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症　　例

Cholelithiasis in Hereditary Spherocytosis: Report of a Case

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Hereditary spherocytosis (HS) is a most common congenital hemolytic disease transmitted by either parent as a mendelian dominant trait[12,19,36]. It results in the production of abnormal red blood cells (RBC) that have increased mechanical and osmotic fragility. The abnormality is manifested as an intrinsic defect of the cell's membrane[25], which causes delayed circulation and ultimate destruction in the spleen. The excessive RBC's destruction will result clinically in biliary tract disease as well as in other disorders[26]. Although the increasing incidence of cholelithiasis in HS has been well recognized, biliary tract surgery in HS remains a relatively uncommon procedure in practice.

Report of a case

A 20-year-old jaundiced female student complaining of severe abdominal pain was admitted to Critical Care Medical Center in our institute on February 15, 1985. Her jaundice had appeared since her birth, although varying in its severity. Because of the attack of similar abdominal pain, she was treated by a physician at the age of 16 and diagnosed as having HS. Family history revealed maternal cholelithiasis, but no hematological disorders was noted in her parents and siblings. Physical examination showed a well-nourished woman of 168 cm in height and 53 kg in weight with a blood pressure of 128/60 mmHG, a regular heart rate of 60/min, a temperature of 37°C, and regular respiration. She had mild jaundice on skin and bilateral conjunctivae. No abnormal breath sounds or heart murmurs were audible and lymphnodes enlargement was not observed over the entire body surface. On abdominal palpation, tenderness without rebound phenomenon on the epigastrium was noted and the spleen was palpable 1 fingerbreadth adjacent to the costal margin at the left upper quadrant. The liver and kidney were not palpable.

Laboratory data including hematology, urinalysis, liver chemistry studies and so on are listed

Key words: Cholelithiasis, Hereditary spherocytosis, Jaundice, Cholecystectomy, Splenectomy.
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Table 1. Pre- and postoperative laboratory data

	Preoperative	Postoperative
RBC ($\times 10^4$)	240	366
Hb (g/dl)	7.9	10.6
Ht (%)	22.1	33.6
Platelets ($\times 10^4$)	24.6	52.4
WBC	5,100	21,800
Reticulocytes (‰)	144	18
Cholesterol (mg/dl)	111	134
GOT (IU)	16	25
GPT (IU)	9	8
Alkaline phosphatase (IU)	51	79
LDH (IU)	151	183
Total bilirubin (mg/dl)	9.9	0.6
Indirect bilirubin (mg/dl)	8.1	0.4
serum Fe (microgram/dl)	91	—
Urinalysis	n.p.	n.p.

in Table 1. Ultrasonogram of the abdomen showed gallbladder stones and splenomegaly, which were also revealed by computed tomography of the abdomen (Fig. 1). Two floating stones in the gallbladder were visualized by endoscopic retrograde cholangiopancreatography, while no other abnormalities were noted in the bile duct and the pancreatic duct (Fig. 2).

With a tentative diagnosis of gallbladder stones in HS, abdominal exploration was carried out on March 25, 1985 through an upper median skin incision. There were no ascites. Removal of the spleen and gallbladder was performed without difficulty. Blood loss was 567 g and pre- or intraoperative blood transfusion was unnecessary. The resected spleen measured $14 \times 9 \times 5$ cm and weighed 565 g, with proliferated red pulps and decreased white pulps on histology. Neither specific inflammation nor malignancy was noted. The gallbladder developed mild chronic

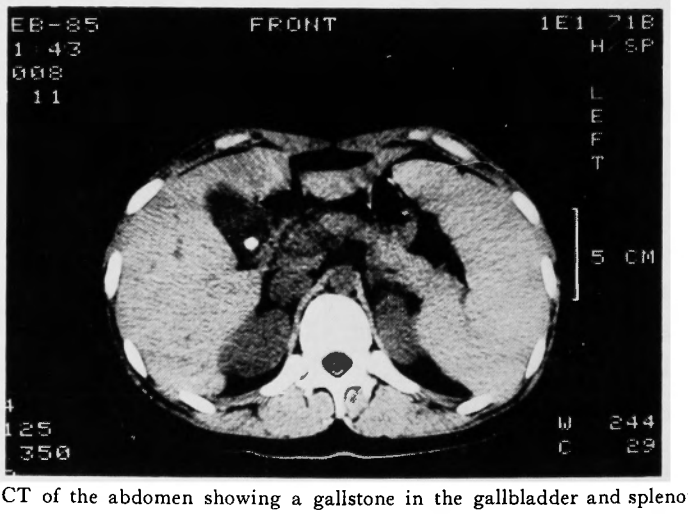

Fig. 1. CT of the abdomen showing a gallstone in the gallbladder and splenomegaly

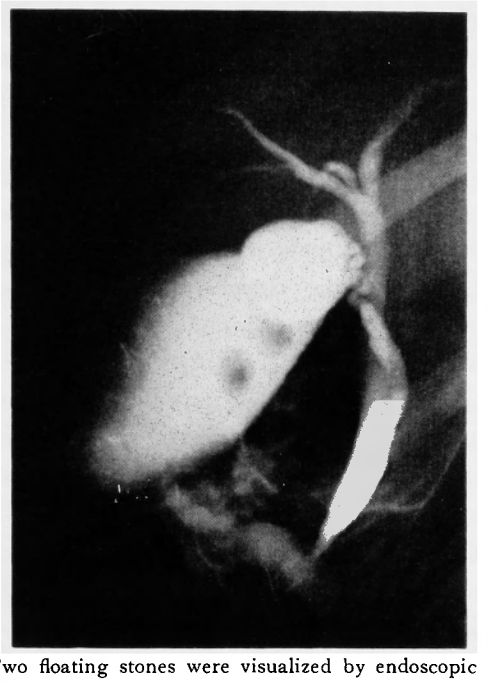

Fig. 2. Two floating stones were visualized by endoscopic retrograde cholangiopancreatography.

inflammation and there were two stones of 0.5 cm in diameter, respectively, which were composed of bilirubin.

Although the number of thrombocytes in the peripheral blood reached $80.3 \times 10^4/mm^3$ transiently, her postoperative course was uneventful with rapid improvement of anemia and regress of jaundice. Postoperative laboratory data are also listed in Table 1. She was discharged 17 days after the surgery and has been in good condition since then.

Discussion

In the survey of 128 HS patients by Japanese Ministry of Health and Welfare, there was no sexual difference, heredity was evidenced in 45 pedigrees (37%) and associated gallstones were noted in 22% of all the patients[24]. Although the incidence of HS in the same family is considered to be 50 percent theoretically, mutation or presence of recessive trait is suspected in the cases being no evidence of heredity[6,18,37]. BELLINGHAM and PRANKERD[6] stated that an estimated 20% to 50% of the cases were sporadic in nature and derived from mutations. The reported incidence of cholelithiasis in HS was 21%[26], 22%[24], 32%[3], 45%[16] and 46%[9]. The incidence was lower in childhood and increased with aging; BATES and BROWN[5] reported 5% in 19 patients aged 10 years and younger, 48% in 40 patients aged 11 to 40 years and 63% in 32 patients aged 40 years and older. KRUEGER[15] reported 8% of 100 patients aged 15 years and younger.

To our best knowledge, 56 surgical cases of cholelithiasis in HS including our own case since 1960 have been reported in the Japanese literature. In 49 cases whose age and sex were recorded,

there were 17 males with a mean age of 22.3±3.1 years, consisting of 5 in their teens and 6 in their twenties, and there were 32 females with a mean age of 29.4±2.5 years, consisting of 8 in their teens, 7 in their twenties and 9 in their thirties. The male-to-female ratio was 1 : 1.9 and no significant difference was noted in the mean age between sexes.

The diagnosis of HS requires spherocytosis and reticulocytosis in the peripheral blood, mechanical and osmotic fragility of RBC, negative Coombs test, excessive autohemolysis and evidence of family history[22]. Generally the diagnosis of HS is easy except for the cases with atypical symptoms[31]. The three major clinical manifestations are jaundice, anemia and splenomegaly. Although the destruction and production of RBC are virtually equivalent, occasional crises due to exacerbated hemolysis sometimes occur. Jaundice is relatively slight in comparison with the level of serum bilirubin because the indirect bilirubin being insoluble in water is hard to combine with the skin elastin and the connective tissues[21]. The presence of subclinical cases not associated with these symptoms may be encountered[3]. MIZOTE et al[20] reported that the incidence was 75% for splenomegaly, 70% for jaundice and 50% for anemia in their collective review. In the present survey, out of 48 cases whose symptoms were described, 39 patients (80%) developed jaundice, 35 (73%), anemia and 31 (65%), splenomegaly. Twenty-six patients (54%) had a history of abdominal pain attack.

The inducing factor of cholelithiasis in HS is generally accepted as follows: indirect bilirubin increased by hemolysis is excreted from the capillary bile ducts and the excessive amount of insoluble bilirubin increases in the bile because of limited ability of reabsorption. BATES and BROWN[5] stated that the degree, rapidity and continuity of hemolysis affected the gallstone formation. Although the main component of calculi is bilirubin in principle, KAMEDA et al[13] stated that the possibility of cholesterol gallstone formation that resulted from the decrease of lecithin-bile salt complex due to the stimulus of bile containing excessive amount of bilirubin on the gallbladder mucosa and change of its permeability. As a matter of fact, the incidence of cholesterol gallstone formation in Japan has increased and there may be incidental coincidence of this calculus in a HS patient. In the present survey, 53 cases were described as to their locations of cholelithiasis; calculi were localized in the gallbladder in 44 patients, in the gallbladder and in the extrahepatic bile duct in 5, in the extrahepatic duct in 3 and in the gallbladder and in the extra- and intrahepatic bile ducts in 2. Components of calculi were demonstrated in 41 cases, of which 34 presented bilirubin stones, 3, mixed stones, 2, black stones and 2, cholesterol stones.

In HS, the spleen plays an essential role in the membrane defect of RBC to express itself as a hemolytic process[26]. Thus, once the diagnosis is established, splenectomy is indicated in virtually all patients[11,28]. Splenectomy improves the symptoms of anemia and jaundice, however, deformity and fragility of RBC are inevitably continuous[7]. The search and removal of the accessory spleen at laparotomy is important for prognosis[4,23]. Occasionally, splenectomy causes a fatal overwhelming sepsis[1,10,17]. In children, splenectomy should be avoided until the age of 5 years[8]. While, OHYABU et al[22] reported the safety of splenectomy in children aged one year and older.

Preoperative or intraoperative performance of blood transfusion on HS patients with anemia

was controversial. If biliary tract operation and splenectomy are simultaneously scheduled, the number of candidates for blood transfusion may increase. Whether blood transfusion may cause crises or not was discussed by many investigators; YOSHIDA et al[35] stated that HS was different in nature from autoimmune hemolytic anemia with virtual hemolysis due to an anti-RBC auto-antibody, and crises due to blood transfusion was hard to occur in HS. BARKER and MARTIN[3] also evidenced no abnormality on pre- and intraoperative blood transfusion in HS patients. Of course, the importance of preoperative cross-matching is stressed[35]. In the present survey, several cases underwent pre- or intraoperative blood transfusion without any maleficence[29,33–35]. Nowadays, development of screening for antibody at blood transfusion is advanced and this transfusion in the cases of surgery to HS is recognized to be possible and safe.

In not only the symptoms but also the surgical procedure, cholelithiasis in HS is not different from that of usual cholelithiasis. Main operation is cholecystectomy with various additional surgery. In the present survey, 53 cases were described with respect to surgical maneuver in detail. Cholecystectomy and splenectomy were performed in 49; two patients[14,30] underwent splenectomy with delayed cholecystectomy and another[2] underwent a mutually replaced procedure. Other 46 patients underwent simultaneously both procedures and among them, 8 patients underwent additional surgery such as choledocholithotomy and so on. From the viewpoint that splenectomy completely removes the cause of lithogenesis, BARKER and MARTIN[3] recommended cholecystolithotomy instead of cholecystectomy, and this maneuver with splenectomy was carried out in two Japanese cases[2,20]. Recently, TANAKA et al[32] reported the effectiveness of partial splenic embolization instead of splenectomy for HS patients. This technique may be useful in patients in whom splenectomy is hazardous despite the necessity of biliary tract operation.

Although only one patient associated with liver cirrhosis showed poor prognosis[27], the surgery for cholelithiasis in HS patients has been safe and in good recovery in the present survery.

Summary

The postoperative course of a 20-year-old female with cholelithiasis in HS undergoing simultaneously cholecystectomy and splenectomy was uneventful. In consideration with the possibility of crises due to infection, biliary tract surgery should not be hesitated in such a patient. If possible, simultaneous splenectomy is advocated. Although our own case received no blood transfusion, this pre- or intraoperative supplement seems to be not hazardous.

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和文抄録

遺伝性球状赤血球症に合併した胆石症の1例

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軽度ないし中等度の黄疸が生下時より持続していた20歳の女性が，腹痛を主訴として来院し，胆嚢内結石と判明した．患者は17歳時に遺伝性球状赤血球症を指摘されており，来院時も黄疸，貧血，脾腫などを伴なっていた．輸血をせずに胆嚢摘出，脾臓摘出を施行し，術後経過は良好であった．同疾患の溶血機転により胆石を合併する例のあることは，よく知られているが，実際の胆道系手術実施例の報告は少ない．自験例を含めて56例の同疾患胆石合併例の胆道系手術例を，本邦文献の1960年以後のものから集計し，症例報告とともに簡単な考察を加えた．