Case Report

Diffuse neonatal hemangiomatosis with a single atypical cutaneous hemangioma

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ABSTRACT

Diffuse neonatal hemangiomatosis (DNH) is an extremely rare but deadly neonatal condition which presents as multiple cutaneous hemangiomas and hemangiomas in 3 or more visceral organs. DNH is usually suspected when multiple hemangiomas are found on the skin of the baby. We hereby present an interesting case in a newborn whose diagnosis was made from multiple intracranial, hepatic, and intramuscular hemangiomas, but with a single and unusual cutaneous manifestation over the right ankle. The patient was asymptomatic at the time of diagnosis. Due to the solitary nature of skin lesion, this report might contribute to a redefining of the term DNH.

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Introduction

Diffuse neonatal hemangiomatosis (DNH) is an extremely rare condition characterized by numerous cutaneous hemangiomas and the involvement of 3 or more extra-cutaneous organs [1,6]. The incidence of red spots on the skin of a newborn would arouse suspicion about a potential diagnosis of DNH and instigate an investigation for visceral hemangiomas. Here we present a case of a newborn baby with a prenatal diagnosis of an intracerebral mass eventually proving to be multiple hemangiomas in brain, liver, and muscles, but with only a single and atypical skin lesion.

Case report

A healthy young woman with an unremarkable medical history, was admitted to the provincial hospital at 39 weeks gestation because of maternal pre-eclampsia and a suspicious fetal brain mass on prenatal ultrasonography (US). The first fetal US
at 36 weeks gestation was unremarkable. At 39 weeks gestation, ultrasonography to estimate fetal weight revealed a hyperechoic mass at the right frontal lobe. No vascular flow was detected within the mass in color sonography. The family has one healthy daughter. There is no known hereditary condition in this family.

The delivery of the male newborn was normal, birth weight 3156 grams, and Apgar scores were 9 and 10 at 5 and 10 minutes, respectively. Physical examination revealed a head circumference of 33 cm, 3 × 3 cm of nonbulging anterior fontanelle, and 0.5 × 0.5 cm of posterior fontanelle. He had normal and equal movement in all extremities. Normal Moro and sucking reflexes were elicited. Heart, lung, and abdominal examinations were normal. No detectable skin lesion was noted at that time. Non-contrast cranial computed tomography (CT) was conducted the day after birth and 3 well-circumscribed, intra-axial lesions of varying size, which were round and hyperdense, were found in the right frontal lobe with an extensive area of brain edema. A further small hyperdense lesion in the left frontal lobe was found (Fig. 1). On day 6 of life, skin discoloration of the right scrotal sac was noticed so scrotal and abdominal US was performed which revealed a hydrocele in the right scrotum and a 4-cm predomi-
nately hyperechoic mass with central hypoechoic area in the left lobe of the liver. Multiphase contrast-enhanced CT and MRI of the upper abdomen performed on days 13 and 17, respectively, demonstrated an avid peripheral nodular arterial

Fig. 1 – Unenhanced axial cranial CT scan shows a hyperdense lesion in the right frontal lobe with surrounding brain edema (white arrow) and another smaller lesion in the left frontal lobe (arrowhead).

Fig. 2 – Axial CT scan of the abdomen in unenhanced (a), arterial (b), and portovenous (c) phases demonstrate a peripheral nodular arterial enhancing mass with progressive fill-in in the left lobe of the liver (white arrow) and a small hypervascular lesion in the right lobe of the liver (black arrow). The central portion of the left lobe mass contains hemorrhage (arrowhead) which appears slightly hyperdense on unenhanced CT, hyperintense on T1-weighted (d), and hypointense on T2-weighted MR images (e). The caudal CT scan in the arterial phase (f) reveals an avid enhancing lesion in the right paraspinal muscle (open arrow).
enhancing mass with evidence of hemorrhage in the left lobe of the liver and other multiple small varying-size hypervascular enhancing lesions in the right lobe of the liver, consistent with hemangiomas (Fig. 2a-d). Abdominal CT also revealed a few strongly enhancing lesions in paraspinal muscles which were compatible with hemangiomas (Fig. 2e). Oral propranolol at a dosage of 3 mg/kg per day was begun for treatment of multiple hepatic hemangiomas and probable intracranial hemangiomas.

Two months later, a follow-up abdominal CT revealed variable response of hepatic hemangiomas. At age 2 months and 11 days old, the baby was brought to our hospital for continuing treatment. The first MR imaging of the brain, age 2 months and 22 days, showed remarkable changes of the cere-
bilateral masses turning to thin-walled cysts with small eccentric strongly enhancing nodules. The largest cyst in the right frontal lobe was sizable and caused bulging of the right-sided calvaria. Also noted were numerous nodular avid enhancing lesions in the cerebral hemispheres, cerebellum, thalamus, pons, choroid plexus, and along the pial and dural surfaces (Fig. 3). All enhancing nodules showed blooming dark signals on the gradient echo resulting from blood product. No hydrocephalus or brain herniation was seen. A multidisciplinary team consisting of a pediatric hemato-oncologist, neurologist, dermatologist, and radiologist concluded that diffuse neontal hemangiomatosis was the most likely diagnosis. At that time, following a meticulous search for cutaneous hemangioma, a 3-mm soft brownish papule on the dorsum of the right ankle was found. Due to the atypical morphology of the skin lesion indicating hemangioma, an excisional biopsy was performed. The histopathology confirmed capillary hemangioma (Fig. 4). GLUT-1 stain was negative and congenital hemangioma was concluded.

Serial brain MR imaging and abdominal CT examinations indicated gradual resolution of all lesions in both the brain and liver. At 9 months after diagnosis, reduction of the intracranial cysts resulted in encephalomalacia in the bilateral frontal lobes without any other enhancement (Fig. 5a, b), and a residual small enhancing hemangioma with calcification in the left lobe of the liver was observed (Fig. 5c, d). The patient was asymptomatic and did not experience any neurological or developmental problems within the 9 months of follow-up.

Discussion

To our knowledge, this is the first reported case of DNH with single atypical cutaneous hemangioma but complete diagnosis by multiple visceral hemangiomas in the brain, liver, and muscles. DNH is an extremely rare but fatal neonatal condition. In general, multiple cutaneous hemangiomas are the warning signs that visceral organs may be affected. When hemangiomas are later discovered in 3 or more organs, DNH is diagnosed. The liver is the most common location of visceral involvement followed by the brain. Other organs include the bowel, spleen, mesentery, heart, lung, and genitourinary system [2]. Although the histology is benign, the mortality rate of DNH is as high as 50%-90% due to various complications such as congestive heart failure from a large volume of arteriovenous shunting, liver failure, consumptive coagulopathy, and bleeding. The skin lesions are typically red papules or nodules and usually 0.5-1.5 cm in size with numbers ranging from 50 to 100 [1,2]. Ten is the least number of lesions on the skin from the total of 16 cases of cutaneous hemangioma with brain involvement reported by Friedland et al. [3]. More than half (9 of 16 cases) of the infants in their study experienced neurological symptoms related to brain hemangioma and 6 cases died.

The first manifestation of our case was an intrauterine fetal brain mass. Fetal brain tumor is rare; the differential diagnosis includes germ cell tumor, glioma, hemangioma, and atypical teratoid rhabdoid tumor. In imaging findings of intracranial hemangioma, intense contrast enhancement and hemorrhage are common features. Multiplicity, intra-axial location and cystic change with sedimentation of intracranial hemangiomas are reported in cases of DNH [2]. Location and imaging appearance of the cerebral masses on the initial CT scan in our case were similar to intracranial hemangiomas in DNH patients; however, cerebral metastasis was still a possibility. The rapid involutive, presence of typical hepatic and intramuscular hemangiomas, and a pathologically proven cutaneous hemangioma, even though single, support the diagnosis of DNH with intracranial hemangiomas. The post-treatment cys-

Fig. 4 – A brownish lesion at the dorsum of the right ankle (a) was proven by histology to be capillary hemangioma. Section (b) shows an unremarkable epidermis. The dermal layer shows numerous vascular ectasia of capillaries in the upper dermis (arrow) with larger diameters in the reticular dermis (arrowhead). The vascular channels show few plump endothelial cells which are separated by normal dermal stromal components. (Hematoxylin and eosin stain, original magnification x200.)
tic change in our case differs from that reported in related literature because the cysts were large and lack sedimentation.

Currently, there is no standard treatment approach or interval follow-up recommendation for intracranial hemangioma. Most small and asymptomatic lesions are managed with observation and spontaneous regression is expected. The most valuable option if the disease is widespread is medical treatment including oral steroids, propranolol, thalidomide, bevacizumab, temozolomide, interferon, and vincristine [5]. Propranolol is currently widely used and is an effective treatment for cutaneous hemangioma. Although propranolol is not a standard prescription for intracranial hemangioma, several recent reports revealed successful involution of intracranial hemangioma after treatment with propranolol [4,5]. For intracranial hemangioma, a 3-month follow-up may be appropriate as our case showed involution of cerebral hemangiomas at 2 months with complete regression at 9 months.

Even though there were no neurological sequelae at the last follow-up of 9 months old, a relatively short-term assessment, a complete evaluation of developmental milestones is necessary.

**Conclusion**

We have described this challenging case of DNH which primarily presented with intracranial hemangiomas with a later
finding of the single and unfamiliar skin lesion. Even if there is no observable characteristic cutaneous hemangioma, intracranial hemangiomas must be considered in multiple intracerebral masses, and prompt investigation for the presence of hemangioma in other organs is required to diagnose DNH. It is critical to get early diagnosis and treatment to minimize severity and mortality [2,6]. Patients with multiple cutaneous hemangiomas are not always DNH, but those with multiple cerebral hemangiomas may be. Further study into the correlation between cerebral hemangiomas and DNH is needed.

**Patient consent**

A written consent was obtained from the parent for publication of this case and any accompanying images.

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