in the synovial fluid but no synovitis or synovial infiltrate (Soebergen, 1982), and in one patient with reticulum cell sarcoma with articular involvement, the diagnosis was established by the demonstration of malignant cells in the synovial fluid at a time when these cells were absent from the peripheral blood and the initial bone marrow specimen (Emkey, 1977). Also large, suspected blast cells in synovial fluid were found in an 81-year-old woman with acute myelogen-

ous leukemia (Weinberger et al., 1981) and like this case, the presence of leukemic cells in synovial fluid was demonstrated in 2 patients with acute lymphoblastic leukemia and adult T cell leukemia. But the demonstration of immature appearing mononuclear cells in synovial fluid is not diagnostic of leukemia, since synovial fluid lymphoblasts have been reported in patients with rheumatoid arthritis (Traycoff et al., 1976).

In the diagnosis of leukemic synovitis, synovial biopsy is more helpful. Spilberg and Meyer found leukemic infiltration in all synovial biopsies performed in 3 patients with leukemia-associated arthritis (Spilberg & Meyer, 1972) but other series have reported negative biopsy results in 3 patients (Weinberger et al., 1981; Fink et al., 1972). Autopsy studies have indicated that leukemic involvement of the synovium has been rare, even with the clinical evidence of arthritis (Thomas et al., 1961), and as in this case, the diagnosis of leukemia rendered by the demonstration of leukemic cells in synovial fluid when leukemic cells were absent in the peripheral blood or bone marrow had been very difficult to obtain.

REFERENCES

Buckingham RB, Rodnan GP: *Arthritis associated with hematologic disorders, storage diseases, disorders of lipid metabolism, and dysproteinemias. In McCarty DJ (ed): A textbook of Rheumatology. Lea & Febiger, Philadelphia, pp1135-1167, 1985.*

Emkey RD: *A case of lymphoproliferative disease presenting as juvenile rheumatoid arthritis: diagnosis by synovial fluid examination. Am J Med 54:825-828, 1977.*

Fink CW, Windmiller J. Sartain P: *Arthritis as the presenting features of childhood leukemia, Arthritis Rheum 13:347-349, 1972.*

Hallidie-Smith KA, Bywaters EGL: *The differential diagnosis of rheumatic fever. Arch Dis Child 33:350-357, 1958.*

Harden EA, Moore JO, Haynes BF: *Leukemia-associated arthritis; Identification of leukemic cells in synovial fluid using monoclonal and polyclonal antibodies. Arthritis Rheum 27:1306-1308, 1984.*

Howqua JA, Mackay IR: *L.E. cells and lymphoma. Blood 22:191-198, 1963.*

Luzar MJ. Sharma HM: *Leukemia and arthritis: including reports on light, immunofluorescent and electron microscopy of the synovium. J. Rheumatol 10:132-135, 1983.*

McCarty GA: *Lymphocytic lymphoma and systemic lupus erythematosus. Arch Pathol Lab Med 106:196-199, 1982.*

Park HG, Seo BK, Lee HY, Lee MC, Choi SJ, Kim NK, Koh CS: *Two cases of sternal "cold" lesions on bone imaging in the metastatic skeletal disease. Kor J Nucl Med 12:167-170, 1983.*

Schaller J: *Arthritis as a presenting manifestation of malignancy in children. J Pediatr 81:793-797, 1972.*

Soebergen EM: *T cell leukemia presenting as chronic polyarthritis. Arthritis Rheum 25:87-91, 1982.*

Spilberg I, Meyer GJ: *The arthritis of leukemia. Arthritis Rheum 15:635-635, 1972.*

Thomas LB, Furkner CE, Frei E, Besse B, Sabernau J: *The skeletal lesions of acute leukemia. Cancer 14:608-621, 1961.*

Traycoff RB, Pascual E, Schumacher HR Jr: *Mononuclear cells in human synovial fluid: identification of lymphoblasts in rheumatoid arthritis. Arthritis Rheum 19:743-748, 1976.*

Valimaki M, Vuopio P, Liewendahl K: *Bone lesions in chronic myelogenous leukemia. Acta Med Scand 210:403-408, 1981.*

Weinberger A, Schumacher HR, Schimmer BM: *Arthritis in acute leukemia: Clinical and histopathological observations. Arch Intern Med 141:1183-1187, 1981.*