Acute Leucemia in a Patient with Juvenile Rheumatoid Arthritis Displaying Cystic Osseous Lesions*

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Juvenile Rheumatoid Arthritis (JRA) is a collagen tissue disease of undetermined origin and presents many problems of diagnosis and management. This disease is thought to represent a nonspecific hypersensitivity reaction by some authors; and hereditary, environmental and constitutional factors, psychological stresses and trauma are believed to be involved in its genesis.[1]

Encountered in approximately 2 % of the adult population, this disease is less frequently seen in children.[2]

The case we are going to present was diagnosed as having Juvenile Rheumatoid Arthritis on her first admission to the hospital and radiological examinations revealed cystic changes in the bones. Five months later on readmission the presence of acute leucemia was detected. This case is thought to be interesting both for the coexistence of collagen and malignant diseases, and for the cystic bone lesions and is forthwith reported.

Case Report

K. S. (Hospital Number 67/29525) was a 13 year old girl admitted to the Pediatric Department of Hacettepe University Medical School, on

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* Work published from the Hacettepe University Medical Center.

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6/30/1967 because of pain and swelling in the joints and inability to walk. Some swelling and pain in the right knee with the pain becoming more severe in the mornings had been first noted three years earlier. Similar manifestations in the other joints developed about a year prior to admission. During the last fortnight there was marked increase in these complaints and the child was unable to sit or walk; various analgesics failed to produce any relief.

Physical examination revealed a mentally alert child who refused to sit or move. She weighed 22 kilograms with a height of 125 cms. and her vital signs were normal. The joints were warm, swollen and deformed. All the extremities were tender and showed muscular atrophy (Figures 1 and 2). Ulnar deviation was present in both wrist joints. Examination of

Figure 1

Figure 2

the right knee joint indicated the presence of effusion in the same. The liver was palpable two centimeters below the costal margin. Splenomegaly, adenopathy or exanthemata were absent.

Laboratory investigations showed the W. B. C. to be 5200/mm^3 with segmented cells being 56% on the peripheral smear. There were abundant thrombocyte clumps. Blood chemistry was normal. Skin and muscle biopsy material was found to be normal. Bone marrow aspirate failed to disclose any evidence of malignancy and was within normal limits.

X-ray examination of the vertebrae, thorax and the skull showed the presence of diffuse osteoporosis with coarsening of the trabecular pattern. Roentgenograms of the long bones of the extremities revealed similar changes with the osteoporosis being more marked in and near the epiphyses. In addition well-demarcated cystic lesions were present in the

epiphyseal regions of some long bones as well as in some of the small wrist bones. The cortical bone adjacent to the cystic areas of destruction showed thinning and in some stress bearing regions there were small compression fractures. In the phalanges there was marked juxtaarticular osteoporosis as typically seen in rheumatoid arthritis (Figures 3, 4 and 5). There was widening and irregularity of the bony margins along the distal radio-ulnar articulation. Marked narrowing of the joint spaces between the carpal bones was present indicating some destruction of the articular cartilage.

Figure 3

In the light of the above findings the patient was accepted as having Juvenile Rheumatoid Arthritis and treatment with corticosteriods was initiated. This was followed by marked clinical and some radiological improvement and the child was discharged on 8/16/1967. The patient was regularly seen in the Out-patient Department while she was kept on treatment with cortico-steroids, aspirin and indocid.

Five months later on 1/14/1968 she had to be readmitted to the hospital with complaints of fever, cough, vomiting and a sore throat of one week's duration. Physical examination at this time revealed petechiae on the skin and gingiva in addition to the previous findings. Hemorrhages

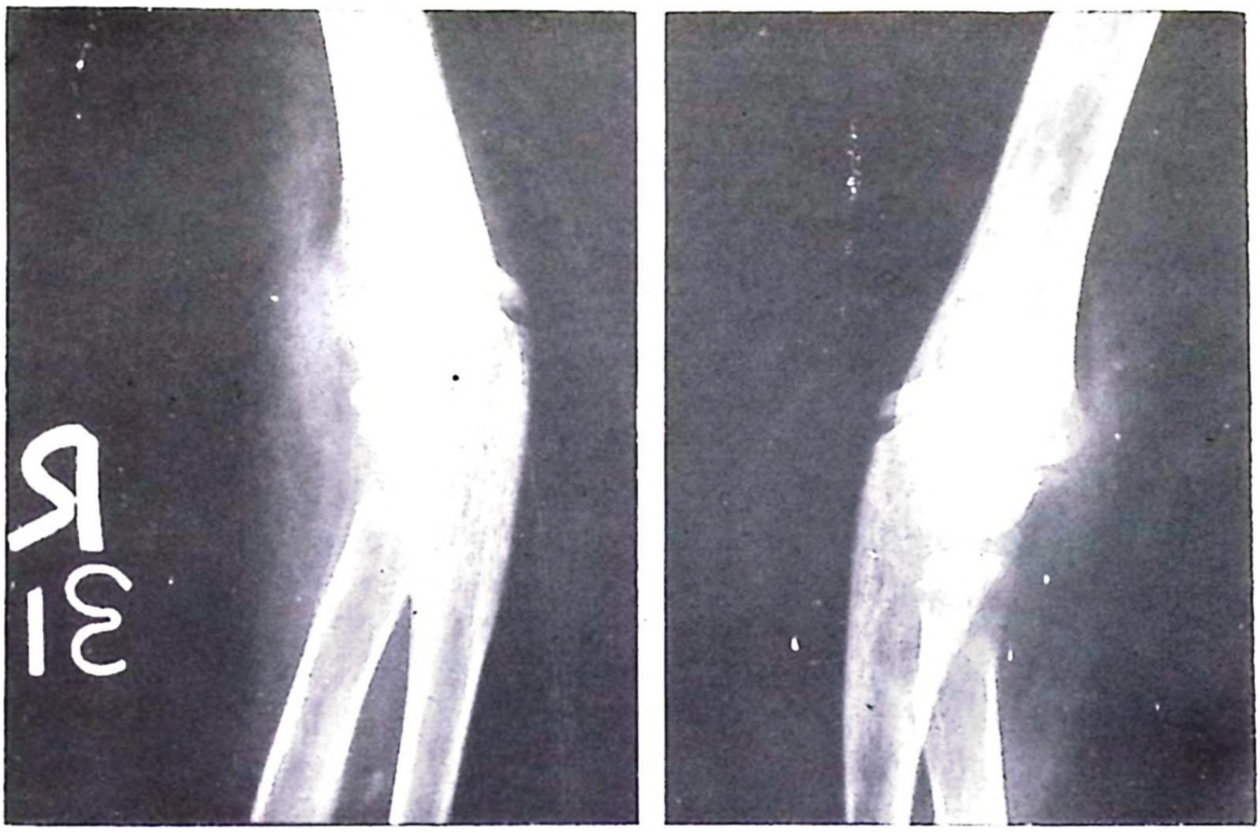

Figure 4

were present in the fundi. Skin and the scleras were icteric. Bone marrow aspirate disclosed numerous blast cells. Thrombocytes were scarce in the peripheral blood smear. Radiological findings were similar to those on the inital admission. The child's problems were complicated by a superimposed broncopneumonia and antibiotic and antileucemic treatment. She expired on 2/2/1968.

Discussion

There are no uniform criteria for the diagnosis of Juvenile Rheumatoid Arthritis. The onset of the disease may be in one of the following three forms:[3]

1 — Acute form (Still's Disease),

2 — Polyarticular form (Adult type of the disease),

3 — Monoarticular form.

1 — The acute form of the disease may convert into the polyarticular form in later stages. Joint pains, high fever, exanthemata, generalised lymphadenopathy, splenomegaly and leucocytosis are the cardinal manifestations of the disease. The average age of patients presenting this form of the disease has been found to be four and a half years. It is

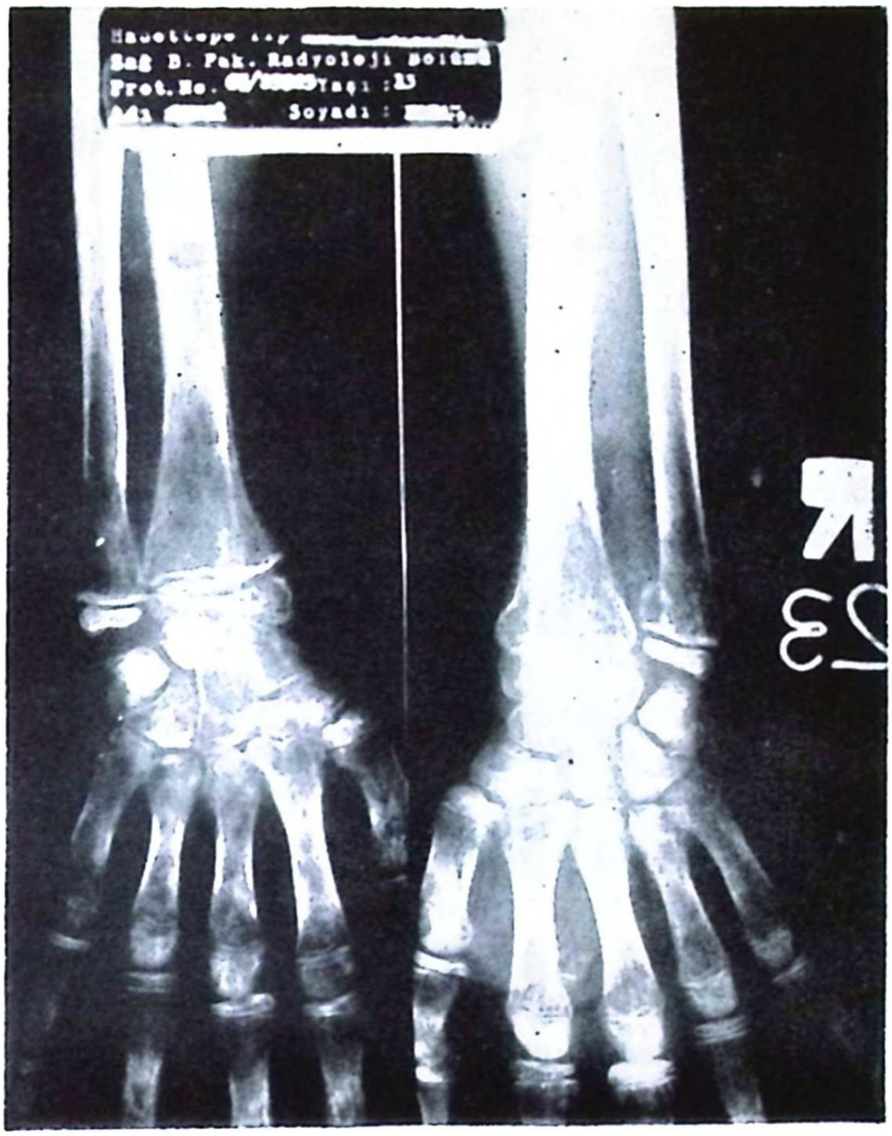

Figure 5

rarely encountered below six months and above ten years of age. The incidence of the disease in males is twice that in females. The joint pains may not be clearly defined in some cases and the diagnosis may be quite difficult. Exanthemata may be seen anytime between a week to nine years following the onset of the other symptoms.[4] In addition to the above symptoms hepatomegaly, myocarditis, pericarditis, pneumonia and vasculitis may be present.

2 — The polyarticular form attacks four or more joints simultaneously. Girls are affected twice as often as boys. The average onset of the disease is calculated to take place at seven years and five months. Though it closely resembles the adult form, rheumatoid factor and subcutaneous nodules are rarely seen. The early stage of the disease may be insidious or fulminant. The first joints to be involved are usually the knees, wrists or the elbows. The diseased joint is warm, swollen and its movement is limit-

ed. Tenderness and redness may be absent. It has a tendency to attack symetrical joints. Cervical vertebrae may be attacked early in the disease. In addition to the joint symptoms systemic findings such as fever, exanthemata, lymphadenopathy and weight loss may be present. There usually is slight leucocytosis and the sedimentation rate and C reactive protein may be increased. Radiological examinations are useful in establishing the diagnosis: Juxta-articular osteoporosis, acceleration of epiphyseal maturation, overgrowth of the metaphyses, and evidence of cartilage destruction may be seen.[5]

3 — In the monoarticular type of the disease, patient's complaints are confined to a single joint for at least a month. This form makes up a third of all the cases of Juvenile Rheumatiod Arthritis and males are attacked by it three times as often as girls. The average age of onset is seven years, and the disease usually begins insiduosly. The knee is the most commonly involved joint. Systemic findings such as fever, irritability, lymphadenopathy, splenomegaly and weight loss may be late in appearance and for a while the patients may appear relatively healthy. Sedimentation rate, rheumatiod factor are normal. Synovial biopsy reveals nonspecific findings. Radiological findings are similar to those in the polyarticular form.

We believe that our patient represents a case of monoarticular rheumatoid arthritis initially, with clinical and radiological findings of this form of the disease with later conversion into the polyarticular form. However two interesting aspects of this particular patient probably warrant further discussion: Primarily how can the cystic bone lesions be explained on the basis of Juvenile Rheumatoid Arthritis? And in the second place, was leucemia present from the onset and did the patient not have rheumatoid arthritis at all?

The changes in the metaphyses of the long bones of the patient on the initial roentgenograms, indeed do resemble bone changes encountered in leucemia and neuroblastoma with malignant infiltration of the bone marrow.[7] [8] [9] However the presence of cartilage destruction in addition to the other findings, normal bone marrow aspirate, the long clinical course of the disease, and the involvement of a single joint initially in our case have made these diagnoses unlikely.

In the presence of osteoporosis and cystic osseous lesions, hyperparathyroidism had also to be excluded in our case. Normal serum chemistry, the normal appearance of the cranial bones and the lamina dura around the teeth, as well as the selective localization of the osteoporosis in the epiphyses helped to rule this possibility out.

Osteogenesis imperfecta similarly could be ruled out because of cystic lesions, selectivity of the osteoporosis, cartilage destruction and the clinical picture.

However, as mentioned above, cystic bone lesions are not typical of Juvenile Rheumatoid Arthritis either. They are occasionally encountered and there are various theories as to their development in rheumatoid arthritis.[11] [12] This particular subject was discussed in the International Rheumatology Congress of 1963. According to Bywaters, the cystic lesions are actually extensions or herniations of the joint space into the spongiosa through the thin subchondral bone where the cartilage is either thin or absent.[11] Physical activity and the muscle tone of the particular extremity have been claimed to be contributing factors in cyst formation. Observations of R. François and G. Van Dain, indicating that the disease is clinically and radiologically more severe in the right arm, would appear to confirm this point. In the series of 153 patients of Castilla et al., cystic lesions were present in twenty and these patients were found to be the ones with the highest physical activity.[13] Our patient also went to school and physically was quite active during periods when the pains subsided. The patients with cystic lesions in the literature are adults and since the cartilage is relatively thick in children the rareness of the cystic lesions in the pediatric age group has been explained on that basis.[11]

In the light of the above discussion the radiological findings in our patient were explained on the basis of rheumatoid arthritis. However the diagnosis of leucemia in the second admission, made the case more interesting and also cast some doubt on the initial diagnosis. Then it has to be remembered that there are many reports about the coexistence of malignant and immune diseases in the same patient.[14-20]

Daniel has shown that connective tissue diseases are present in 0.58 % of patients with solid tumors and that their incidence increases to 1.86 in patients with malignant lymphomas.[14] Of the 270 patients with collagen tissue disease of Christianson, 6.7 % had malignant disease and one of these was lymphoblastoma.[20]

Lea has pointed out the coexistence of rheumatoid disease and leucemia but has concluded that this may be just coincidence since only 0.1 of his patients had this combination.[18] Nilsen has reported a Hodgkin patient with lupus erythematosus and has written about the coexistence of lymphomas and autoimmune diseases.[17] He claimed that the findings of the autoimmune disease may subside when lymphoma is added to the picture, since in his particular patient L. E. cells disappeared when Hodgkin's disease became manifest. Camarata has pointed out

that rheumatoid disease and malignant lymphoma may imitate one another or may be present in the same patient together, immunologic events making it possible for them to coexist.[15]

In view of some clinical and radiological findings which can only be explained on the basis of rheumatoid disease we think it is reasonable to accept our patient as a case in whom both Juvenile Rheumatoid Arthritis and leucemia were present.

Summary

A 13 year- old leucemic child with rheumatoid arthritis is presented. The interesting aspects of the patient are the presence of cystic osseous lesions in active joints and the coexistence of leucemia. This case is believed to be yet another example of coexistence of malignant lymphomas and autoimmune diseases.

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