Cirrhosis of Liver Simulating Congenital Cyanotic Heart Disease

By R. C. Hansoti, M.D., and N. J. Shah, M.D., M.R.C.P.

CENTRAL CYANOSIS in cirrhosis of liver was first observed by Fluckiger in 1884. Subsequently, there have been a few reports of desaturation of arterial blood in this condition. It is unusual, however, for cases of cirrhosis of liver to show dyspnea, central cyanosis, and clubbing and thus to simulate congenital cyanotic heart disease. In the last 3 years we examined seven such patients who were diagnosed as cases of congenital cyanotic heart disease. In this communication, the clinical features of these seven cases are described and the pathogenesis of cyanosis is discussed.

Material and Method

Our material consists of seven patients with severe cyanosis and gross clubbing simulating congenital cyanotic heart disease seen between 1962 and 1965 who showed no evidence of intracardiac shunt but were found to have cirrhosis of liver probably with intrapulmonary arteriovenous shunt.

Clinical history was obtained with special reference to the duration of cyanosis, clubbing, and other symptoms, as well as history of antecedent jaundice, alcoholism, umbilical sepsis, and hematemesis, and a complete clinical examination was performed in all cases.

Routine investigations consisting of hematocrit value, chest X-ray, a 13-lead electrocardiogram, barium examination of the esophagus, liver-function tests, and spectroscopic examination of the blood were performed in all.

Every patient was subjected to right heart catheterization and selective right ventricular and pulmonary angiography. Transsplenic portal splenography was carried out in all. In three instances this was performed with a serial changer with plates covering the upper abdomen and chest to observe portopulmonary fistulas if possible. In two patients selective right lower lobe pulmonary arteriography was performed.

A needle biopsy of the liver was obtained in six patients and an open biopsy in one. An open-lung biopsy of the right lower lobe was performed in one.

Results

Five of the patients were male and two were female; all were between 12 and 21 years of age; all of them showed severe cyanosis, gross clubbing, and severe effort intolerance of 2 to 4 years' duration (fig. 1). Four patients also complained of a lump in abdomen, and one observed a soft swelling on the right forearm and swelling of ankles and wrists. There was no history of antecedent jaundice, alcoholism, protein malnutrition, umbilical sepsis, or hematemesis in any patient.

Every patient had severe cyanosis and gross clubbing, warm hands, wide pulse pressure, a grade-II/VI ejection systolic murmur, and a normally split second heart sound with normal aortic and pulmonary components at the pulmonary area. The spleen was enlarged in all and grossly so in six. The liver was palpable 1 to 3 fingerbreadths below the costal margin in all. One patient had marked swelling of the ankles and wrists due to osteo-

Figure 1

Patient had severe cyanosis and gross clubbing (case 1).
arthropathy. He also had a hemangioma on the lateral aspect of the upper part of right forearm. He exhibited marked wingflap tremors of the outstretched hands, but there was no Kayser-Fleischer ring nor any other neurologic abnormality. Two patients had arterial spiders and telangiectasias on their chest, back, and arms. One patient showed a marked caput medusae and another a few engorged veins on the abdomen. None of the patients showed evidence of free fluid in the abdomen.

Slight enlargement of the heart with somewhat increased pulmonary vascularity was present in three, and chest X-rays were normal in the remaining four patients. The electrocardiogram was within normal limits in all. Barium swallow demonstrated esophageal varices in three patients. There was a mild degree of polycythemia in six. Spectroscopic examination of the blood revealed no abnormality.

The liver-function tests were abnormal in six patients (table 1). The serum globulin was raised in six; in two patients in whom plasma electrophoresis was performed, the rise was largely due to γ-globulin. Bromsulfalein retention was increased and flocculation tests were positive in five.

Intrasplenic pressure was raised in all patients (table 2). In none of the three cases, on whom a serial changer was used with the film covering the upper abdomen and the chest, was the portal vein visualized. A few collateral vessels were seen near the splenic hilus and a large vein was seen to open into the inferior vena cava in all three (fig. 2). No communications were seen between portal and pulmonary veins. Of the remaining four patients in whom only a single film was exposed, the intrahepatic pattern was visualized in two and was found to be distorted. Portal vein collateral channels were observed in all four and in one a large venous channel seemed to open into the inferior vena cava. In the other three cases the course of these collateral channels could not be ascertained.

Table 3 shows the pressures in the right heart chambers to be normal in all. There was marked desaturation of the femoral arterial blood in all, which could not be restored to normal by inhalation of 100 per cent oxygen for 10 minutes. Pulmonary venous samples were obtained in three and were found to be markedly desaturated.

Selective right ventricular angiography (three per second) revealed no intracardiac shunt in any case. The pulmonary vasculature appeared blotchy in all (fig. 3). In patients 1 and 2, on whom a selective right lower lobe pulmonary arteriography was performed (six

<table>
<thead>
<tr>
<th>Liver-Function Tests</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma protein,</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>6.5</td>
<td>7.2</td>
<td>5.8</td>
<td>6.0</td>
<td>7.0</td>
<td>6.8</td>
<td>5.5</td>
</tr>
<tr>
<td>albumin</td>
<td>3.0</td>
<td>3.0</td>
<td>2.8</td>
<td>2.4</td>
<td>2.8</td>
<td>3.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Gm. per cent globulin</td>
<td>3.5</td>
<td>4.2</td>
<td>3.0</td>
<td>3.6</td>
<td>4.2</td>
<td>3.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Thymol-turbidity, units</td>
<td>10</td>
<td>12</td>
<td>7</td>
<td>7</td>
<td>9</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Thymol flocculation</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Cephalin cholesterol flocculation</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Bromsulfalein retention at 45 minutes after injection of 5 mg./Kg.</td>
<td>9.5</td>
<td>20</td>
<td>10</td>
<td>12</td>
<td>10</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

*Electrophoretic study of plasma proteins, serum cholesterol, and cholesterol ester estimation and estimation of SGOT and SGPT was performed in cases 1 and 2.

In case 1 results were albumin 3 Gm. per cent, \( a_1 \) globulin 0.31 per cent, \( a_2 \) globulin 0.60 per cent, \( \beta \) globulin 1.19 per cent, \( \gamma \) globulin 1.47 per cent, SGOT 52 units, SGPT, 18 units.

In case 2 results were albumin 3 Gm. per cent, \( a_1 \) globulin 0.30 per cent, \( a_2 \) globulin 0.38 per cent, \( \beta \) globulin 0.72 per cent, and \( \gamma \) globulin 2.8 per cent.
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Table 2

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Intrasplic pressure, mm. Hg</th>
<th>Portal vein</th>
<th>Intrahepatic pattern</th>
<th>Collateral channels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>15</td>
<td>Not visualized, ? blocked</td>
<td>Not visualized</td>
<td>Few small vessels near hilum. A large channel opened into the inferior vena cava</td>
</tr>
<tr>
<td>2*</td>
<td>30</td>
<td>Not visualized, ? blocked</td>
<td>Not visualized</td>
<td>Few small vessels near hilum. A large channel opened into the inferior vena cava</td>
</tr>
<tr>
<td>3*</td>
<td>22</td>
<td>Not visualized, ? blocked</td>
<td>Not visualized</td>
<td>Few collateral vessels. A large channel opened into the inferior vena cava</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>Dilated</td>
<td>Abnormal pattern</td>
<td>Large collateral vessels, course obscure</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>Dilated</td>
<td>Abnormal pattern</td>
<td>Few collateral vessels, a large vein probably opening into inferior vena cava</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>Not visualized, ? blocked</td>
<td>Not visualized</td>
<td>Large collateral vessels, course obscure</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>Not visualized, ? blocked</td>
<td>Not visualized</td>
<td>Large collateral vessels, course obscure</td>
</tr>
</tbody>
</table>

*Portal splenography on a serial changer with plates covering upper abdomen and chest did not reveal porto-pulmonary anastomosis in any of these.

per second), multiple small pulmonary arteriovenous aneurysms were evident (fig. 4).

Histologic examination of the needle biopsy of the liver in six cases and open biopsy in one (case 1) revealed portal cirrhosis of the liver (fig. 5).

Open-lung biopsy performed in one patient (case 1) showed a collection of arterial spaces filled with blood and crowded in certain areas. These probably represent pulmonary arteriovenous microaneurysms (fig. 6).

Discussion

Our study shows that patients suffering from cirrhosis of liver rarely may show severe

Figure 2

Splenogram showing enlarged spleen. Few portal collateral channels at the splenic hilum. A large channel opening into the inferior vena cava and nonvisualization of intrahepatic pattern (case 1).

Figure 3

Pulmonary angiogram showing blotchy appearance (case 1).
Cyanosis and clubbing and closely simulate congenital cyanotic heart disease. The occurrence of this condition in the younger age group and the invariable presence of an ejection systolic murmur at the pulmonic area make the semblance complete. A normally split second heart sound with normal aortic and pulmonary components, normal electrocardiogram, and almost normal cardiac shadow on chest X-ray are against the diagnosis of congenital cyanotic heart disease. Hepatic and massive splenic enlargement are usual and point to the liver. Only in one of our seven patients was the spleen not palpable though enlarged as seen on splenography. Portal collateral vessels and evidences of hepatic failure are helpful for the diagnosis of cirrhosis of the liver but they are not invariably present. Engorged veins on the abdomen were seen only in two of our patients, who also had esophageal varices. One patient had esophageal varices alone, while four had neither engorged abdominal veins nor esophageal varices. Telangiectasia and arterial spiders were seen only in two. One patient had marked osteoarthropathy of ankles and wrists. Such osteoarthropathy in cirrhosis of liver was observed by Hijmans Van den Bergh.2 Liver-function tests usually show some impairment, but may be normal as in two of our cases. Liver biopsy demonstrated portal cirrhosis in all.

Intraspinal pressure is usually raised. In all the three patients on whom splenography was performed on a serial changer with plates covering the upper abdomen and the chest, the portal vein was not visualized. A large channel was seen to open into the inferior vena cava (fig. 2). The intrahepatic pattern was not visualized in any of these three, nor was there any evidence of portopulmonary venous shunt. In the remaining four patients, splenography was performed with only a single plate. Two of these four showed a deranged intrahepatic pattern indicative of cirrhosis of liver, while in the other two the portal vein was not visualized. The absence of visualization of the portal vein is likely to be due to portal vein block, as it was not vis-

### Table 3

<table>
<thead>
<tr>
<th>Case</th>
<th>Pressure, mm Hg</th>
<th>Venous oxygen saturation</th>
<th>General situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/7</td>
<td>25/3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>25/7</td>
<td>25/0</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>20/5</td>
<td>20/2</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>25/3</td>
<td>25/3</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>28/6</td>
<td>28/6</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>25/6</td>
<td>25/0</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>28/6</td>
<td>28/4</td>
<td>4</td>
</tr>
</tbody>
</table>

*The femoral artery and pulmonary venous oxygen saturation did not rise to normal on inhaling 100 per cent oxygen for 10 minutes.*
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Figure 4

Selective pulmonary angiography showing multiple tiny pulmonary arteriovenous aneurysms (case 1).

ualized in any of the plates on a serial angiogram. It could, however, be due to the dye draining away into the inferior vena cava through the large channel with its torrential flow.

Right heart catheterization was normal in all cases. There was no evidence of intracardiac right-to-left shunt on selective right ventricular angiography. Femoral arterial blood showed an oxygen saturation ranging from 69 to 82 per cent. Pulmonary venous samples obtained in three cases were highly

Figure 5

Liver biopsy (case 1) showing irregular areas of fibrous tissue traversing the parenchymatous tissue, pseudolobulation, and regenerating nodules.

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Figure 6

Lung biopsy (case 1) showing collection of arteriolar spaces filled with blood and crowded in certain areas.
desaturated. The femoral arterial and pulmonary venous oxygen saturation could not be restored to normal on inhaling 100 per cent oxygen for 10 minutes. This excludes uneven ventilation and diffusion defect as a cause of systemic arterial desaturation. The pulmonary angiograms were abnormal in all patients and showed a blotchy appearance (fig. 3).

The cause of desaturation of the arterial blood in cirrhosis of liver has been investigated by a few workers. Rydell and Hauffbauer demonstrated multiple small arteriovenous fistulas in the lungs by injecting the pulmonary vessels of a young man dying of juvenile cirrhosis of liver with cyanosis and clubbing of 10 years’ duration. Rodman et al. were unable to demonstrate such fistulas in their cases of alcoholic cirrhosis. Portopulmonary venous anastomosis via mediastinal veins has been described by Calabresi and Abelmann and Schoenmacker and Vieten. Recent studies by Shaldon et al. using radioactive krypton (Kr) have shown shunts between portal and pulmonary veins to be rare, and Fritts et al. found this shunt to be small. It is unlikely that such a shunt can ever be large enough to produce significant desaturation of systemic arterial blood, as portal vein oxygen content is high and total portal flow is only about 20 per cent of the cardiac output. Keys and Snell postulated a shift in oxygen dissociation curve; however, Rodman et al. found a normal dissociation curve in 19 of their 20 cases. This factor does not appear to be important in causing cyanosis.

In three of our patients in whom splenography was performed on a serial changer with plates covering the upper abdomen and the chest a huge channel carrying most of the portal vein blood was seen to open into the inferior vena cava (fig. 2). There was no evidence of any portopulmonary venous fistulas in any of these three cases. Clearly then, at least in these three cases, there was no question of any significant portopulmonary venous shunt. Even anatomically this is a difficult path to pursue, since portal collateral vessels open into the azygos veins and thus drain into the right atrium.

In two cases a high-speed (six per second) selective right lower lobe pulmonary arteriography was performed and this demonstrated multiple small pulmonary arteriovenous aneurysms (fig. 4). This left no doubt that in these two cases at least the pulmonary arterial venous aneurysms accounted for the shunt. In retrospect, it appears that the blotches in all other cases represent pulmonary arteriovenous aneurysms. Thus it is fairly certain that shunt through these multiple tiny pulmonary arteriovenous aneurysms causes cyanosis.

Small pulmonary arteriovenous aneurysms may be difficult to demonstrate on biopsy. In one of his two cases Hales demonstrated pulmonary arteriovenous fistulas on postmortem injection of pulmonary vessels but which could not be detected on pulmonary angiography and histology. In one patient (case 1) where open-lung biopsy was performed, a collection of large arteriolar spaces filled with blood were seen crowded in certain areas (fig. 6). These probably represent pulmonary arteriovenous microaneurysms. The etiologic origin of these pulmonary arteriovenous aneurysms is uncertain and, though they could be congenital, the relatively short history suggests that they are acquired. Vascular malformations like arterial spiders and telangiectasia are known to develop in cirrhosis of the liver. The angioma on the right forearm in one of our patients was also acquired; there was no history of trauma. How cirrhosis of liver causes these vascular malformations remains uncertain. The predilection of these pulmonary arteriovenous microaneurysms to occur in juvenile cirrhosis is unexplained.

The cause of cirrhosis in these cases is uncertain. There has been no history of jaundice, alcoholism, or severe protein malnutrition. Antia and Bharadwaj were also unable to arrive at the etiology of cirrhosis in most of their cases of cirrhosis of liver in children studied in Bombay.

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The systolic murmur was almost certainly due to hyperkinetic circulation.

Summary and Conclusion

Seven patients with cirrhosis of the liver with severe cyanosis and gross clubbing simulating congenital cyanotic heart disease were subjected to right heart catheterization and angiography, splenography, liver-function tests, and liver biopsy. In three cases splenography was performed on a serial changer with plates covering the chest and upper abdomen. No portopulmonary fistulas could be demonstrated. In all three patients the portal vein was not visualized and a large channel was seen to open into the inferior vena cava. In two patients a selective right lower lobe pulmonary angiography was performed at six plates per second. This demonstrated numerous tiny pulmonary arteriovenous microaneurysms, which probably were responsible for the cyanosis.

The clinical features and the pathogenesis of the condition are discussed.

Acknowledgment

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References


But words are things; and a small drop of ink,
Falling, like dew, upon a thought produces
That which makes thousands, perhaps millions, think.
—Lord Byron. Don Juan, Canto III, Stanza 88.
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