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Abstract

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KEYWORDS: intravascular coagulopathy, hepatic hemangioma, Kasabach-Merritt syndrome

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A CASE OF GIANT CAVERNOUS HEMANGIOMA OF THE LIVER COMPLICATED BY INTRAVASCULAR COAGULOPATHY

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Abstract. A case of liver hemangioma complicated by intravascular coagulopathy is presented because of the rarity of the association. Hemangioma of the liver was suspected by palpation of the liver tumor, scintigraphy and x-ray examination, and confirmed by selective hepatic arteriography in combination with exploratory laparotomy. Intravascular coagulopathy was established by demonstrating secondary fibrinolysis and consumption of platelets and coagulation factors. Unconjugated hyperbilirubinemia due to micro-angiopathic hemolytic anemia was also present. The clinical course of the clotting abnormalities was basically a chronic one with an occasional acute or subacute defibrination process associated with further enlargement of the hepatic tumor. These provide sufficient evidence that the intravascular coagulopathy was closely related with the hemangioma in the liver. Neither ligation of a presumed nutritional artery of the hemangioma nor radiation therapy caused any demonstrable reduction in the tumor size.

Key words: intravascular coagulopathy, hepatic hemangioma, Kasabach-Merritt syndrome

Cavernous hemangioma of the liver, first reported by Eiselsberg (1), is a rare condition in Japan and is usually discovered incidentally during laparotomy or autopsy. In 1940, Kasabach and Merritt (2) reported a case of 2-month-old boy with a massive cutaneous hemangioma associated with thrombocytopenia and purpura. Defibrination process in hemangiomatosis was also documented by Hagedorn *et al.* (3). The Kasabach-Merritt syndrome or intravascular coagulopathy may occur with giant cavernous hemangioma of the liver, although their simultaneous occurence is rare, only 6 cases having been reported. The present case had a giant cavernous hemangioma of the liver complicated by intravascular coagulation and is reported because of the rarity of this association as well as the extensive evaluation of both of the pathological conditions.

CASE REPORT

A 44-year-old man visited our clinic complaining of general malaise and abdominal distension. For several years, he had suffered from heartburn and epigastric pain after meals. The existence of liver disease was pointed out to him by a physician in March 1974 when the same symptoms recurred together with a chill and high fever. General malaise developed in February 1975. The stomach showed ptosis and deviation to the left in a gastrointestinal tract examination. An oral cholecystography failed to demonstrate a gallbladder.

In May, he noticed an abdominal distension and was referred to our clinic because of an extensive hepatomegaly. At our out-patient clinic, chest x-ray films revealed an elevation of the right hemidiaphragm. Scintiscanning of the liver with ^{99m}Tc-phytate, ^{67}Ga-citrate and ^{198}Au-colloid failed to show uptake of the radioisotopes into the right lobe of the liver (Fig. 1). No calcification was seen in plain films of the abdomen. He was hospitalized on July 2, 1975 for further examination of the liver. There was no family history suggestive of an abdominal tumor or hemangioma and no past history of being exposed to vinyl chloride monomers. He had an accident of being hit by a tractor in the abdomen in 1973.

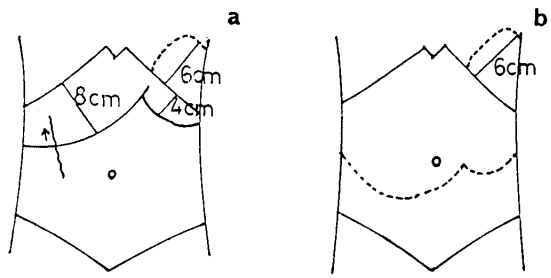

Fig. 2. a, Liver edge determined by palpation and spleen dullness by percussion on admission. Venous dilatation, flowing upwards, is also shown. b, Liver dullness on the fourth hospital day. Palpation of the liver was impossible thereafter.

Physical examination revealed jaundice in both the skin and sclerae, retention of ascitic fluid, elevation of the upper limit of liver dullness to the fourth rib, and extension of the liver edge to 8 and 4 cm below the right and left costal margins, respectively (Fig. 2a). The liver was smooth, elastically soft, dull-edged and tender. No bruit or thrill was present over the liver tumor.

Laboratory investigations showed a red cell count of 404×10^4 per mm^3, hemoglobin 12.4 g per 100 ml, packed cell volume 38.0%, reticulocyte count 0.8%, white cell count 4,100 per mm^3, platelet count 31×10^4 per mm^3, a blood film within normal limits except for red cell fragmentation, Rumpel-Leede

phenomenon negative, bleeding time (Ivy) 4 min, clotting time (Lee-White) over 20 min, clot retraction poor, Thrombotest 60.0%, prothrombin time 16.5 sec (normal, within 16.0 min), Normotest 101.3%, erythrocyte sedimentation rate 2 mm in one h and 4 mm in two h, serum bilirubin 3.10 (conj. 0.71) mg per 100 ml, no abnormalities in other liver function tests, hepatitis B surface antigen and antibody negative, α-fetoprotein 15 ng per ml, direct and indirect Coombs test negative and antinuclear factor negative. The results of venous pressure measurement were 130 mm saline in the right and left upper extremities, 307 mm saline in the right leg and 298 mm saline in the left leg and circulation time (arm to tongue) 17.0 sec. Laboratory tests for evaluation of the unconjugated hyperbilirubinemia were: osmotic fragility of red cells normal, fecal urobilinogen 155 mg per 100 g feces and salicylamide glucuronide formation (4, 5) 67.5%.

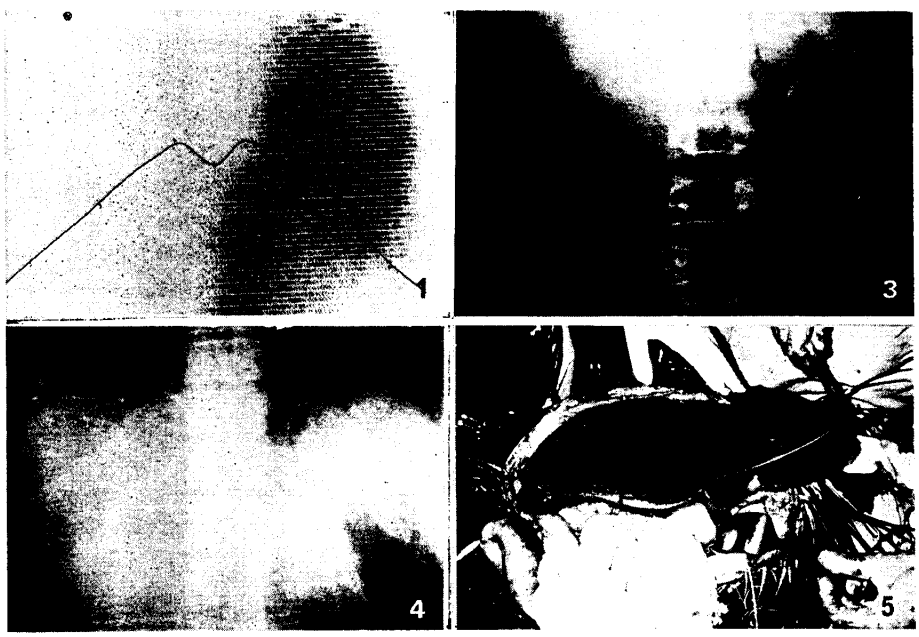

Fig. 1. Liver scintigram with ^{99m}Tc-phytate showing a filling defect in the right hepatic lobe. No uptake was observed with ^{67}Ga-citrate and ^{198}Au-colloid either (these pictures not shown).

Fig. 3. Intravenous pyelogram showing marked shift of the right kidney to the left. The kidney was demonstrated at the fourth lumbar spine.

Fig. 4. Selective celiacography showing a characteristic "cotton wool-like" pooling of contrast medium.

Fig. 5. Cavernous hemangioma at operation. A view of the right hepatic lobe mostly occupied by hemangioma tissue with a sponge-like consistency and wine color.

These results were all within normal limits and failed to confirm that the hemolysis was due to either intracorpuscular abnormalities or a defect in glucuronide formation. Further examination of the coagulation disorder revealed a fibrinogen level of 110 mg per 100 ml, partial thromboplastin time 14.6 sec (normal, 11–13 sec), recalcification time 92.4 sec and plasmin activity, plasminogen activator and euglobulin lysis time within normal limits. Fibrinogen and fibrin degradation products were not measured at this time.

On the fourth hospital day, a further enlargement of the liver was noticed, as shown in Fig. 2b. This was associated with the development of anemia and a slight decrease in the platelet count: red cell count 360×10^4 per mm^3; hemoglobin 11.7 g per 100 ml; packed cell volume 37.0%; reticulocyte count 1.1%; white cell count 3,600 per mm^3; platelet count 24×10^4 per mm^3. Development of unconjugated hyperbilirubinemia was noticed one week after the episode: bilirubin 3.52 (conj. 0.73) mg per 100 ml. These data suggested the occurence of hemolysis associated with intravascular coagulation. Alimentary examination of the gastrointestinal tract revealed a further shift of the stomach and the intestine to the left by a homogeneous dense shadow in the right upper quadrant approaching the pelvis. An intravenous pyelogram showed that the right kidney was at the level of the fourth lumbar spine (Fig. 3). An echogram demonstrated a giant tumor image with a depth of 20 cm. The tumor occupied two thirds of the abdomen. This was suggestive of the presence of a dermoid cyst or teratoma of the liver. Selective celiacography revealed a characteristic "cotton wool-like" pooling of contrast medium 2 to 23 sec after injection (Fig. 4).

Based on the presumptive diagnosis of hemangioma of the liver and because of a stepwise aggravation of the disease state, the patient was referred to the First Department of Surgery in our hospital to undergo an exploratory laparotomy attempting to resect the tumor. Before operation, the abnormalities in coagulation were checked again: fibrinogen 88 mg per 100 ml, prothrombin 80%, Factor V 50%, thrombin time 19.9 sec (normal, within 16.0 sec), plasma prothrombin time 16.1 sec (normal, 11–13 sec), cryofibrinogen(6) (++), ethanol gelation test (7) (−), protamine sulfate test (8) (−), fibrinogen and fibrin degradation products 128 μg per ml, serial thrombin time (9) 27.1 sec (normal, 30 sec) at 30 min. These data indicate consumption of coagulation factors with secondary fibrinolysis, that is, the occurence of intravascular coagulopathy. A myelogram showed a normal nucleated cell count and hyperplasia, anisocytosis and polychromasia of the red cell series.

At operation, the right lobe of the liver was noted as extending to 25 cm below the xyphoid process. It was occupied mostly by tumor tissue (Fig. 5). The caudate lobe was electric bulb-sized and was replaced by hemangioma tissue. The left lobe also contained multiple small hemangiomata. Visceral organs had

shifted from their original sites to the left in the abdominal cavity; the right kidney crossed over the spine. Resection of the tumor was abandoned, because ligation of the right hepatic artery, which was regarded as a nutritional artery of the hemangioma tissue, failed to cause a reduction of the hemangioma in size and because the caudate lobe was situated in close contact with the inferior vena cava. During operation, oozing of the blood was marked because of the presence of intravascular coagulopathy.

Since ligation of a presumed nutritional artery of the hemangioma caused no reduction in the tumor size, postoperative radiation was attempted. A total dose of 3,000 rad over four weeks was without effect on the tumor size and coagulopathy.

No further radiation was performed because of subsequent leukopenia.

DISCUSSION

The incidence of hemangioma of the liver has been reported by Ochsner (10) as 2.3% at autopsy and has been shown by Malt (11) and Adam (12) to be highest, 42.3 and 84.1%, respectively, among benign tumors of the liver. In Japan, the incidence is relatively low (0.25%) (13), and only 56 cases of hemangioma of the liver found at abdominal operation or autopsy have been reported, including the present case (14, 15).

Preoperative diagnosis of hemangioma of the liver is difficult, because patients rarely become symptomatic, liver functions are not impaired appreciably in most cases, and plain x-ray examination of the abdomen rarely shows calcification in the hemangioma (16). Only 2 of 67 (17) and 1 of 37 cases (18) have been reported to be correctly diagnosed preoperatively. A useful finding for diagnosis of liver hemangioma provided by selective hepatic arteriography is a characteristic "cotton wool-like" pooling of contrast medium, scattering in the tumor and persisting for a short period of time. Laparoscopic examination is also useful, 10 cases having been diagnosed in our clinic in combination with selective hepatic arteriography. This is, however, contraindicated for a risk of bleeding when the patient is complicated with intravascular coagulopathy as was the case in the present report. The final diagnosis of liver hemangioma in the present case was made by selective celiacography from the characteristic "cotton wool-like" pooling of contrast medium and by exploratory laparotomy.

Radical operative treatment of hepatic hemangioma comprises extirpation of the tumor or hepatic resection. Ligation of branches of the hepatic artery (19, 20) or portal vein (21-23) and/or radiation therapy (24, 25) is indicated when radical treatment is not possible. Anticoagulant therapy or, paradoxically, plasmin therapy (26, 27) is also recommended depending on the stage of the coagulopathy. The hemangioma in the present case was inoperable and radia-

tion therapy was applied.

The association of a hepatic hemangioma with intravascular coagulopathy is a very rare pathological condition and only a few cases have been reported (15, 28–32). In the present case, the consumption of platelets and coagulation factors, as revealed by hematological examinations, indicated the presence of intravascular coagulation. These abnormalities in coagulation were found throughout the entire course of the illness, conforming to the concept of chronic intravascular coagulation-fibrinolysis syndrome (33), although the extent of decrease in coagulation factors was somewhat pronounced when further enlargement of the liver occurred. The acute or subacute defibrination process associated with the tumor enlargement provides evidence that the intravascular coagulation present in this case was closely related to the hemangioma tissue localized in the liver. The unconjugated hyperbilirubinemia found in the present case is thus attributable to micro-angiopathic hemolytic anemia (34), as was suggested by Owen *et al.* (33). The symptoms of intravascular coagulopathy could be divided into two, those due to thrombosis and those related to bleeding, both being observed in the present case.

Accordingly, in hemangioma of the liver, the possibility of intravascular coagulation should be always considered, even though the complication is an infrequent pathological condition.

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