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Infantile Hemangioendothelioma Treated with High Dose Methylprednisolone Pulse Therapy

Infantile hemangioendothelioma is a severe disease with a high mortality. It is characterized by multiple hemangioma affecting the skin and visceral organs. We report that high doses of methylprednisolone pulse therapy improved symptoms and signs of infantile hemangioendothelioma in a male neonate, and completely resolved the hepatic and cutaneous hemangioendothelioma on follow up.

Key Words: *Hemangioendothelioma; Methylprednisolone Pulse Therapy; Neonate*

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INTRODUCTION

Infantile hemangioendothelioma (IHE) is characterized by multifocal benign vascular lesions, typically involving both the liver and skin (1). It is a histologically benign tumor with potentially life-threatening complications. The chief complaint is abdominal mass. Other symptoms and signs include hepatomegaly, high-output cardiac failure, skin hemangioma, thrombocytopenia, hypofibrinogenemia, hemolytic anemia and peritoneal bleeding. Females outnumber males by two to one. Its natural history is variable, but up to two-thirds of symptomatic patients, especially those who experience heart failure and jaundice, may die (2, 3). Various therapeutic options have been suggested according to the extent of the lesions. We report a case of IHE with congestive heart failure in a neonate who was successfully treated with high dose methylprednisolone pulse therapy.

CASE REPORT

A male infant weighing 4.51 kg was delivered by normal vaginal delivery at 38 weeks of gestation. He was admitted to the Pediatric Department for evaluation as too large for his gestational age with tachypnea four days after delivery. On physical examination, pulse rate was 146/min and respiration rate was 84/min. Multiple hemangiomas of various size were detected on the skin (Fig. 1) and oral mucosa. The infant had congestive heart failure with respiratory distress and a cardiothoracic ratio of 70% on chest radiography. The liver was palpable 4 cm below the right costal margin. All laboratory findings on admission were normal. He was treated with digitalis and diuretics, but his condition continued to deteriorate with increasing respiratory distress and cardiomegaly. On ten days after delivery, capillary hemangioma was confirmed on microscopic examination of a skin lesion. Laboratory examinations showed hyperbilirubinemia (total bilirubin 20.9 mg/dL, direct bilirubin 3.1 mg/dL) and elevated alpha-fetoprotein (20,790 ng/dL). An abdominal sonogram demonstrated hepatomegaly and multiple variable-sized hypoechoic masses with increased Doppler flow signals in the liver. Post-contrast abdominal CT scanning revealed homogeneous intense enhancement of multiple hepatic nodule, of which density was low on pre-contrast CT scan, and markedly dilated abdominal aorta above the level of renal artery. We also observed characteristic MRI findings of IHE in this neonate (Fig. 2). We began high dose methylprednisolone therapy (30 mg/kg/day), which was administered intravenously for one hr, every other day for six times. After that, methylprednisolone (30 mg/kg/day) was injected once a week with oral prednisone (2 mg/kg/day) given every other day for eight weeks. Within four weeks after starting the therapy, heart failure and hepatomegaly were markedly improved.

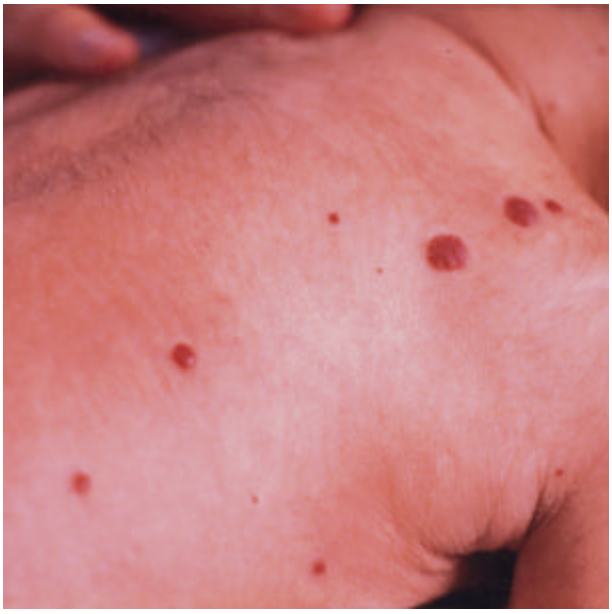

Fig. 1. The patient at seven days of age. Multiple hemangiomas of various sizes on the skin of trunk are shown.

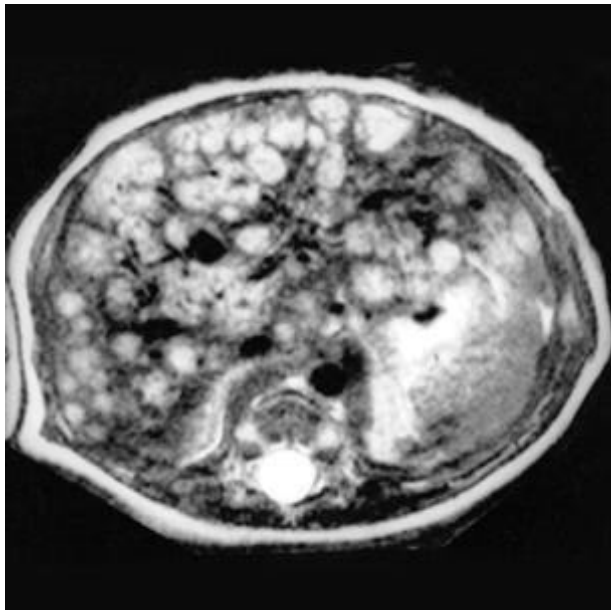

Fig. 2. Multiple variable sized nodules are scattered in the liver, which are high signal intensity on T_2W_1 MRI scan.

All laboratory findings were within normal limits. At the age of four months, the multiple hepatic masses had completely disappeared on follow-up abdominal CT scan (Fig. 3), and skin hemangioma was improved. The infant's general condition was good on follow-up.

DISCUSSION

IHE of the liver is a rare tumor that may occur as a solitary lesion or multifocal nodules, and appears as discrete, nonencapsulated, vascular tumors which vary in size from a few millimeters to 15 cm. The disease usually presents with the following typical triad: multiple enlarging cutaneous hemangiomas, hepatomegaly and congestive heart failure. It is associated with a high mortality rate if congestive cardiac failure develops in patients less than six weeks old. If untreated, the infant's chance of death rises to 50% within two weeks of onset (4). Dehner and Ishak (5) subdivided this tumor histologically into Type 1 and Type 2. For most patients, needle biopsy is very dangerous in infantile hepatic hemangioendothelioma, so ultrasonogram, CT, MRI, ^{99m}Tc RBC scan or angiography are used for diagnosis.

Despite the fact that this tumor is histologically benign, treatment is difficult. Because complete resection is impossible and operation is risky, various conservative treatments such as radiotherapy (6), steroid therapy (7), hepatic artery ligation or embolization (4,8) and interferon therapy (9) have been used. There has been widespread use of steroids to shrink the immature hemangiomatous tissues since Touloukian (10) first reported their successful use in an eight-month-old infant. Until now, the dosages of prednisolone used for treatment have been between two and ten mg/kg/day. However, many argued that the side effects of high doses of steroids and their complications were serious, and many studies also showed treatment failure (11-13). The adequate dosage and treatment methods of steroid therapy and their mechanism are not well known. However, it has been pre-

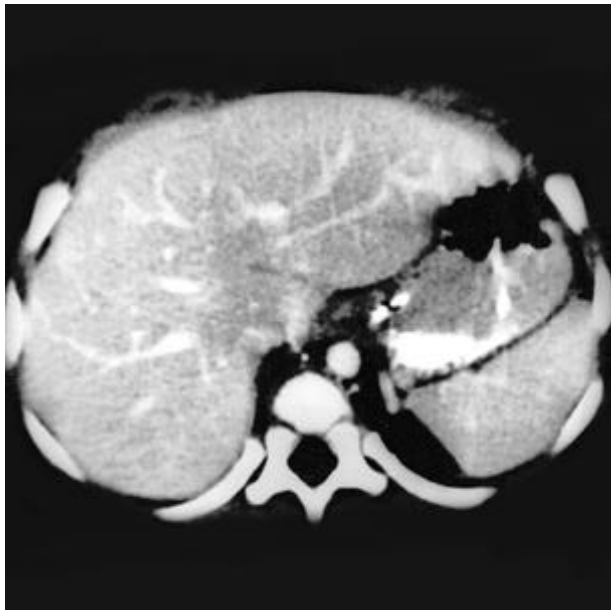

Fig. 3. Follow-up Abdominal CT scan: intrahepatic multiple masses disappeared completely at four months of age.

viously demonstrated that steroids restore the reactivity of the vascular bed in the mesentery of the adrenalectomized rat, and heightens its sensitivity to topically applied epinephrine (14). The vascular channels within the hemangioma are lined with immature endothelial cells, which may be particularly sensitive to systemic corticosteroids and undergo similar changes.

Enjolras et al. (13) reviewed 25 cases of alarming hemangiomas in infancy. Treatment response varied: total failure (30%), rapid improvement (30%) and doubtful response (40%). Liver hemangiomas had a high mortality, and all three infants with hepatic involvement died. In our case, we were unable to control the congestive heart failure in our patient with any conservative medication, and his condition continued to deteriorate with increasing respiratory distress and cardiomegaly. Poor prognosis was expected due to the early age of onset, severe congestive heart failure, severe jaundice and multiple nodules in the entire liver. Therefore, we decided to treat the infant with high dose methylprednisolone, which had been frequently used in our hospital without severe side effects. Methylprednisolone pulse therapy was introduced by Mendoza and Tune (15) for the treatment of steroid resistant focal segmental glomerular sclerosis. During the treatment, we checked the infant's blood pressure and other vital signs, blood and urine sugar, electrolytes and others for known side effects of steroids. There were no significant side effects, and the infant's response was very good. The size of multiple hepatic masses had decreased by the first follow-up abdominal CT scan at 2 months of age, and skin hemangioma had improved.

In summary, we report that high dose methylprednisolone pulse therapy improved the symptoms of infantile hemangioendothelioma in a male neonate and completely resolved the hepatic and cutaneous hemangioendothelioma on follow-up.

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