CASE REPORT

Diffuse Neonatal Haemangiomatosis: A Rare Cause of Haemorrhagic Shock and Refractory Coagulopathy in the Newborn

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Summary

A term newborn infant developed hypovolaemic shock shortly after birth. She was pale with gross hepatomegaly. She required multiple boluses of intravenous fluids, blood products as well as inotropic support. Blood investigations showed persistent thrombocytopenia, anaemia and disseminated intravascular coagulopathy (DIC). She also developed heart failure. She finally succumbed on the eleventh day of life. Autopsy revealed haemangiomatosis involving the liver, lungs, gastrointestinal tract, kidneys and adrenals.

Key Words: Diffuse Neonatal Haemangiomatosis, Corticosteroids

Case Report

The mother was a 25-year-old primigravida. Her pregnancy was uneventful except for mild pregnancy-induced hypertension near term. Her husband was a 32-year-old construction worker and their marriage was non-consanguinous. There was no family history of still birth, neonatal death or blood disorders.

She had spontaneous onset of labour at the 39th week of amenorrhoea. The labour progressed well. Cardiotocography (CTG) was normal. There was no maternal fever, foul-smelling or meconium-stained liquor. The second stage lasted 13 minutes. A female infant weighing 2310 grams was born via spontaneous vertex delivery with an Apgar score of 9 and 10 at 1 and 5 minutes, respectively.

One hour after delivery the infant was noted to be pale while still in the labour room. She was hypothermic (skin temperature 34.9°C), pale and inactive. She was also tachypnoeic and grunting although auscultation of her lungs revealed normal breath sounds. Her heart rate was 170 beats/min. The apex of her heart was not

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displaced. Her peripheral perfusion was poor. There was no skin lesion. The liver edge was palpable 6cm below the right subcostal margin. There was no liver bruit or tenderness. There was no subaponeurotic haematoma or cephalohaematoma. The placenta and umbilical cord were grossly normal.

After rewarming, her skin temperature improved to 36.2°C but she remained pale and tachycardic with poor perfusion. Her perfusion improved after 2 intravenous bolus doses of 20mls/kg of normal saline. She was then transferred to the neonatal intensive care unit (NICU).

During the next 12 hours, she remained pale, hypotensive and anuric despite having been transfused boluses of 90ml/kg of normal saline, 20mls/kg of blood and fresh frozen plasma. She was commenced on intravenous infusion of adrenaline, dopamine and dobutamine. Intravenous crystalline penicillin and gentamicin were also commenced as infection could not be ruled out. However cultures of blood, urine and swabs taken from the umbilicus, rectum and nose were negative. Serology for congenital infections namely toxoplasma, rubella, cytomegalovirus, herpes simplex and syphilis were negative.

Ultrasound examination of the brain revealed bulky choroids plexus without evidence of subdural or subarachnoid haemorrhage. An abdominal ultrasound performed by the paediatric radiologist did not reveal any evidence of bleeding in the adrenals, liver or kidneys. Neither was there any evidence of free fluid in the peritoneal cavity. The initial blood investigations showed haemoglobin of 11.3 g/dl, platelet count of 103,000/mm^3, serum creatinine of 109 micromol/L, prothrombin time (PT) of 68.7 seconds with International Normalisation ratio (INR) of 5.3 and activated partial thromboplastin time (APTT) of more than 180 seconds. The peripheral blood film which was taken after the patient had been transfused did not reveal any significant finding.

Her blood pressure eventually stabilized after about 24 hours. Her urine output slowly improved. However she had persistent haematuria and intermittent epistaxis. Enteral feeding was withheld as she developed rectal bleeding. Her coagulation profile showed prolonged PT, APTT and low fibrinogen levels. The platelet counts ranged between 29,000 to 94,000/mm^3. She required regular transfusion of platelets, fresh frozen plasma and cryoprecipitate. She had liver dysfunction as evidenced by elevated liver enzymes (ALT of 306 U/L, AST of 2306 U/L, ALP of 250 U/L), direct hyperbilirubinaemia and hypoalbuminaemia.

She remained haemodynamically stable until the seventh day of life when she required assisted ventilation for type 2 respiratory failure due to congestive heart failure and pulmonary oedema.

The pulmonary oedema resolved with treatment. However she remained ill and her coagulopathy persisted. On the 9th day of life she did not have any spontaneous movements. Repeat cranial ultrasound showed loss of normal brain configuration with grade 4 intraventricular haemorrhage. Repeat renal ultrasonography showed loss of corticomedullary differentiation and reduced renal blood flow. The baby finally succumbed on the eleventh day of life. The cause of death was multi-organ failure secondary to hypovolaemic shock as a result of visceral haemorrhage.

Autopsy revealed haemothorax and haemoperitonium. Histopathological examination of the lung tissues showed dilated vessels and areas of haemorrhage. The liver was enlarged and nodular. Sections from the liver showed loss of normal architecture with numerous vascular channels occupying almost the entire liver. Both

kidneys showed areas of haemorrhage and infarcts. Sections from the kidneys showed presence of vascular proliferation and haemorrhage in the calyceal systems and tubulointerstitial region. Similar findings were seen in the gastrointestinal tract and adrenals. These findings were consistent with the diagnosis of diffuse haemangiomatosis. The skin biopsy was normal.

Discussion

Diffuse neonatal haemangiomatosis (DNH) is a rare disorder characterized by the presence of multiple cutaneous and visceral haemangiomas which appear at birth or shortly after. However there are cases in which only the skin is affected and also instances in which cutaneous involvement is absent but there is extensive visceral haemangiomatosis, usually involving the liver[1]. Between 1966 to 1997 only 68 cases were reported in the literature. It is three times more common in females. There is no hereditary factor identified. Holden and Alexander in 1970 established 3 minimal diagnostic criteria for the diagnosis of DNH[2]. They were i) onset in the neonatal period, ii) no evidence of malignancy and iii) involvement of 3 or more organ systems as found in our patient.

The most commonly affected organs besides the skin (100%) were liver (72%), lungs (42.6%), central nervous system (35.3%) and gastrointestinal tract (29.4%). Our patient was unusual as there was no cutaneous manifestation. Complications of haemangiomas include Kasabach Merritt Syndrome (KMS) in which there is thrombocytopenia secondary to local consumption of platelet and high output congestive cardiac failure (CCF) due to arteriovenous shunting in the lesions. The overall mortality rate for DNH was 50% and the mean age at death was 9.8 weeks. The causes of death are CCF (38.2%), haemorrhage (11.8%), hydrocephalus (8.8%), multi-organ failure (8.8%), KMS (5.9%), others (11.8%) and not mentioned in 11.8%. The mortality rate was significantly higher in patients with CHF and KMS as well as in patients with five or more organs involved.

There is no universally accepted protocol for the specific treatment of DNH. Because of its rarity, it is difficult to conduct prospective and controlled studies to compare various treatment strategies. The most recent guidelines suggest that treatment should be started with corticosteroids (2-4 mg/kg/day)[3]. If no effect is seen after 2-4 weeks, interferon alpha is recommended. The response to steroid is good in 30%, bad in 30% and doubtful in another 40% of patients. In good responders, growth of the haemangioma usually arrests within 3 weeks. The duration of treatment ranges between one month to 2 years.

Interferon alpha has been shown to be effective in patients with life-threatening or vision-threatening haemangiomas which failed to respond to steroid therapy[3]. However this was described only in more localized lesions.

This case illustrates that in a newborn with haemorrhagic shock, refractory coagulopathy and persistent thrombocytopenia without any obvious site of bleeding, the diagnosis of DNH should be considered even in the absence of cutaneous lesion. The presence of congestive heart failure also increased the likelihood of this diagnosis. Early empirical steroid therapy may improve the outcome.

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