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Tuberculous Poly Arthritis
A Review With Patient Presentation and Discussion

G. Samar, M.D. H. Basty, M.D. E. Saebi, M.D.

Tuberculous poly arthritis is an important and serious local manifestation of a systemic disease , which may, if untreated, lead to complete joint destruction. Compared to other extrapulmonary sites, poly articular involvement is rare, occurring in less than 1 per cont of patients with tuberculosis [1]. The rathogenesis , pathology , clinical aspects, diagnosis and treatment are discussed.

One patient is presented to illustrate the following important clinical problems concerning this disease : (1) Clinical evidence of tuberculosis may be present many years before diagnosis. One must think of it to diagnose it. (2) A previous history of tuberculosis or exposure, no matter how remote, is important and should always be sought when destructive bone and joint lesions are present. (3) Any monoarticular arthritis, particularly with a destructive skin test should be performed as a minimum.(4) Multiple sites of bone and joint involvement commonly occur

* Pahlavi Medical School, Tehran University.

and must always be considered. (5) Approximately 50 per cent of the patients with bone tuberculosis do not have concomitant tuberculosis in the lung. (6) Pathologic specimens which are compatible with tuberculosis or granuloma should be suspect, even if the organism is not demonstrated. (7) When tuberculosis is present, adequate chemotherapy should be instituted prior to surgical procedures if possible. (8) Good treatment results from chemotherapy alone are possible, even in far advanced joint disease, In unusual instances surgical intervention may be necessary to improve joint function. (9) Persistent bone pain particulary in the spine should suggest evaluation for tuberculosis.(10) Early diagnosis is essential since excellent therapy is available and far advanced destruction and long suffering and disability can be avoided.

Pulmonary tuberculosis remains by far the most common form of the disease, but any organ system can be involved. Early detection and treatment are essential just as they are with the pulmonary form. Our purpose is to emphasize these facts as they particularly relate to skeletal tuberculosis. A general discussion of skeletal tuberculosis is followed by the presentation of one patient with this disease recently diagnosed and treated.

Pathogenesis

It is generally belived that skeletal tuberculosis is caused by dissemination of bacilli by the blood stream early in the course of the initial infection . In some instances spread to bone appears to result from lymphatic drainage from another area of tuberculosis such as tuberculosis of the pleura or kidney spreading via the periaortic lymph nodes with erosion into the spine. Burke[2] in 1950 concluded that his experimental studies in animals, using a

mixture of colloidal thorium dioxide and finely divided lampblack injected into the pleural space as well as anatomic and clinical findings, suggested that most cases of Pott's disease are the result of lymph-borne dissemination of the tubercle bacilli. In children and probably also in adults, skeletal involvement may be the only manifestation of systemic disease and, like the pulmonary form, may smoulder for years before it is discovered. It has been long suspected that trauma may play an important role in the pathogenesis of bone tuberculosis. This is a logical suspicion since the weightbearing joints are most frequently involved.

Pathology

The basic lesion is almost always a combination of osteomyelitis and arthritis. Invasion of the joint space may be either direct via the blood stream or indirect from lesions in epiphyseal bone eroding into the joint space. We suspect the latter is the most common means of invasion but in most cases it is impossible to be sure. Initially the synovium develops an inflammatory reaction followed by formation of granulation tissue. Effusion develops in which fibrin may precipitate, forming so-called "rice" bodies . This pannus of granulation tissue then begins to erode and destory cartilage and eventually cancellous bone, ultimately leading to progressive demineralization and caseation necrosis. The cartilage is destroyed peripherally first, preserving the joint space for a considerable length of time. Tuberculosis infection does not produce proteolytic enzymes which can destory cartilage, as occurs in pyogenic arthritis. This preservation has important clinical implications.

Eventually in far advanced disease, para-osseous abscesses may develop which involve the tissue surrounding the joint to form the so-called "cold" abscess. Erosion

and sinus tract formation may eventually develop.

The healing process in bone is similar to that found in the lung. Fibrous tissue is formed which in joint usually results in fibrous and possibly osseous ankylosis.

Clinical Aspects

In adults, skeletal tuberculosis usually occurs in the joints most subject to trauma. The spine is involved in approximately 50 per cent of the cases, the hip in 15 per cent, the knees in 15 per cent and the wrist, ankle, elbow, shoulder and other bones in 20 per cent. Jones and Miller [3] recently reported thirty-six cases of skeletal tuberculosis detected over a seven year period which followed this approximate distribution. Over seventy per cent of the lesions found in 230 cases reported by LaFond[4] occurred in the spinal column, hip, knee or sacroiliac joints. Any other bone in the body can be involved and the diagnosis is often difficult and frequently not properly considered. For instance, tuberculosis of the ribs occurs in approximately five per cent of all cases of bone and joint tuberculosis and is by far the most common inflammatory process involving the ribs[5]. Hunt[6] in describing five patients with skeletal tuberculosis pointed out that there may be a change in the nature of tuberculosis of the bone, older people being seen more often and with lesions in unusual locations. Two of his patients had lesions in the tarsus and one each had hip, proximal humerus or sternoclavicular joint involvement. Multiple skeletal involvement or even widespread dissemination of the tuberculosis in bone is possible and should always be considered when a patient presents with multiple osteolytic lesions[7].

Pain is generally the most common complaint. Tuber-

culosis should always be considered when evaluating the cause of skeletal pain. There may be joint swelling and limitation of motion. Eventually a " cold " abscess may occure. Such abscesses are found in the majority of cases with far advanced disease.

Diagnosis

Early diagnosis is essential since preservation of cartilage and joint space persists early in the disease, and if the condition is properly diagnosed and treated, good joint function will result. Unfortunately. misdiagnosis and delay are common. Walker[8] reports that of eighteen new cases of skeletal tuberculosis seen during a year's time, nine were at first misdiagnosed with an average delay in diagnosis of one year and seven months. Considering all eighteen patients, the time of onset of symptoms until confirmation of the diagnosis varied from three months to four years.

The tuberculin skin test remains one of the most valuable diagnostic tools and is usually positive in skeletal tuberculosis. However, a negative skin test does not absolutely rule out tuberculosis. If the first strength or intermediate strength purified protein derivative test is negative, a second strength test should always be performed. A tuberculin skin test should be a routine part of the evaluation of any destructive arthritis or bone lesion, particularly when it is monoarticular or in the spine.

Confirmation by culture is highly desirable and leaves no doubt about diagnosis. Joint fluid or " cold " abscess aspirate should be examined by smear and culture. If necessary, a biopsy specimen of tissue and a culture should be obtained preferably at an early date so that there is no unnecessary delay in treatment. A pathology report

of granulation tissue compatible with tuberculosis is sufficient evidence to begin therapy.

Good roentgenograms are invaluable in helping to establish the diagnosis and to follow the progress of the disease during therapy. Early lesions are easily missed and soft tissue swelling may be the only abnormality. Later, in long bones, small localized areas of osteoporosis occur subchondrally, often associated with a surrounding ring of sclerosis. Subsequently, varying degrees of cortical and cartilage destruction take place within months or years can result in complete destruction of the joint space. Changes in the spine are first noted as a slight narrowing of the intervertebral space. Later the adjacent vertebral bodies develop destructive lesions with eventual collapse and formation of varying degrees of scoliosis and kyphosis often referred to as gibbus formation.

The differential diagnosis of skeletal tuberculosis should include sarcoid arthritis and pyogenic arthritis caused by bacteria and fungi. Arthritis occurs commonly with sarcoidosis and may be a polyarthritis or, rarely, monoarticular arthritis which is intermittent or persistent[9]. Other signs and diagnostic criteria for sarcoidosis can usually be made. Bone lesions are commonly seen or roentgenograms in sarcoidosis and usually are cystlike localized areas of bone destruction. In advanced stages there may be considerable bone destruction and deformity.

Frequently bacterial arthritis is monoarticular. The knee is commonly involved, In the acute form the clinical history is more acute than in tuberculosis and commonly there is penetration of the joint cavity by a wound. Roentgenograms are often of little diagnostic help in acute infections. In chronic infections there is usually some nearby

osteomyelitis. loss of articular cartilage , narrowing of joint space and general rarefaction and erosion of the articular ends of adjacent bones. Chartier et al.[10] noted a decrease in the total incidence of bacterial arthritis primarily as a result of a decrease in the chronic form.

Stone and Bonfiglio [11] emphasized not only the rarity but also the difficulties in making the diagnosis of pyogenic vertebral osteomyelitis in the adult . Such patients may pressent with symptoms and findings similar to those of vertebral tuberculosis and only needle aspirates or biopsy and culture will distinguish between them. There appears to be a high incidence of diabetes in patients with vertebral pyogenic osteomyelitis.

Disseminated fungal infection commonly involves bone. In coccidioidomycosis there appears to be a predilection for points of tension or ligaments, giving a "punched-out" appearance resembling a cyst . Histoplasmosis may invade bone marrow but has not been reportrd in bone cortex or cartilage. The bones, particularly the ribs and vertebrae, are commonly involved in North American blastomycosis and are indistinguisable from those found in tuberculosis. Cryptococcosis may produce multiple widely disseminated lesions in bone which in appearance suggest coccidioidomycosis or sarcoidosis rather than tuberculosis . Actinomycosis may also involve bone and must be differentiated from tuberculosis, usually by biopsy.

The so-called "atypical" mycobacterial infections have recently been the subject of more clinical awareness. Several reports have appeared implicating these organisms as causes of bone and joint disease[12-14]. These organisms may be difficult to isolate and are frequently resistant to the usual antituberculosis drugs. Clinically there is little

to differentiate this disease from tuberculosis although a case simulating rheumatoid arthritis has been reported[15].

Neoplasms in bone can mimic tuberculosis. Often such lesions are metastatic from tumors of the breast, lung or prostate. Finding the primary lesion helps to establish the etiology of the bone lesion. Since bone lesions caused by tumor are much more common than tuberculosis, the latter diagnosis is more likely to be overlooked, resulting in unnecessary delay and risk in treating a completely curable disease.

Treatment

Although treatment used to be exclusively in the hands of the orthopedists, now it should primarily involve the internist. Since the advent of chemotherapy, surgery is much less often necessary and much safer than before. Skeletal tuberculosis of the spine when associated with considerable destruction warrants surgical fusion because of the chance of collapse with paraplegia. However, with effective chemotherapy early in the disease, spinal fusion should not be necessary. Synovectomy, debridement, removal of necrotic bone and abscess material in patients with far advanced disease of peripheral joints may be necessary and can be successful without arthrodesis; however, it should be delayed until after the patient has received chemotherapy for two or three months. With effective chemotherapy, surgical intervention is only rarely indicated and should be reserved to prevent deformity, to improve function and to arrest disease that had not responed to drugs. If the diagnosis is made when the disease is in its early stages or even it is moderately advanced, good joint func-

tion can be expected to result with drug treatment alone.

The drugs of primary choice for the treatment of skeletal tuberculosis are the same as those for other forms of tuberculosis: isoniazid (INH), para-aminosalicylate (PAS) and streptomycin. When organisms are available, drug sensitivity studies should be made and if necessary, one or more of the so-called secondary drugs used. They may also be indicated where allergy or toxicity to a primary drug is present or when retreatment becomes necessary. Iproniazid (Marsilid) was thought to be a specific and more effective drug than isoniazid for traetment of skeletal tuberculosis. Recommendations for its use have appeared in fairly recent literature[16]. The significant toxicity of this drug and the present evidence that there is no clinical difference in its effectiveness as compared to isoniazid preclude its use. In the past some have considered six to twelve months of chemotherapy to be sufficient for most patients with skeletal tuberculosis[17]. The general consensus and recommendations now are that chemotherapy should be given without interruption for at least two years [18]. In general, at least two of the effective chemotherapeutic drugs should be used. Isoniazid may be continued alone for an indefinite period after the disease has been controlled. This is an important consideration in the elderly patient or in one with an underlying disease process in whom reactivation of the tuberculosis is possible[19].

Case Report

A seventeen year old woman entered Pahlavi Hospital with a two months history of increasing pain and swelling of her right elbow and her left ankle. One month prior to admission low grade fever, night sweats, anorexia, weight loss and chronically draining fistula appeared on her left susorbital. the patient denied having cough, chest pain or

hemoptysis.

Physical examination on admission revealed a young woman in no acute distress, with a temperature of 38 c regular pulse of 116 beats/minute and a blood pressure of 110/60 mm Hg.

There was 1 to 2 cm. fistula draining serous material, on her left sus-orbital. Examination of the chest revealed decreased breath sounds at the base of the left lung. The right elbow and the left ankle were markedly swollen, fluctuant and tender.

Laboratory data included a normal complete blood count, urinalysis, blood urea nitrogen, electrolytes and liver function studies. A skin test with intermediate strength purified protein derivative showed 24 mm induration at forty-eight hours. Erythrocyte sedimenation rate was 100 mm/hour. Chest films showed a left pleural effusion a small infiltrate in the upper lobe of the left lung (Fig. 1) Roentgenograms of the involved joint revealed marked soft tissue swelling and extensive articular destruction. (Fig 2,3). Arthrocentesis yielded purulent fluid which failed to grow out pyogens. Biopsy of the lesion revealed caseating granuloma . Histologic examination and culture of necrotic tissue , obtained from the involved joint , demonstrated caseating graruloma and grew M. tuberculosis.

The patient was treated with 400 mg INH, 800 mg ethambutal and 1 gr streptomycin daily; within six months her chest lesions cleared, she became afebrile, and her joint swelling markedly decreased. She underwent arthroplasty of her ankle to regain joint function and is continuing on antituberculous therapy.

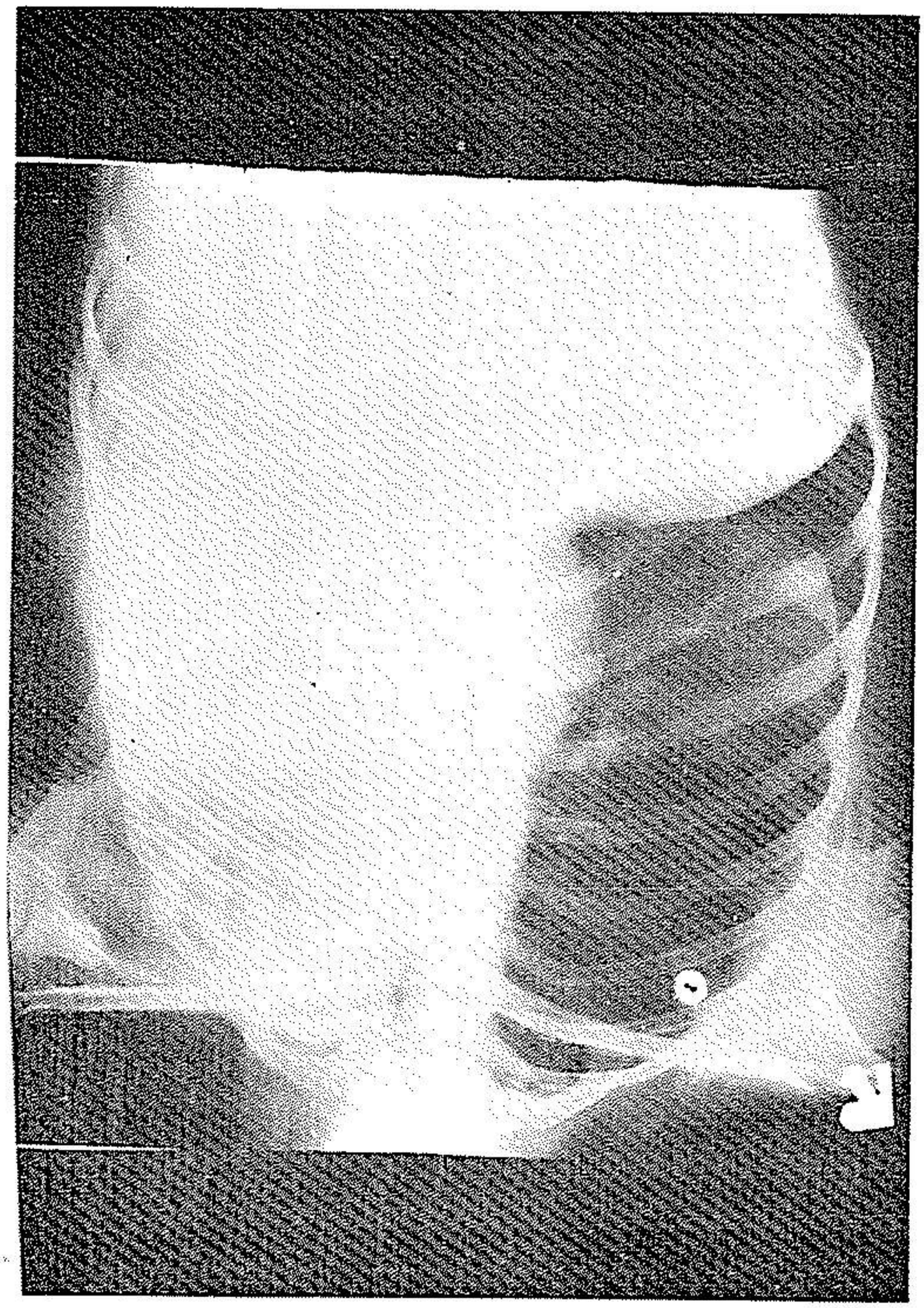


Fig. 1

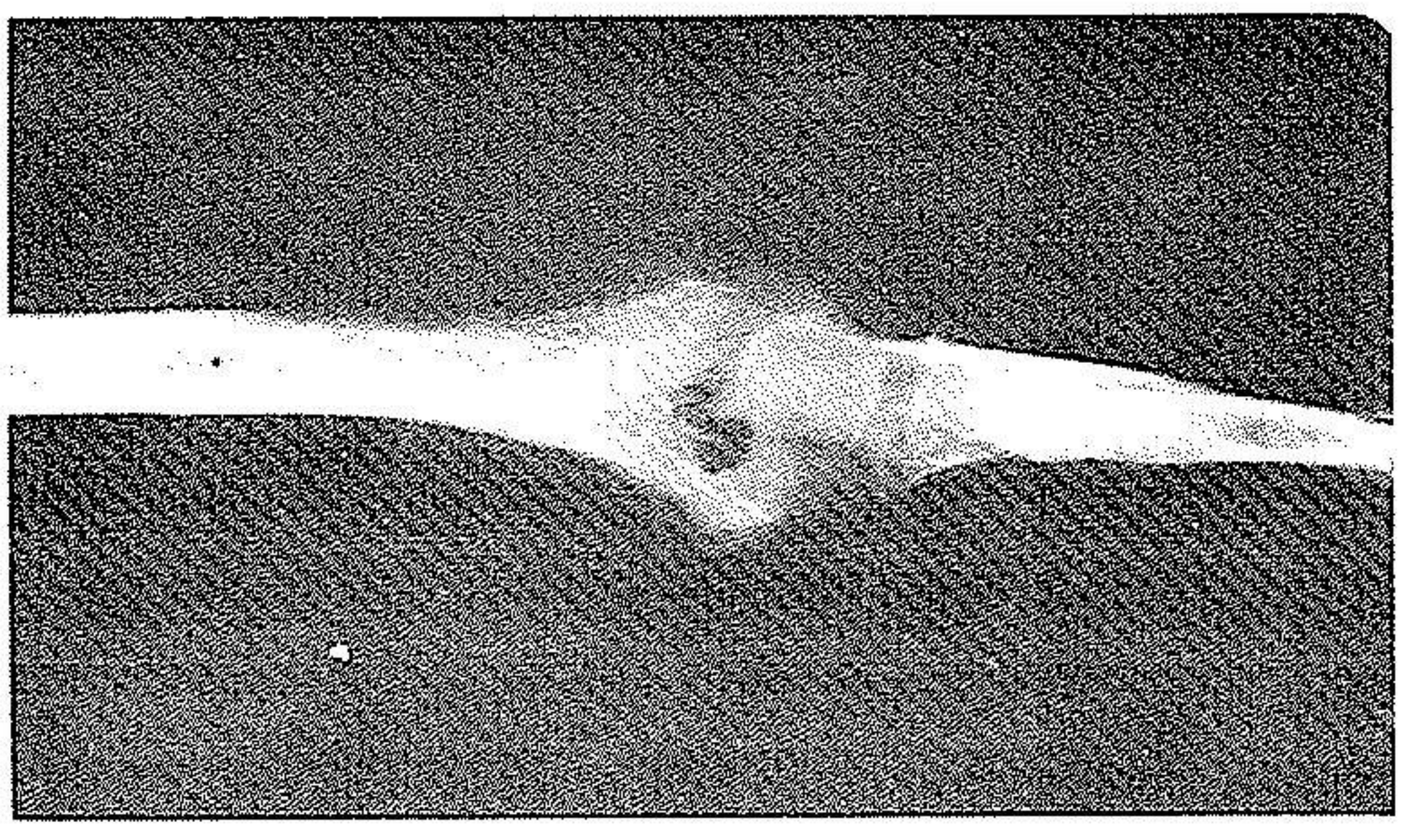
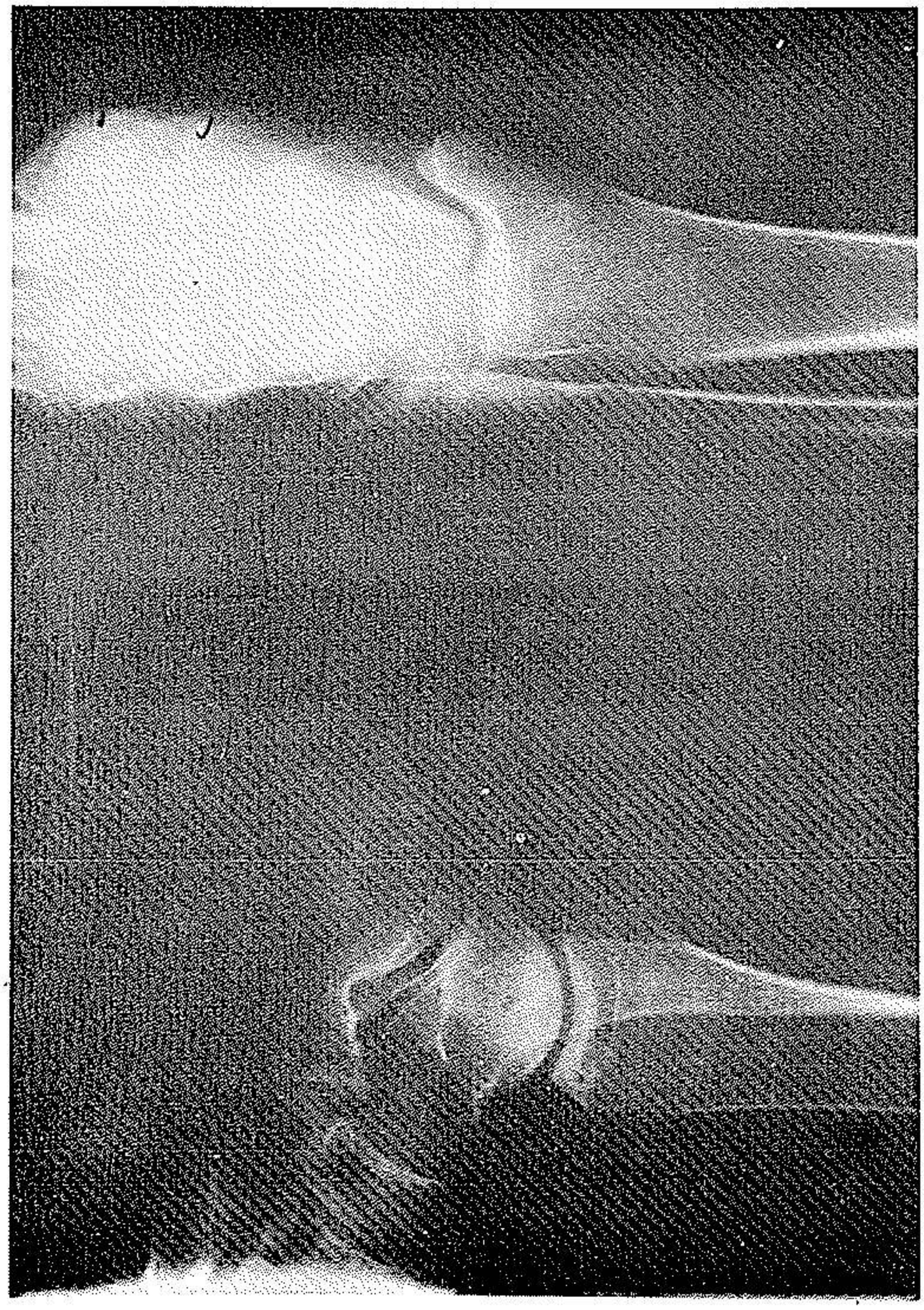


Fig. 2:



Discussion

In this patient active pulmonary tuberculosis developed with concomitant hematogenous dissemination to joint, bone and pleura, cultural confirmation of articular tuberculosis was obtained from synovial tissue. Articular tuberculosis, like other forms of extrapulmonary tuberculosis, is usually due to reactiviation of a hematogenously seeded focus and need not be associated with active tuberculosis elsewhere [2021]. The characteristic pathologic and x-ray findings in articular are caused, in large part, by the pattern and anatomy of the local vascular supply[22-24]. For example, the metaphyseal capillaries loop sharply in the area of the epiphyseal plate. The diameter of the afferent loops is 8, and more numerous efferent loops is from 15 to 60. Thus, efferent blood flow is slower and more turbulent[24]. The metaphyseal capillaries also lack effective phagocytic cells [25] and are thus less able to defend against infection . Furthermore, in adults, there are extensive anastomoses of metaphyseal and epiphyseal vessels. These features, which are conducive to bacterial localization and growth, may account for the synovial reflection[26] found in resected tuberculous joints. Therefore, the early changes seen on roentgenograms in our patient include joint space narrowing, metaphyseal and subchondral erosions, and cysts.

The weight-bearing joints seem to be more commonly affected. It is difficult to say if the daily microtrauma of weight bearing predisposes these joints to infection. Certainly, joint size and vascular supply cannot be the only factors involved in the predisposition of septic joint disease, as the shoulder would be more commonly involved.

Failure to diagnose tuberculous arthritis delays definitive therapy allowing further joint destruction. Therefore,

prompt recognition of this disorder is important. Our patien. tested was tuberculin-positive, and had roentgenologic abnormalities of the involved joint. Tuberculous artheritis sould be suspected if these features are present. Nevertheless, the definitive diagnosis is made by careful and appropriate examination of synovial fluid and tissue. For example, acid-fast bacilli were seen on direct smear of 25 per cent of synovial fluids studied. This procedure, then, should not be omitted.

Although the definitive diagnosis of tuberculous arthritis was obtained by culture and histologic examination with equal frequency, biopsy gives earlier diagnosis.

The chemotherapy of articular tuberculosis is the same as that for most other forms of tuberculosis. Any antituberculous drug regimen, which includes streptomycin, or para-aminosalicylic acid or ethambutol in addition to isoniazid, is virtually effective in all cases in which infection is due to M. tuberculosis. The patients whose course we most recently observed responded well to chemotherapy and immobilization [27].

Tuberculous arthritis should be considered in all patients presenting with monoarticular arthritis of insidious onset. A normal chest film, the absence of constitutional symptoms or the absence of other foci of active tuberculosis should not dissuade one from the diagnosis. Patients should undergo skin tests for tuberculin sensitivity. Although a positive skin test does not indicate active disease in the absence of anergy, a negative skin test makes the diagnosis unlikely. Moreover, synovial fluid and synovial tissue specimens should be obtained promptly from these patients and should be cultured in Dubos liquid culture medium [28].

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