Liver failure Due to Diffuse Neonatal Hemangiomatosis

Keywords: Hemangioma; Diffuse hemangiomatosis; Liver failure; Neonatal; Propranolol

Abstract

The term Diffuse Neonatal Hemangiomatosis (DNH) has been used to describe multifocal vascular lesions affecting the skin and organs with the liver being the organ most frequently involved. Although spontaneous regression is the rule, complications such as a high cardiac output caused by portovenous or arteriovenous shunts can occur. Liver lesions can be potentially lethal due to severe complications such as fulminant hepatic failure. Mortality varies between 60-80% in the first months of life without treatment. Propranolol has been reported as an effective and well-tolerated treatment for cutaneous hemangiomas and more recently in hepatic hemangiomas. We report the case of an infant with a diffuse neonatal hemangiomatosis with hepatic hemangioma, which caused liver failure and successfully responded to treatment with propranolol.

Introduction

Congenital vascular lesions are relatively common disorders that have multiple forms of presentation, some with a tendency to resolve spontaneously and others associated with hemangiomatous lesions of internal organs. Depending on their location they can cause heart failure, anemia, hepatic failure, ocular and brain disorders, and even death [1].

Hemangiomas are benign vascular tumors composed of proliferating endothelium. They typically occur during the first two months of life in 90% of cases. Benign neonatal hemangiomatosis (BNH) is diagnosed when five or more skin lesions are present. When vascular lesions affect the skin and viscera the disease is known as Diffuse Neonatal Hemangiomatosis (DNH), which is a serious systemic disorder that is present in 1 to 2.6% of infants born at term. Many publications emphasize the severity of DNH, citing a mortality of 60-80% [2].

Lister first described DNH in 1938 [3], and in 2008 Leauté reported regression of hemangiomas in children treated with propranolol [4]. Since then, several series have confirmed the benefit of propranolol in the involution of infantile cutaneous hemangiomas and for the treatment of isolated hemangiomas in other locations [5,6].

Case Report

The patient is a 45-day-old male infant with respiratory distress, tachypnea, intercostal retractions and nasal flaring. In the last 24 hrs, he refused to eat. On physical examination, he had a heart rate of 160 beats/minute and an oxygen saturation of 89%. Multiple papule-like purple lesions compatible with hemangiomas were noted. These were 1-3 mm in diameter and located on his thorax, abdomen and extremities, in addition to a 1 mm lesion on his scalp. His skin also presented generalized jaundice. In the chest, a holosystolic grade III/VI murmur was heard. The abdomen was found distended with hepatomegaly 4 cm below the right costal border at the midclavicular line and with grade II splenomegaly.

Initial laboratory tests revealed hemoglobin of 10.9 g/L, a hematocrit of 30.9%, leukocytes 9,260/mm³ and platelets 243,000/mm³. Liver function tests showed total bilirubin 10.9 mg/dL, direct bilirubin 1.9 mg/dL, indirect bilirubin 9 mg/dL, albumin 3 g/dL, AST 160 U/L, ALT 178 U/L, LDH 585 U/L, alkaline phosphatase 246 U/L.

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Liver hemangiomas, especially those that are multiple and large, are associated with high mortality. One complication is high-output congestive heart failure (51%) because these lesions simulate the hemodynamic alterations of a left-right shunt.

The clinical presentation can vary and include liver dysfunction [9,10], hyperammonemia, hepatosplenomegaly (5.3%), renal failure (10.6%) and hypothyroidism (5.3%). Although the spontaneous regression is the rule with the liver hemangiomas, complications such as a high cardiac output caused by portovenous or arteriovenous shunts can occur like in our patient.

Liver failure is a rare complication with high mortality and is suspected with elevated transaminases, coagulopathy and encephalopathy. A mortality rate of 60-80% without treatment has been reported [4,5,11,12].

However, with proper treatment mortality is reduced to 27%.

Treatment is aimed at preventing complications. Several therapeutic options have been described including observation, use of interferon alfa-2b, vincristine, vinblastine, cyclophosphamide, steroids, propranolol or non-pharmacological treatments, such as radiation therapy, embolization or surgery [13].

Corticosteroids limit proliferation of blood vessels and induce early regression. They are first-line treatment for severe and complicated infantile hemangiomas. The response rate varies from 30-50% [14,15].

The efficacy of propranolol in the treatment of hemangiomas has been described since 2008. Its mechanism of action remains unclear; however, some suggested mechanisms are a cytotoxic effect on endothelial cells, inhibition of matrix metalloproteinase, and modulation of stem cell differentiation [16,17].

We report the case of an infant with DNH with liver failure secondary to liver hemangiomas. Based on reports that propranolol has been effective in the treatment of hemangiomas in children, we offered this therapy to our patient who showed dramatic improvement of liver failure, demonstrated by the recovery of liver metabolism and synthesis.

**Conclusion**

Diffuse neonatal hemangiomatosis is a rare and potentially fatal disease. Due to its rapid development, early intervention is necessary to prevent progression or produce regression.
In this case, liver failure secondary to DNH occurred, which resolved effectively with steroids and propranolol. The primary cause of liver failure was the hepatic hemangiomas. The administration of propranolol had a fast and consistent therapeutic effect allowing control of the complications caused by hemangiomas. It also shortened the natural history of the disease (proliferation phase) and contributed to its resolution with good tolerance.

References