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Diffuse neonatal hemangiomatosis presenting as congestive heart failure

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ABSTRACT Diffuse neonatal hemangiomatosis is a rare condition with a very high mortality rate if left untreated. We report a neonate having around 490 cutaneous and multiple diffuse liver hemangiomas presenting as congestive heart failure. Prompt treatment was instituted with decongestive drugs and prednisolone for anticipated life threatening complications due to hepatic hemangiomas. Propranolol was added later as it is known to precipitate congestive failure and also to avoid long-term complications of steroids. The child responded well. However, there is no consensus regarding the initial line of management, which needs to be individualized keeping in mind the efficacy, long-term side effects of the drug and the clinical presentation.

Introduction

Diffuse neonatal hemangiomatosis (DNH) is a rare condition with a very high mortality rate (50-90%) if left untreated [1]. Hemangiomas otherwise are the most common vascular tumours of infancy with excellent prognosis. However, the presence of multiple hemangiomas is associated with a strong possibility of visceral organ involvement, which is termed diffuse neonatal hemangiomatosis [2]. Visceral lesions are most commonly found in the liver followed by nervous system, intestine, lungs, rarely skeletal system and proliferate till infancy. The common causes of mortality are high-output cardiac failure as a result of arteriovenous shunting in liver or haemorrhage in intestine or brain [3]. Prompt treatment with corticosteroids or beta blockers like propranolol inhibits the proliferation, promotes early regression of hemangiomas and is life saving [4].

Case Report

A 20-day-old, full term male baby with birth weight of 2.5 kg was referred to the out-born nursery of our tertiary care hospital with a history of insidious onset respiratory distress, difficulty in feeding since day 5 of life and multiple cutaneous hemangiomas since birth. The baby was delivered by caesarean section at a private hospital with an uneventful antenatal

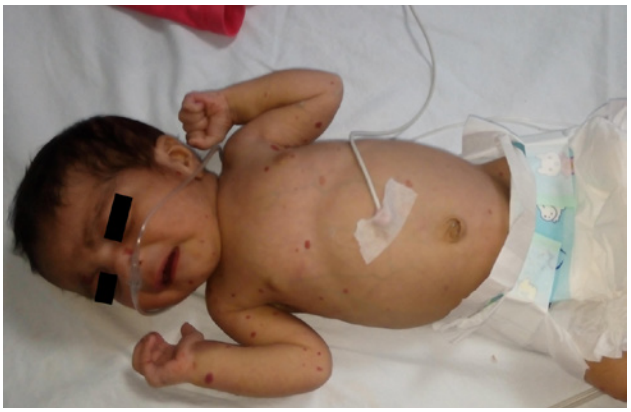

Figure 1. Multiple maculopapular cutaneous hemangiomas. [Copyright: ©2017 Agarwal et al.]

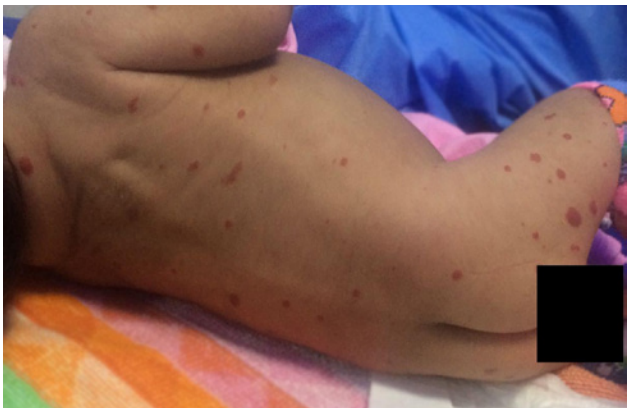

Figure 2. Multiple maculopapular cutaneous hemangiomas. [Copyright: ©2017 Agarwal et al.]

and perinatal course. At birth there were multiple cutaneous hemangiomas widely spread all over the body. Baby was discharged on fourth day of life on exclusive breastfeeding. On day 5, he developed tachypnea and diaphoresis over the forehead during feeding that gradually progressed over the next 15 days. On admission to our institute, the baby was euthermic with tachycardia (heart rate -170/min), tachypnea (respiratory rate- 70/min), hypoxia (SpO2 at room air- 80%) and mild cyanosis. Blood pressure was 86/53 mm of Hg and was similar in all four limbs. All central and peripheral pulses were well palpable and there was no pre- or post-ductal difference in oxygen saturation. There were multiple maculopapular cutaneous hemangiomas (around 490) ranging from pin head size to 1.5 cm x 1.5 cm spread all over the body (Figure 1 and 2). Cardiac examination revealed grade 3/6 systolic murmur in left sternal border with fine crepitations in chest. On abdominal exam there was huge firm liver, 6 cm below the costal margin. The possibility of congenital heart disease with congestive heart failure was made, and the baby was managed accordingly with fluid restriction and diuretics. Sepsis screen was negative, and x-ray chest showed cardiomegaly with pulmonary plethora. Echocardiography revealed severe pulmonary hypertension (systolic gradient 88 mm Hg) with patent ductus arteriosus and right to left shunt. USG abdomen revealed multiple diffuse hemangiomas in liver, with the maximum size being 14 mm x 13 mm (Figure 3). A whole body MRI confirmed the ultrasound and echo findings and ruled out CNS, renal, intestinal and skeletal involvement. Thyroid functions were normal. Prompt treatment was instituted with prednisolone (2 mg/kg/day) for anticipated life threatening complications due to hepatic hemangiomas. Congestive heart failure responded in three to five days with the continuing anti-congestive therapy. After five days, propranolol (2 mg/kg/day) was added with a plan to

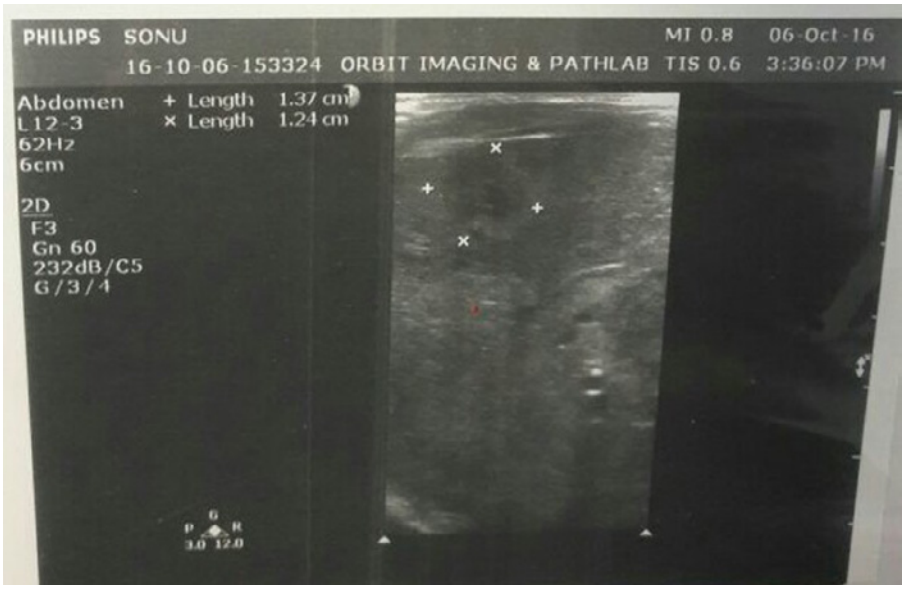

Figure 3. Echocardiography revealed severe pulmonary hypertension. [Copyright: ©2017 Agarwal et al.]

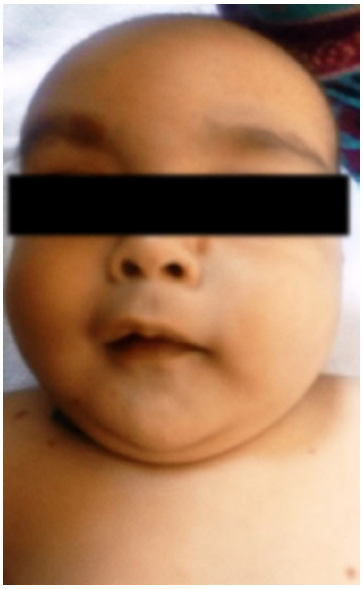

Figure 4. After treatment, some cutaneous lesions regressed while some changed from bright red to wine color. [Copyright: ©2017 Agarwal et al.]

taper steroids in four weeks to avoid long-term complications of steroids. However, they had to be tapered at three weeks due to intercurrent systemic bacterial infection.

After eight weeks, an ultrasound of the abdomen demonstrated decrease in size of hepatic lesions. Echocardiography showed resolving pulmonary hypertension (PG-32mm of Hg), and decrease in right ventricular hypertrophy. Some cutaneous lesions regressed while some changed from bright red to wine color (Figure 4). The baby was continued on the same treatment with careful monitoring of adverse effects of propranolol like hypoglycemia, bradycardia, hypotension, and airway hyperreactivity. The baby is now thriving well without any side effects of propranolol or increase in size of lesions.

Discussion

DNH is potentially a fatal condition owing to the involvement of vital organs resulting in hemodynamic alterations and haemorrhages. DNH occurs most commonly in Caucasian infants, with females being affected more often than males (3:1) [5]. Our patient was a male baby with multiple cutaneous hemangiomas involving the whole body and diffuse hemangiomas in the liver and clinical presentation of congestive heart failure (CHF). CHF is an unusual presentation of DNH in neonates and can be mistaken for a variety of congenital heart diseases. The other likely differentials like Kasabach-Merrit syndrome and PHACES were ruled out with absence of thrombocytopenia, bleeding manifestations or brain tumor.

The vascular lesions are made up of proliferating endothelial cells, which in the early stage form vascular channels filled with blood cells. The proliferative capacity of these immature endothelial cells is maintained for a limited period during postnatal life due to various angiogenic peptides and vascular endothelial growth factor (VEGF) [6]. Hence, these hemangiomas tend to increase initially for 8-12 months (proliferative phase), followed by regression over the next 1-5 years (involuting phase), with continuous improvement until 6-12 years (involuted phase). An early diagnosis and prompt treatment inhibits the progression and induces regression of the vascular lesions, thus reducing the mortality to 27% [7].

Although a variety of medical and surgical treatment options are available, drug therapy is the primary mode of treatment, and most cases of infantile hemangiomas with visceral involvement have been successfully treated by corticosteroids as the first-line agents [8,9]. However, keeping in mind their adverse effects in the long run, we reviewed the literature for other medical options. Propranolol, due its vasoconstrictor and inhibitory effects on endothelial and fibroblast growth factor, has shown promising results in early induction of cell apoptosis, involution of hemangiomas and arteriovenous formations (AVMs) [8,14]. Previously, it was considered second-line treatment in cases of non-resolution of infantile hemangiomas or of failure of other treatments, but recently, it has been used successfully as a first-line agent in DNH with vital organ involvement (10-13). However, complete failure of treatment and rebound growth following cessation of treatment with this drug has also been documented [14,15]. Also, beta adrenergic blockers have to be used cautiously in the presence of severe heart failure as they may further decrease the cardiac function and induce cardiac failure. Hence, we instituted immediate treatment with corticosteroids, and propranolol was started after resolution of CHF with a plan to taper steroids in four weeks. The response to this treatment was satisfactory.

A multimodal and individualized treatment approach may be necessary in life threatening and complicated cases of DNH as there is no specific drug of choice. Randomized trials with corticosteroids and beta blockers would be ideal, but considering the rarity of this disease, it seems less feasible. Hence, reporting of such cases and sharing the personal experiences would help to establish the most effective medical treatment.

Key Message

Although a consensus regarding the exact number of hemangiomas defining DNH has not been reached, it should be suspected in all cases of multiple infantile hemangiomas with or without systemic manifestations. Number of cutaneous lesions as less as three have also been reported to have hepatic hemangiomas on routine ultrasound. [8]. Early diagnosis and prompt medical treatment is lifesaving, as it is a potentially fatal condition. The first-line management needs to be individualized, keeping in mind the efficacy, long-term side effects of the drug, and the clinical presentation.

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