Peliosis Hepatis Associated with Idiopathic Restrictive Cardiomyopathy

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A rare case of peliosis hepatis associated with idiopathic restrictive cardiomyopathy is reported. A 75-year-old man was admitted for evaluation of marked edema and jaundice. Serum total bilirubin was elevated above 20 mg/dl. The liver biopsy under laparoscopy revealed marked sinusoidal dilatation and retention of red blood cells, which was consistent with a diagnosis of peliosis hepatis. Cardiac catheterization revealed right ventricular filling disturbance without specific findings on endomyocardial biopsy, suggesting idiopathic restrictive cardiomyopathy. The level of serum total bilirubin decreased in association with improvement of edema after drip infusion of furosemide therapy.

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Introduction

Peliosis hepatis is an unusual disorder characterized by multiple blood filled cavities in the hepatic parenchyma. Regarding the etiology of peliosis hepatis, many hypotheses such as congenital malformation (1), androgenic anabolic steroid (2) or oral contraceptive administration (3), and acquired immuno-deficiency syndrome (4) have been proposed. On the other hand, restrictive cardiomyopathy is also a rare disorder characterized primarily by abnormal diastolic filling. Here, we report a patient with peliosis hepatis who had idiopathic restrictive cardiomyopathy. The relationship between the two conditions is discussed.

Case Report

A 75-year-old male patient was admitted to our hospital on November 11, 1996, for evaluation of marked edema and jaundice. He had been well until September 1996 when swelling of the lower legs, dyspnea, and jaundice developed gradually and he was admitted to a local hospital. He used to drink excessively before he quit drinking 25 years ago. The edema disappeared after administration of diuretics, but the cause of edema was undetermined and serum bilirubin remained elevated. He visited our hospital with worsening symptoms after

discharge.

On physical examination, there was marked pitting edema in the lower legs. The abdomen was distended and fluid wave was demonstrable. The liver and spleen were not palpable. The penis and scrotum also showed marked edema. The chest was clear to percussion and auscultation.

Laboratory data after admission are summarized in Table 1. Results of urinalysis were normal. Hematological examination revealed mild anemia and a slight decrease in platelet count. Liver function test showed marked elevation of total bilirubin and alkaline phosphatase, moderate serum transferase elevation, and a decrease in serum cholinesterase, total cholesterol, and albumin. Serum electrophoresis disclosed an increase in the gamma globulin fraction. Viral markers for hepatitis B or hepatitis C were all negative. Serologic tests for autoantibodies were all negative.

Chest X-ray film showed no abnormal findings (cardiothoracic ratio 46%). The pericardium was not thickened in lateral view. An electrocardiogram showed first degree arterioventricular block with nonspecific ST-segment and T-wave changes. Abdominal ultrasound and computed tomography (CT) scan revealed dilatation of inferior vena cava and hepatic vein, and small amount of ascites was detected. There was no evidence to substantiate a diagnosis of liver cirrhosis or obstructive jaundice on radiographic examination. An

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Table 1. Laboratory Data on Admission

Urinalysis	n.p.	γ -glutamyl transpeptidase	95 IU/l
Peripheral blood		Thymol turbidity test	5.2 Kun-U
White blood cell count	3,920/mm ³	Zinc sulfate turbidity test	15.9 Kun-U
Red blood cell count	378×10 ⁴ /mm ³	Blood urea nitrogen	16.5 mg/dl
Hemoglobin	11.7 g/dl	Creatinine	0.8 mg/dl
Hematocrit	36.7%	Total cholesterol	133 mg/dl
Platelet	11.8×10 ⁴ /mm ³	Fasting plasma glucose	77 mg/dl
Prothrombin time	52.5%	Ammonia	86 μ g/dl
Hepaplastin test	22.6%		
Blood Chemistry		Serological test	
Total protein	5.7 g/dl	C-reactive protein	1.53 mg/dl
albumin	48.0%	Hepatitis B surface antigen	(-)
α_1	3.2%	Hepatitis B surface antibody	(+)
α_2	6.6%	Hepatitis B envelope antigen	(-)
β	10.4%	Hepatitis B envelope antibody	(+)
γ	31.8%	Hepatitis B Viral DNA	(-)
Total bilirubin	6.2 mg/dl	Hepatitis B Viral polymerase	(-)
Direct bilirubin	3.9 mg/dl	Hepatitis C antibody	(-)
Aspartate aminotransferase	58 IU/l	Antinuclear antibody	×20
Alanine aminotransferase	31 IU/l	Anti-mitochondrial antibody	(-)
Alkaliphosphatase	539 IU/l	Anti-smooth muscle antibody	(-)
Lactate dehydrogenase	272 IU/l		
Cholinesterase	71 IU/l		

echocardiogram showed no abnormal findings except for first degree tricuspid valve regurgitation.

All medication was discontinued to rule out drug-induced hepatitis. However, bilirubin progressively elevated above 15

mg/dl. Thus, laparoscopy was performed for further examination. The laparoscopy showed dark brown liver with scattered dark red spots (Fig. 1). The liver biopsy specimen revealed marked sinusoidal dilatation and retention of red blood cells (Fig. 2). Fibrosis and infiltration of inflammatory cells were not seen. Marked sinusoidal dilatation was observed only in part of the biopsy specimen obtained (Fig. 3). Silver stain of the specimen showed disruption of reticulin framework (Fig. 4). These laparoscopic and pathologic findings were consistent with a diagnosis of peliosis hepatis.

Figure 1. Laparoscopic examination, showing dark brown liver with scattered dark red spots.

Figure 2. Light microscopic appearance of HE stain of the liver biopsy specimen with higher magnification (×200) showing marked sinusoidal dilatation and retention of red blood cells.

Figure 3. Light microscopic appearance of HE stain of the liver biopsy specimen with lower magnification ($\times 40$) showing that sinusoidal dilatation was observed only in part of the specimen.

Figure 4. Silver stain of the liver biopsy specimen showing disruption of reticulin framework ($\times 60$).

Inferior vena cava venography, which was performed to rule out obstruction to venous outflow, revealed marked regurgitation from the inferior vena cava into the hepatic vein (Fig. 5). Right-sided and left-sided cardiac catheterization was per-

Figure 5. Inferior vena cava venography showing marked regurgitation from inferior vena cava into hepatic vein.

Table 2. Hemodynamic Measurements

Heart rate	67 (beat/min)
Aorta (systolic/diastolic)	92/58 (mmHg)
Left ventricle (systolic/diastolic/mean)	94/3/15 (mmHg)
Right ventricle (systolic/diastolic/mean)	27/11/13 (mmHg)
Right atrium (mean)	13 (mmHg)
Inferior vena cava	13 (mmHg)
Pulmonary artery (systolic/diastolic)	23/15 (mmHg)
Pulmonary capillary wedge	12 (mmHg)
Cardiac index	1.8 (l/min/m ²)

Figure 6. Pressure curve from the left atrium and the right ventricle.

Figure 7. Clinical course.

formed to observe cardiac function (Table 2). Coronary and a left ventricular angiographic examinations were normal. Although the pressure curve from the right ventricle did not show the typical dip and plateau pattern, the pressure curve from the right atrium showed prominent x and y descents (w shape), suggesting that the right ventricular filling was disturbed (Fig. 6). Endomyocardial biopsy was performed, but no specific finding was obtained. Congo red stain was negative. These results indicate a diagnosis of peliosis hepatis associated with idiopathic restrictive cardiomyopathy.

After drip infusion of furosemide (240 mg/day) together with a small dose of dopamine (2 µg/kg/min), the leg edema gradually decreased and subsequently the bilirubin level decreased to 10 mg/dl (Fig. 7). However, after discontinuing drip infusion, the leg edema increased and subsequently bilirubin became elevated above the level of 20 mg/dl. Drip infusion of furosemide and dopamine were administered again, which decreased edema and bilirubin in the same way. He is now treated with an injection of 40 mg of furosemide once a day together with 120 mg of furosemide orally, and the level of bilirubin has stabilized at about 10 mg/dl.

Discussion

Though several hypotheses have been proposed, the mechanism of peliotic cavity formation is not clear. Ultrastructural lesions of the liver suggest that primary alterations of the sinusoidal barrier and secondary changes to increased pressure and hypoxia contribute to the formation of peliotic cavity (5).

Longstanding right-sided heart failure due to cardiomyopathy or pericardial constriction may lead to liver abnormalities which resemble our case. The fact that the level of serum bilirubin decreased in association with improvement of edema

suggests that liver congestion contributed to liver abnormalities in the present case. However, cardiac cirrhosis shows striking congestion and centrilobular necrosis followed by linking of central zones with fibrosis. In this case, fibrosis was not seen and marked sinusoidal dilatation was observed only in part of the biopsy specimen obtained, which makes the diagnosis of cardiac cirrhosis unlikely. Thus, it is unlikely that liver congestion was the primary cause of liver abnormalities. There are two different types of peliosis hepatis: the original parenchymal type in which the blood cysts are not distinctly lined; and the phlebotatic type with endothelial or fibrous lining (6). Silver stain showed disruption reticulin framework, which may classify our case as the phlebotatic type. However, the division between the 2 types may not be as clear as suggested above and both types may be present in the same patient. Peliosis hepatis is potentially reversible to a certain degree unless serious underlying conditions exist (7). Though the primary cause of peliotic cavity formation in the present case is still uncertain, it is assumed that underlying restrictive cardiomyopathy and subsequent liver congestion made the peliotic changes irreversible.

Despite the application of a variety of hemodynamic criteria (8), distinguishing constrictive pericarditis from restrictive cardiomyopathy is difficult. Since constrictive pericarditis is a surgically curable disease, the distinction is of clinical importance. Endomyocardial biopsy has proven useful in establishing the diagnosis of specific forms of restrictive cardiomyopathy such as amyloidosis (9). However, in patients without specific pathologic findings, the need for surgical interventions must be considered. Imaging technologies such as CT scanning (10) or magnetic resonance imaging (MRI) (11) appear to be a sensitive means of detecting an abnormal pericardium. The present patient was diagnosed as having restrictive cardiomy-

opathy because neither CT scanning nor MRI detected a thickened pericardium. Thus, a thoracotomy was not performed.

In summary, we encountered a case of peliosis hepatis associated with idiopathic restrictive cardiomyopathy. The level of serum total bilirubin decreased in association with improvement of edema. Liver biopsy under laparoscopy was useful for differential diagnosis. A diagnosis of peliosis hepatis should be included in the differential diagnosis of patients with jaundice.

References

- 1) Weir MR, Decherd J, Beathard G. A unique case of peliosis hepatis. *Tex Rep Biol Med* **27**: 1105, 1969.
- 2) Nadell J, Kosek J. Peliosis hepatis. Twelve cases associated with oral androgen therapy. *Arch Pathol Lab Med* **101**: 405, 1977.
- 3) Ockner RK, Davidson CS. Hepatic effects of oral contraceptives. *N Engl J Med* **276**: 331, 1967.
- 4) Czapar CA, Weldon-Linne CM, Moore DM, Rhone DP. Peliosis hepatis in the acquired immunodeficiency syndrome. *Arch Pathol Lab Med* **110**: 611, 1986.
- 5) Zafrani ES, Cazier A, Baudelot AM, Feldmann G. Ultrastructural lesions of the liver in human peliosis. A report of 12 cases. *Am J Pathol* **114**: 349, 1984.
- 6) Yanoff M, Rawson A. Peliosis hepatis – An anatomic study with demonstration of two varieties. *Arch Pathol* **77**: 159, 1964.
- 7) Bagheri SA, Boyer JL. Peliosis hepatis associated with androgenic-anabolic steroid therapy. A severe form of hepatic injury. *Ann Intern Med* **81**: 610, 1974.
- 8) Vaitkus PT, Kussmaul WG. Constrictive pericarditis versus restrictive cardiomyopathy: a reappraisal and update of diagnostic criteria. *Am Heart J* **122**: 1431, 1991.
- 9) Schoenfeld MH, Supple EW, Dec GW Jr, Fallon JT, Palacios IF. Restrictive cardiomyopathy versus constrictive pericarditis: role of endomyocardial biopsy in avoiding unnecessary thoracotomy. *Circulation* **75**: 1012, 1987.
- 10) Sutton FJ, Whitley NO, Applefeld MM. The role of echocardiography and computed tomography in the evaluation of constrictive pericarditis. *Am Heart J* **109**: 350, 1985.
- 11) Soulen RL, Stark DD, Higgins CB. Magnetic resonance imaging of constrictive pericardial disease. *Am J Cardiol* **55**: 480, 1985.