A Case of Viral Hepatitis with Pleural Effusion

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A 27-year-old male was admitted to the Toho University Hospital with icterus and massive right pleural effusion containing 4.0g/dl of protein. The hepatocellular dysfunction and positive HBs antigen were revealed and he was diagnosed as typical acute viral hepatitis, type B. Evaluation for his pleural effusion presented no evidence of pulmonary parenchymal disease, tuberculosis, or other systemic disorder. Since the effusion resolved with normalization of liver function tests, it is most likely that the effusion was a complication of viral hepatitis. Cases with pleural effusion as the presenting sign of viral hepatitis are rare in the recent medical literature. A survey of publications disclosed the presence of this association in at least 11 patients, not including our own.

Key Words: Viral hepatitis, Liver biopsy, HBs antigen, Pleural effusion.

A 27-year-old businessman was admitted to the Toho University Hospital in September of 1976 for evaluation of icterus and pleural effusion. The patient had been well until 2 weeks prior to admission when he noticed general fatigue, anorexia, abdominal fullness and epigastric discomfort. He was entertained by a physician with the diagnosis of hepatitis. At that time, it was noted that serum glutamic oxaloacetic transaminase was 397 units, serum glutamic pyruvic transaminase was 501 units, while serum bilirubin level was normal. About 5 days after, dry cough, easy fatigability and nausea occurred and dark urine was noticed. He had never been exposed to hepatotoxins including ethanol, and received neither surgical treatment nor blood transfusion. Physical examination revealed a jaundiced man in mild respiratory distress with a blood pressure of 110-70mmHg, a regular pulse of 90 beats per minute, and a body temperature of 36.5°C. The sclerae, palate and

skin were icteric, but without rash. No lymphadenopathy was noted. There were dullness, decreased tactile fremitus and decreased breath sounds over the lower half of the right chest. The remainder of the chest was clear to auscultation. Cardiac examination revealed no rubs or murmurs. The liver was palpable 3cm below the right costal margin with a tender, soft, sharp edge. The spleen was not palpable. There was no shifting dullness or fluid wave. Neurological and mental examinations were negative.

Laboratory data showed hepatocellular injury and the following values: serum glutamic oxaloacetic transaminase, 214RF units; serum glutamic pyruvic transaminase, 300RF units; alkaline phosphatase, 142 international units; lactic dehydrogenase, 238 international units; icterus index, 55; total bilirubin, 5.8mg/dl; thymol turbidity test, 17.6SH units; zinc sulfate test, 11.4SH units; total protein, 6.3g/dl; γ -globulin, 20.8%; total cholesterol, 204mg/

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Table 1. Cases of pleural effusion associated with viral hepatitis (bibliographical)

Authors	Year	Number of Cases	Nature of Fluid Protein (g/dl)
Gross & Gerding	1971	1	exudative 4.8
Katsilabros et al	1972	4	
Owen & Shapiro	1974	1	exudative
Forster et al	1975	5	exudative 3.0-4.0
(Sugimoto et al)	1977	1	exudative 4.0

Fig. 3. Chest roentgenogram on the 20th day after admission. Pleural effusion completely disappeared.

Fig. 1. Chest roentgenogram on admission. Massive right pleural effusion is evident.

Fig. 4. Slight dissociation of hepatic cell cords with scattered necrotic lesions and diffuse fatty degeneration are seen. Binucleated cells are numerous. Edema and fibrosis with slight cell infiltration are seen in portal triad. (H. E. stain)

Fig. 2. Clinical course.

dl. HBs antigen was positive and α -fetoprotein was also elevated.

Chest roentgenogram (Fig. 1) revealed a right pleural effusion. By thoracentesis 80ml of yellow fluid with a specific gravity of 1.032 and total protein of 4.0g/dl was

Fig. 5. Kupffer cell mobilization in the parenchyma with iron uptake strongly suggests viral hepatitis. (Perls' method for iron)

Fig. 6. Moderate collapse of lobular architecture is evident. (Reticulin stain)

Fig. 7. HBs antigen is negative. (Shikata's method)

obtained. Microscopically, numerous reactive mesothelial cells and a few of matured lymphocytes and neutrophilic cells, but no malignant cell were seen. Gram stain and Ziehl-Neelsen stain were negative for bacteria, mycobacteria and fungi. Antibodies of viruses for Coxsackie A-9, B-1, Adeno and Cytomegalovirus were not elevated in the fluid.

Cultures of sputum and morning gastric aspirations were negative. Tuberculin skin test was positive, but chest films of lateral decubitus and postthoracentesis showed no evidence of parenchymal lung disease. Antibodies of viruses in serum for Influenza A, B, Parainfluenza I, II, Coxsackie A-9, B-1, B-3, Adeno, Mumps, Herpes simplex, Cytomegalovirus and R. S. virus were not elevated. Although Parainfluenza III and Rubella were slightly elevated, no changes were seen 3 weeks later. Electrocardiogram was within normal

limits. An upper gastrointestinal X-ray series and barium enema study were normal. Liver scintiscanning showed no abnormalities.

Following the right thoracentesis, the patient was treated conservatively with bed rest and a high caloric diet. Furosemide 40mg per day was administered for 10 days. During the first 10 days of hospitalization, the patient's condition was gradually improved and the liver size decreased accompanied by a return of the liver function tests toward normal (Fig. 2). Twenty days after the admission, pleural effusion completely disappeared on the chest roentgenogram (Fig. 3), although diuretics had already been stopped. In this chest film no pulmonary parenchymal lesion was evident. About a month after the admission, values of transaminases and total bilirubin were completely normal and titer of α -fetoprotein was decreased (Fig. 2). Liver biopsy was performed on the 58th day of hospitalization.

Microscopically (Fig. 4), a slight dissociation of the hepatic cell cords with minimal necrotic lesions and diffuse fatty degeneration were present in the lobulus. Binucleated cells were increased. Edema and fibrosis with a slight cell infiltration mainly of lymphocytes and some neutrophilic cells were seen in portal triad. A specimen stained by Perls' method (Fig. 5) showed a scattered iron uptake into Kupffer cells. On reticulin stain (Fig. 6), collapses of the lobular architecture was evident. A specimen stained by Shikata's method¹⁾ (Fig. 7) was negative for HBs antigen.

The patient was discharged on the 14th day after the liver biopsy.

DISCUSSION

Although the route of transmission was not clear in this patient, his typical course and positive HBs antigen in the serum strongly suggested the diagnosis of acute viral hepatitis, type B, in spite of the presence of pleural exudation, which was

the primary presenting sign. The histological finding was also consistent with the clinical diagnosis, with the exception of fatty degeneration, which is not the feature of viral hepatitis. Fatty degeneration may be associated with hepatitis, especially in a severe case, or in a patient overnourished during the convalescent period²³. Moderately collapsed liver lobuli seen in the biopsy specimen taken on the 58th day of hospitalization, suggested that the hepatic damage in this patient might have been considerably severe.

Pleural effusion is well known as an occasional complication in hepatic diseases. In a series of 436 cases with pleural effusion, Leuallen and Carr³³ reported that 2% of the cases were due to liver cirrhosis. Johnston and Loo⁴¹ reviewed 200 cases with cirrhosis and found the incidence of pleural effusion to be 6% (12 cases). In these patients, the pleural fluid was a transudate and the effusion was on the right in 8, on the left in 2, and bilateral in 2. These authors, by injecting radioiodinated albumin into the pleural and peritoneal cavities and intravenously, suggested that the pleural fluid was derived from the peritoneal fluid. Lieberman et al⁵¹, in a study of 330 cases with cirrhosis and ascites, reported that the incidence of hydrothorax was 5.4% (18 cases).

In hepatitis, pleural effusion may be more usual than is commonly believed. In a prospective Italian study⁶¹, 70% of 156 patients with hepatitis had at least a small pleural transudation ranging in quantity from 2 to 50ml and occasionally seen before the patients became noticeably jaundiced.

Exudative pleural effusions large enough for clinical detection have recently been observed as a complication of acute viral hepatitis⁷¹⁻¹⁰¹ (Table 1). The case of this association was first reported by Gross and Gerding⁷¹ in 1971. An 18-year-old girl with right-sided massive serous effusion containing 4.8g/dl of total protein was presented. The effusion of this patient, initially suspected for tuberculosis, resolved

accompanied by normalization of the liver function test. Adding to this report, effusions were seen in 4 cases out of 2500 patients with viral hepatitis, during a 10-year period in a Greek hospital⁸¹. However, in this description, the nature of effusions was not clarified.

Owen and Shapiro⁹¹, in 1974, reported a case of 42-year-old male who had skin rash, anergy, exudative pleural effusion of the right chest and transient hematuria, presenting mildly depressed serum complement (C₃) as the initial sign of viral hepatitis. Forster et al¹⁰¹, in 1975, presented 3 cases of acute and 2 of chronic aggressive hepatitis associated with pleural effusion rich in protein (3-4/gdl). In 2 of these cases, positive test for HBs antigen in the fluid was demonstrated. These facts suggest a certain immunological factor or direct invasion of the virus as the cause of associated pleuritis. Further evidences are expected to know the real nature of this complication.

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