A Rheumatic Syndrome with Laennec's Cirrhosis

By WILLY N. PACHAS AND ROBERT S. PINALS

A MILD inflammatory polyarthritis may be noted in the prodromal stage of viral hepatitis[1] and during the course of chronic or "lupoid" hepatitis.[2] The occurrence of a similar rheumatic syndrome during the recovery phase of Laennec's cirrhosis is the subject of this report.

PATIENTS AND METHODS

During a 3-year period 30 patients with cirrhosis were seen in consultation because of musculoskeletal complaints. In Table 1 the diagnoses in these patients are listed. Although there were no cases of deforming rheumatoid arthritis, 13 patients presented with a mild inflammatory polyarthritis which is described below. During this period of 3 years 387 patients (38 per cent women) were admitted to the hospital with a diagnosis of cirrhosis. Since we did not question or examine the majority of the patients, the true incidence of arthritis is unknown.

A latex fixation test, by the tube dilution method,[3] and indirect fluorescent antibody test for antinuclear factor, using mouse liver as substrate,[4] was performed on the patients with arthritis and on a control group of 104 consecutive patients admitted to the hospital with cirrhosis. In addition, sensitized sheep cell agglutination tests were performed on the arthritis patients (by Dr. Edgar Cathcart).

ILLUSTRATIVE CASE REPORT

A 56-year-old woman with chronic alcoholism of long duration was admitted to the hospital because of abdominal swelling, anorexia and right upper quadrant pain. She was disoriented and slightly icteric. Multiple spider angiomata, moderate ascites and an enlarged, tender liver were noted. Liver function tests were abnormal (Fig. 1) and barium swallow revealed esophageal varices. She had a stormy hospital course with pleural effusion, encephalopathy, and massive gastrointestinal bleeding. After successful portocaval shunt surgery there was remarkable improvement in liver function and in the various clinical manifestations of her disease. About 6 weeks after discharge from the hospital she developed polyarthralgia and morning stiffness lasting 2 to 3 hours. The shoulders, elbows, hands and low back were especially painful. She was unable to make a complete fist, and moderate soft-tissue swelling was noted in the metacarpophalangeal and proximal interphalangeal joints. Shoulder motion was somewhat limited and painful. Joint symptoms persisted for almost one year. She was left with mild flexion contractures of the proximal interphalangeal joints of 2 fingers on the same hand. Roentgenograms showed periarticular demineralization and soft-tissue swelling in the hands. Several latex fixation and antinuclear tests were negative. She has been followed for over one year since cessation of joint symptoms. The liver disease has not progressed.

Table 1.—*Musculoskeletal diagnoses in 30 patients with chronic liver disease who were seen in consultation during a 3-year period.*

Gouty arthritis	8
Chronic bursitis	3
Septic arthritis	2
"Lupoid" hepatitis	2
Spondylolisthesis	1
Hemochromatosis with arthritis	1
Mild inflammatory polyarthritis	13

DESCRIPTION

The 13 patients with inflammatory polyarthritis had many clinical features in common. All but one were women, in contrast with the 38 per cent frequency of women among the control group of hospitalized cirrhotics. Their mean age was 47 (range 33-56). All had a history of chronic al-

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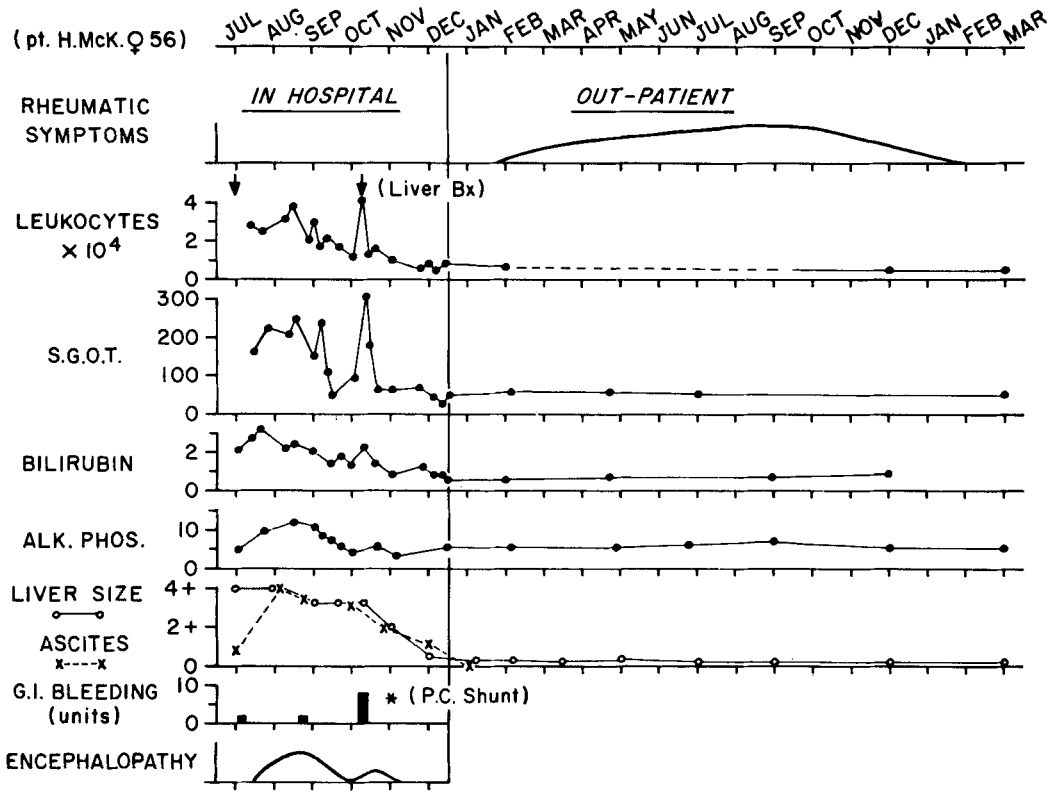

Fig. 1.

coholism and showed clinical and laboratory evidence of hepatic decompensation when admitted to the hospital. These findings are summarized in Table 2. Liver biopsy was performed in 5 cases and histologic changes compatible with Laennec's cirrhosis were noted in all.

There was a striking chronological relationship between the hepatic and rheumatic disorders. In 12 of the 13 patients the rheumatic syndrome first appeared coincident with substantial improvement in liver function and in the various stigmata of cirrhosis. Several patients noted joint pains soon after discharge from the hospital. In the one case in which this pattern was not observed, rheumatic symptoms appeared while the liver was still severely decompensated, but remarkable improvement in liver function occurred soon afterward. Three patients had a past history of mild and vague musculoskeletal complaints, but not of the same type and severity as in their present episode.

In its clinical characteristics the rheumatic syndrome resembled a mild form of rheumatoid arthritis. All of the patients complained of stiffness in the morning and following periods of immobilization during the day. Seven patients felt that cold or damp weather aggravated their symptoms. All had tenderness and pain on motion of the involved joints and mild to moderate soft tissue swelling. There was a tendency toward symmetrical distribution in most of the cases. The shoulders, elbows and knees were the most frequently affected joints. In 6 cases the shoulders were the earliest and most severely involved joints. Limitation of motion was noted in several joints but was never severe, and resolved completely except for one patient who had persistent mild flexion contractures of the proximal interphalangeal joints of 2 fingers.

Table 2.—*Frequency of clinical findings in 13 patients with cirrhosis who subsequently developed arthritis.*

spider angiomata	11
jaundice	9
ascites	8
hepatomegaly	13
splenomegaly	6
esophageal varices	10
encephalopathy	5
SGOT>50	11
leukocytosis	5

Two patients had small bilateral knee effusions. In one of these fluid was aspirated. There was a good mucin clot and 8000 W.B.C./mm^3, of which 77 per cent were neutrophiles. Five patients complained of low back pain, and 7 of myalgia which was especially prominent in the upper arms and thighs. Electromyograms in 2 of these showed a normal pattern.

Radiologic findings were mild and nonspecific. In hand films, soft tissue swelling and juxta-articular demineralization was noted in several cases, but there were no erosive or destructive changes and the joint spaces were maintained. Four patients had small calcific deposits in the rotator cuff of the shoulders. In one of these the deposit disappeared coincident with improvement in joint symptoms. In 2 patients small calcifications at the attachment of the triceps to the olecranon were noted.

The disease has run a benign course in all patients. Seven have had a complete remission after a period of rheumatic symptoms lasting for several months, the average being about 8 months. The others continue to have mild, intermittent pain and stiffness but, in all cases, this is much less severe than at the onset. Two patients have been lost to follow-up. The others have been observed for 1 to 3 years. Most have reduced their consumption of alcohol and have not had progression of liver disease.

There was no significant difference in the incidence of positive latex fixation and antinuclear antibody tests and hyperglobulinemia between the group of 13 patients with arthritis and a series of 104 consecutive cirrhotic patients without arthritis (Table 3). Latex fixation tests were positive in low titer in 2 patients with arthritis. Two different patients had positive antinuclear antibody tests with a homogeneous pattern of nuclear fluorescence. The sensitized sheep cell agglutination test was negative in all of the patients with arthritis. L.E. preparations were negative, with the possible exception of one case in which atypical cytoplasmic inclusions were seen. This patient had no clinical evidence of "lupoid" hepatitis and had a negative antinuclear antibody test.

Discussion

It is likely that if this rheumatic syndrome had been observed in otherwise healthy individuals a diagnosis of mild rheumatoid arthritis would have been made in most cases. Indeed, in every case the criteria for definite rheumatoid arthritis, as proposed by the American Rheumatism Association,[5] were fulfilled. Since mild and early cases of rheumatoid arthritis are often sero-negative,[6] the absence of positive tests for rheumatoid factor in most of the patients would not be surprising. The greater incidence in women is also in accord with the findings in rheumatoid arthritis. However, one must somehow account for the uniform chronological relationship between the hepatic and rheumatic disorders. It is well known that amelioration of rheumatoid arthritis may follow the development of hepatocellular damage and that relapse may occur with recovery of liver function.[7] Possibly these cases represent latent rheumatoid arthritis, becoming clinically manifest when the suppressive influence of liver disease is removed. The mechanism by which liver disease modifies rheumatoid arthritis has never been precisely defined. Inability of the damaged liver to metab-

Table 3.—*Laboratory findings in cirrhotic patients with arthritis and in a control group with cirrhosis but no arthritis.*

	With Arthritis		Without Arthritis	
	No. Pos.	Total	No. Pos.	Total
Positive latex (> 1:80)	2	13	20	104
Positive Antinuclear Factor	2	13	19	97
Mean Total Serum Protein (± SD)		6.96 ± 0.90		6.61 ± 0.94
Mean Serum Globulin (± SD)		3.80 ± 0.66		3.81 ± 0.83

olize corticosteroids formerly had been suggested as a likely explanation,[8] but the finding of normal plasma cortisol values in cirrhotic patients fails to support this hypothesis.[9] However, the recent demonstration that the normal diurnal pattern of cortisol secretion may be absent in chronic liver disease,[10] as in Cushing's syndrome, provides evidence that altered corticosteroid metabolism may be the basis for the "anti-rheumatic" effect of hepatocellular damage.

In the absence of a significant difference in serum globulin and antinuclear factor between the patients with arthritis and a control group of cirrhotic patients without arthritis, it would be difficult to invoke "lupoid hepatitis" as an explanation for this rheumatic syndrome. Although the joint symptoms associated with "lupoid" hepatitis may be similar, they do not occur specifically during the phase of hepatic recompensation. Calcium deposits were demonstrated radiographically in 4 cases in the shoulder, but it is not possible to assign a pathogenetic role to them. The incidence of calcifications in the non-rheumatic control group is unknown. Moreover, most of the involved joints did not show calcifications. The possibility that serum hepatitis from blood transfusions caused the arthritis in these patients seems remote. Rheumatic symptoms in viral hepatitis are transient and usually occur during the prodromal stage of the illness.[11] In all of the cases reported herein, liver function continued to improve after the onset of arthritis.

In conclusion, this rheumatic syndrome in Laennec's cirrhosis may be an unusual clinical expression of some metabolic change taking place in the healing liver, but the nature of this change and the mechanism whereby the joints are affected remain obscure.

Summary

An inflammatory polyarthritis has been observed in 13 patients with Laennec's cirrhosis, during the phase of hepatic recompensation. 12 of the patients were women. The clinical picture resembles a mild, non-progressive rheumatoid arthritis, but the actual relationship to that disease is unclear. The incidence of positive latex fixation and antinuclear antibody tests in this group did not differ from that in a control group of cirrhotic patients.

Summario in Interlingua

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