Diffuse Neonatal Hemangiomatosis

Hyun-Jin Kim, M.D., Nack-In Kim, M.D.

Department of Dermatology, College of Medicine, Kyung Hee University, Seoul, Korea

Diffuse neonatal hemangiomatosis (DNH) is a rare entity with the distinctive features of multiple hemangiomas of the skin and internal organs, which may result in a fatal outcome if widespread involvement of the internal organs.

We report a case of DNH with cutaneous and hepatic involvement. The significant regression in the vascular lesions was achieved with systemic corticosteroid therapy. (Ann Dermatol 15(1) 17~20, 2003).

Key Words: Diffuse neonatal hemangiomatosis, Corticosteroid

Diffuse neonatal hemangiomatosis (DNH) is a rare disorder first recognized at birth or during the neonatal period. DNH is characterized by the multiple cutaneous hemangiomas and visceral hemangiomas involving three or more organ systems. The internal organs commonly affected are the liver, gastrointestinal tract, brain, lung and the eyes. The cutaneous and associated visceral lesions increase in number and size after birth. Clinical feature and outcome depend on their location, size, number and response to therapy. In the widespread involvement of internal organs, DNH can be life-threatening, if left untreated.

Many treatment modalities have been used to reduce the mortality of the DNH, including systemic corticosteroid, interferon-α, irradiation, the ligation or embolization of the feeding vessels of hemangiomas. We report a case of DNH with cutaneous and hepatic hemangiomas, successfully managed with corticosteroid.

CASE REPORT

A four-week-old female infant visited our department for the evaluation of multiple, scattered, cherry-red papules and plaque on trunk, extremities, scalp, palms and soles. The lesions had first been noticed 2 weeks after birth by her parents and had rapidly increased in number and size. She was born of 29-year-old healthy mother without significant disease. Vaginal delivery was undergone at full-term and the birth weight was 3,400 gm. The immediate newborn condition was good and her Apgar score was 9. But the skin lesions were increasing in number and size for the neonatal period. Physical examination revealed an alert, well-crying, well-nourished baby without cyanosis, jaundice, and dyspnea. Vital signs including body temperature, heart rate, respiration and blood pressure were within normal limits. The skin lesions were variable in size with the range from pinpoint to 1.8 × 1.0 cm in diameter and total 23 lesions were widely distributed over the trunk, extremities, scalp, palms and soles (Fig. 1A, B). Ophthalmologic examination revealed no abnormalities.

Laboratory evaluation revealed that a complete blood count including platelet, bleeding time, clotting time, prothrombin time, partial thromboplastin time, liver function test, renal function test, serum electrolytes, VDRL, urinalysis and occult blood in stool were within normal limits or negative. A chest radiography, electrocardiography and echocardiography showed unremarkable findings.
Abdominal and pelvic ultrasonography showed multiple hepatic masses, 1.5-2.4 cm in diameter, in the right lobe of liver, suggesting hemangiomas, which were confirmed by chest and abdominal computed tomographic (CT) scan (Fig. 2A). No internal organs other than liver showed abnormal findings. Brain computed tomographic scan showed no parenchymal abnormalities, but high signal intensity was observed above left parietal area, suggestive of a cephalhematoma due to birth injury. Histopathologic finding of the skin lesion on the back revealed numerous dilated vessels and the angiomatous proliferation of endothelial cells in the upper dermis (Fig. 3).

Fig. 1. Scattered, multiple, variable sized hemangiomas are noted on trunk (A), perineum and low extremities (B).

Fig. 2. Before treatment abdominal CT shows multiple masses (arrows) on the right lobe of liver (A), and after treatment follow-up ultrasound shows significant decrease of their size and number(arrows) (B).

Fig. 3. Skin biopsy of the lesion on the back shows numerous dilated vessels lined by single layer of endothelial cells in upper dermis. And some endothelial cell proliferations are seen. (H&E stain, ×100).

Fig. 4. The skin lesions regressed significantly 7 months after the initial treatment.

Treatment with oral prednisolone (2mg/kg/day)
was initiated. After four weeks of therapy, the skin lesions stopped growing and spreading, and started decreasing in size and number. After six weeks of therapy, it was tapered to 1.5 mg/kg/day. And then, it was gradually tapered. After 4 months of the initial therapy, when the skin lesions decreased in number and size significantly, the corticosteroid was discontinued. Three months later, almost all cutaneous skin lesions disappeared (Fig. 4) and hepatic hemangiomas significantly decreased in size (Fig. 2B).

**DISCUSSION**

Cutaneous hemangiomas are present at birth or appear shortly thereafter in approximately 10% of all neonates. Generally, the lesions are solitary and regress spontaneously. But uncommonly the patients may have diffuse, widespread involvement of skin and internal organs.

In 1970, Holden and Alexander described the term, "diffuse neonatal hemangiomatosis (DNH)" present the diagnostic criteria of the following: (1) Onset in the neonatal period; (2) No evidence of malignancy of hemangiomas; (3) three or more organs involved. In 1999, Lopriore and Markhorst suggested that the inclusion criteria for DNH should be expanded to include patients with only cutaneous hemangiomas. DNH is characterized by multiple hemangiomas at birth or shortly thereafter affecting the skin and visceral organs. Most affected organs except the skin are liver, gastrointestinal tract, brain, lung, oral cavity and the eyes. In our patient, multiple hemangiomas affected the skin and liver shortly after birth and revealed no evidence of malignancy in Histopathologic finding. The clinical course of DNH is progressive vascular proliferation especially during the first 6 months of life and early death in infants with multiple organ involvement, if left untreated. The complications of DNH are serious and often lead to death. Death usually results from high-output congestive heart failure due to arteriovenous shunting in the hemangiomas, gastrointestinal bleeding, obstructive jaundice, central nervous system sequelae due to space-filling hemangiomas and Kasabach-Merritt syndrome following the consumption of platelet and clotting factors in the hemangiomas.

The management of DNH still remains. Many treatment modalities have been challenged to reduce the mortality of the DNH, including systemic corticosteroid, interferon-α, irradiation, the ligation or embolization of the feeding vessels of hemangiomas. High dose corticosteroid (2-5 mg/kg/day) has been recommended as the method of choice since the first successful experience of Fost and Esteterly in the management of Kasabach-Merritt syndrome. The mechanism by which corticosteroids induce a regression of hemangiomas is not clear. It has been suggested that proliferating blood vessels are sensitized to endogenous circulating vasoconstrictors by the corticosteroids. Another suggested mechanism is that corticosteroids occupy receptors in hemangioma tissue and block the factors involved in their growth. In this case, oral prednisolone 2 mg/kg/day was initially administered to the patient and showed good results without any adverse effect.

Interferon-α is recommended for life- or vision-threatening hemangiomas unresponsive to corticosteroids. Its action mechanism remains unknown. Several mechanisms have been suggested that it inhibits endothelial cell migration and proliferation, that it inhibits other step in angiogenesis and that it down-regulates the expression of basic fibroblast growth factor (bFGF), angiogenic factor. In this case, Interferon-α was not be used because of the good response to corticosteroid without any side effects. To the best of our knowledge, four cases of DNH have been reported in Korean literatures. All the cases revealed favorable outcomes with good response to corticosteroid only or Interferon-α in addition. Two cases had cardiac failure.

Multiple capillary hemangiomas in a newborn child should raise suspicion for a diagnosis of DNH. The risk of visceral involvement increases with the number of cutaneous hemangiomas. Because hemangiomas undergo the rapid progressive enlargement for 8-18 months of life and possibly lead to serious complications and death if left untreated, early recognition of the disease and appropriate therapy are crucial in the management of the neonates with multiple cutaneous hemangiomas.

Clinical evaluation for the affected neonates should be directed towards possible involvement of the organs other than skin and therefore in-
clude a thorough physical examination with particular emphasis on cardiac status, central nervous system involvement and ocular involvement. A complete hematologic work up including platelet count, prothrombin and partial thromboplastin time should be done. Frequent analysis of urine and stool for occult blood is requisite. Echocardiography is a useful and noninvasive tool of the diagnosis of high output cardiac failure. Ultrasonography is valuable to detect hepatic hemangiomas and hydrocephalus. CT scan is useful in the detection of intracranial hemangioma and in the evaluation for intrathoracic and intraabdominal involvement. Magnetic resonance imaging can be a valuable diagnostic aid.

This case is DNH with cutaneous and hepatic involvement, without serious complications. She was thoroughly evaluated for almost all internal organs, responded well to oral prednisolone 2mg/kg/day and had a favorable outcome. In addition, she revealed no side effects due to long-term use of corticosteroid. We believe that this patient revealed the favorable outcome because of prompt diagnosis, close evaluation and appropriate therapy.

REFERENCES