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# Rapidly Progressive Pancytopenia, Hepatomegaly, and Abnormal Lung Uptake of Colloid in Systemic Lupus Erythematosus: Possible Saturation of Reticuloendothelial System with Blood Elements

## Authors

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## Rapidly Progressive Pancytopenia, Hepatomegaly, and Abnormal Lung Uptake of Colloid in Systemic Lupus Erythematosus: Possible Saturation of Reticuloendothelial System with Blood Elements

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*A patient with systemic lupus erythematosus developed severe abdominal pain and tender hepatomegaly associated with progressive pancytopenia and elevated serum levels of circulating immune complexes. Liver scintigram demonstrated extreme hepatomegaly with poor colloid uptake and splenomegaly with increased colloid uptake. An unusual accumulation of colloid in the lungs was also noted.*

Systemic lupus erythematosus (SLE) is a typical immune complex disease. In experimental animals, circulating immune complexes (IC) have been shown to be removed by the reticuloendothelial system (RES), especially by the liver (1-3). The saturation of hepatic uptake, however, has not been well documented in the human disorder, but has been experimentally documented in mice (2,3). In this paper, we present an interesting case of SLE which manifested pancytopenia associated with a rapidly enlarging tender liver and avid colloid uptake by the lungs. The combination of these abnormalities must be rare in SLE because a similar case could not be found in the literature. Based on studies of liver scintigram, liver enzymes, serum IC, and hemogram, saturation of hepatic uptake was considered to be responsible for these abnormalities.

### Case Report

A 22-year-old woman was admitted to the University Hospital in September, 1980 because of severe right upper quadrant pain associated with enlarging liver and rapidly progressive pancytopenia of four weeks' duration (Fig. 1). The patient also had arthralgia and spiking fever.

Past history and family history were not contributory.

On physical examination, the patient was grossly pale. Funduscopy revealed cotton wool spots and hemorrhages. The liver was palpable 7 cm below the right costal margin with a rounded edge and severe tenderness. Splenomegaly could not be confirmed by

*Subsequent clinical and laboratory studies raised the possibility of saturation of the reticuloendothelial system in the liver by circulating immune complexes and blood cells, a condition demonstrated in experimental animals, but not hitherto well documented in the human immune complex disorder.*

physical examination because of abdominal tenderness. Laboratory tests revealed a leukocyte count of 1600/ $\mu$ l with 48% neutrophils, 44% lymphocytes, and 8% monocytes; hemoglobin, 5.9 g/dl; hematocrit, 18.6%; reticulocyte count,  $4.8 \times 10^9$ / $\mu$ l. Liver enzymes were normal at this time. The following studies were normal: urinalysis, stool guaiac tests, direct and indirect Coombs' tests, serological tests for syphilis, and latex fixation test. Serum levels of haptoglobin, folate and B<sub>12</sub> were normal. Lupus erythematosus (LE) cell preparations and tests for the antinuclear factor (ANF) were positive; CH50 level was 12 units (normal 30-40). Anti-RNP and anti-Sm antibodies were negative. Levels of IC [Clq deviation test (4)] and anti-ds DNA antibody [Millipore-filter assay (5)] were 70% (normal <30) and 56.9% (normal <5), respectively. Bone marrow aspiration was normal with a megakaryocyte count of 105/ $\mu$ l.

The diagnosis of SLE was considered to be established on the basis of arthralgias, hematological abnormalities, positive LE-cell preparations, positive ANF, and positive anti-ds DNA antibody. Therapy was initiated with 60 mg

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## Pancytopenia, Hepatomegaly, and Abnormal Lung Uptake in SLE

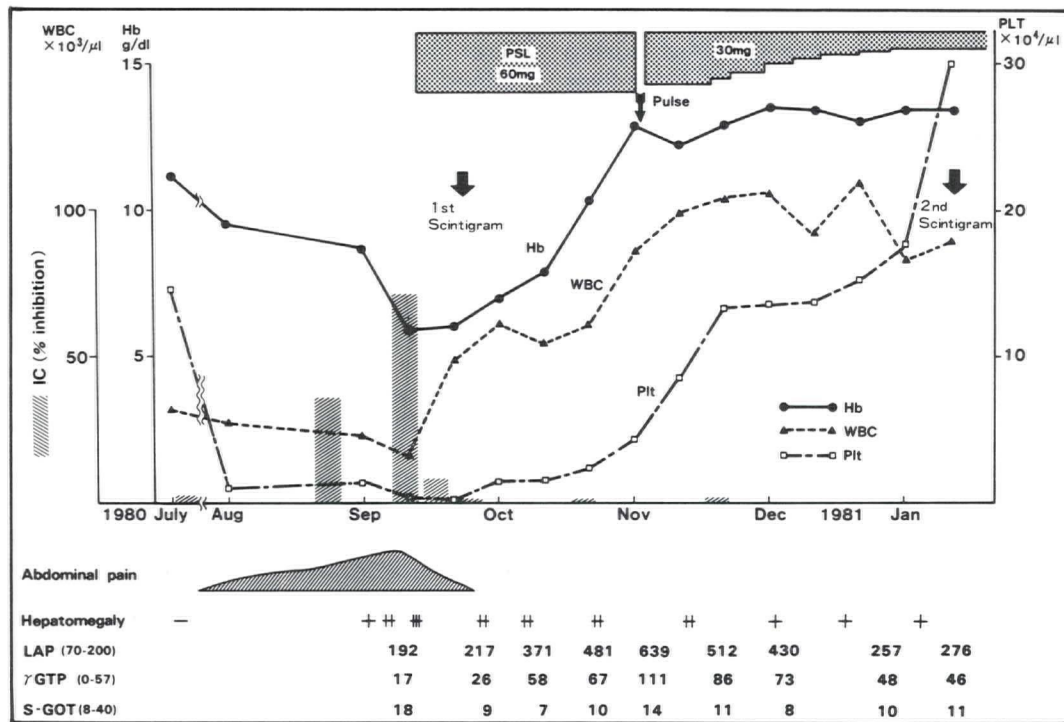


Fig. 1

Changes of the levels of hemocytes, IC, and liver enzymes during treatment. Abdominal pain and hepatomegaly became prominent with high IC level and pancytopenia. LAP and  $\gamma$ -GTP elevated following hepatomegaly.

Hb: Hemoglobin (12-16 g/dl); WBC: White blood cell (4000-9000/ $\mu$ l); Plt: Platelet (15-35 $\times$ 10<sup>4</sup>/ $\mu$ l); IC: Immune complexes (0-30%); LAP: Leucine aminopeptidase (70-200 G.R. unit);  $\gamma$ -GTP:  $\gamma$ -G-lutamyltransferase (0-57 IU/l); ( ) indicates normal ranges

daily of prednisolone. As shown in Fig. 1, the patient responded well to the treatment with improvement of anemia, leukopenia, and abdominal pain. However, the platelet count remained around 10,000/ $\mu$ l. After two months of treatment, a "pulse therapy" was given for persistent thrombocytopenia with subsequent improvement. From the first visit in July, the IC level rose gradually and peaked in mid-September, 1980. The level rapidly decreased after prednisolone treatment was given.

On September 26, liver scan was performed using 7 mCi of <sup>99m</sup>Tc-phytate. Twenty minutes after the colloid was injected intravenously, camera studies were carried out in the anterior, posterior, right lateral, and right oblique projections (Fig. 2). The images confirmed severe hepatomegaly with poor colloid uptake and splenomegaly with increased colloid uptake. Of interest was an unusual accumulation of colloid in the lungs, indicating increased lung uptake as defined by Keyes, et al (6). A second liver scintigram, performed after hematologic recovery in January, 1981, showed almost normal images of the liver and spleen and disappearance of abnormal colloid uptake by the lungs.

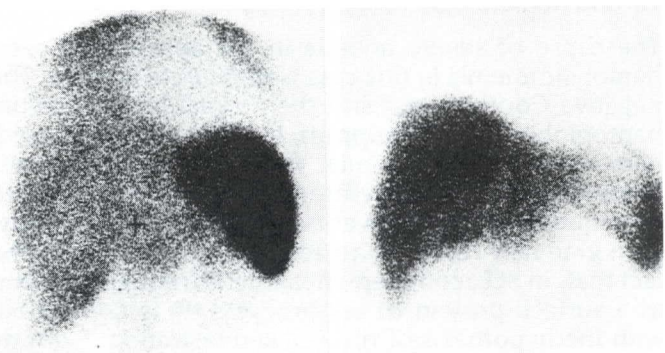


Fig. 2

Left: Liver scintigrams (same magnification) performed on September 26, 1980. Marked hepatomegaly with poor colloid uptake. Note unusual lung and prominent spleen uptake.

Right: Performed on January 14, 1981. Liver size, uptake of colloid by liver and spleen are almost natural. Lung uptake is no longer demonstrated.

The levels of  $\gamma$ -glutamyltransferase ( $\gamma$ -GTP) and leucine aminopeptidase (LAP), which were elevated during hepatomegaly, became normal as the size of the liver and hematological values improved (Fig. 1). The level of alkaline phosphatase (Al-P) was slightly abnormal in parallel with these enzymes. Levels of GOT and GPT remained within the normal ranges. The HBAg remained negative. After four months of prednisolone therapy, all the hematologic and serologic abnormalities which were present on admission became normal, and the patient was discharged receiving a maintenance dose of prednisolone.

### Comment

A striking feature in this case was that progressive pancytopenia and elevation of the levels of circulating IC developed concomitantly with acute hepatomegaly and that the scintigram taken at that time confirmed extreme hepatomegaly with poor colloid uptake associated with an abnormal pulmonary and splenic uptake. In addition, levels of liver enzymes indicating biliary tract obstruction paralleled changes in the liver size. Mannik demonstrated that experimentally prepared immune complexes are preferentially removed by the liver (1). It is only after the liver is saturated that the lungs and the bone marrow function like the reticuloendothelial system. In our case, we assume that the liver had been saturated by immune complexes and sensitized hemocytes, hence the colloid shift to the spleen, the lungs, and the bone marrow. The severe abdominal pain was attributed to rapid expansion of the liver capsule. The results of subsequent liver scintigram studies after clinical and hematologic recovery support this assumption.

The cause of severe anemia in the absence of overt hemolytic anemia in this case is difficult to explain. The negative Coombs' test and the normal level of serum haptoglobin do not support the possibility of autoimmune hemolytic anemia. In experimental animals, complement-bearing erythrocytes have been shown to be sequestered by the liver in the absence of antibody, then gradually return intact to the circulation (7,8). The fact that, in SLE, complement alone is frequently found as a surface protein of erythrocytes (9) is compatible with the hypothesis of red cell sequestration. Garratty and Petz reported that eight of ten commercial "broad-

spectrum" antiglobulin sera failed to react with cells strongly sensitized with complement which were obtained from patients with hemolytic anemia (10). Sequestration rather than hemolysis may have been responsible for the anemia in our case. The abnormally reduced hepatic colloid uptake may be explained by the presence of both IC and blood cells adherent to the surface of Kupffer cells through C3b receptors. Elevated levels of  $\gamma$ -GTP and LAP with normal levels of SGOT and SGPT during the first months of hospitalization could be the result of saturated sinusoids obliterating the biliary tracts.

Diagnosis of acute and chronic hepatitis and malignant tumor can be excluded on the basis of the levels of GOT and GPT along with the hospital course. Steatosis of the liver, reported as a common hepatic disorder in SLE (11), is also unlikely; the patient had developed hepatomegaly before prednisolone therapy, and the liver size returned to normal with the treatment. Thus, accumulation of IC and sequestration of blood cells seems the most reasonable explanation for the hepatomegaly.

Hepatomegaly is present in 30-40% of SLE cases, and the incidence of cytopenia is significant in those patients (11). This correlation supports our concept that the liver is at least partly responsible for the sequestration of sensitized hemocytes in this disease.

The presence of another independent blood dyscrasia is excluded by the results of laboratory studies and the clinical course.

Klingensmith, et al (12) described six patients with collagen-vascular diseases among 27 patients with increased lung uptake during liver scintigram. To explain their findings, they raised the possibility of diffuse liver disease and decreased hepatic clearance of colloid. Our concept is compatible with their theory; the presence of diffuse liver abnormality is apparent from the abnormal liver image.

It has been shown that clearance of particles mediated by these RES membrane receptors is independent of the clearance of aggregated albumin, which is not mediated by receptors (13). It seems probable, however, that the uptake of colloid by the liver may be impeded when the degree of saturation by IC and blood cells is extreme.

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