CASE REPORT

Hereditary Hemorrhagic Telangiectasia – Early Childhood Presentation with Hepatic Failure

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ABSTRACT

Hereditary hemorrhagic telangiectasia (HHT) is a vascular dysplasia in which capillary bed is absent with direct draining of arterial blood into venous circulation. Due to increased pressure there is increased risk of bleeding. The classical triad consists of telangiectasias, epistaxis and a positive family history. This defect can involve any organ system, especially lungs, brain and liver; but hepatic vascular malformations in HHT usually remain silent until fifth or sixth decade of life. However, if symptomatic, it usually results in only mild liver dysfunction in adults. Herein, we report a rare case showing extensive hepatic involvement in HHT leading to hepatic failure at a younger age. Hepatic screening is traditionally not recommended at early age while pulmonary and cerebral screening must be done. Based on this case, we recommend hepatic screening even in a young patient with HHT.

Key Words: *Hereditary hemorrhagic telangiectasia. Osler-Weber-Rendu syndrome. Arteriovenous malformations.*

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) or Osler-Weber-Rendu syndrome is an autosomal, dominantly inherited vascular malformation syndrome characterised by skin or mucosal telangiectasias and arteriovenous malformations (AVMs) that occurs in 1 in 10,000 individuals.[1] The established clinical diagnostic criteria, Curaçao criteria for HHT, requires the presence of three of the following four features: recurrent epistaxis, multiple skin telangiectasias, visceral AVMs or telangiectasias, and a first-degree family member with HHT. Having three criteria confirms the diagnosis.[2] AVMs in HHT often remain clinically silent in early childhood. Liver AVMs are present in 78% of adult HHT patients but only 8% are symptomatic, while 47% of pediatric HHT patients have hepatic AVMs, usually not presenting in childhood.[3]

Liver transplantation offers a viable treatment option in adult patients with hepatic involvement refractory to medical management.[3] Early screening for pulmonary and cerebral AVMs in pediatric HHT are recommended due to risk of life-threatening sequelae. However, hepatic screening has not been routinely recommended since hepatic symptoms of HHT are not considered to manifest until late adulthood.

Here, we report a case of pediatric HHT referred to us for evaluation of deranged liver functions showing extensive liver involvement at a very young age, demonstrating that HHT-related hepatic decompensation can occur at an early age.

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Received: January 04, 2018; Accepted: May 08, 2018.

CASE REPORT

A 2.5-year, developmentally normal, male child, presented with failure to thrive and recurrent episodes of epistaxis since 8 months of age. He also had multiple episodes of cough and dyspnea, occasionally requiring hospital admission. In the months preceding presentation to us, telangiectasias started appearing around mouth and patient became noticeably cyanotic. There was no family history of telangiectasias and bleeding from any site. The child was product of consanguineous marriage as the parents were first cousins.

On examination, the child was malnourished with height and weight below the 3rd centile. He had central cyanosis and clubbing with mild tachycardia and tachypnea. His temperature and blood pressure were normal. There was no jaundice but there were multiple small telangiectasias around his mouth and eyelids, with additional lesions on his arm and upper back. Examination of respiratory and cardiovascular systems was unremarkable. On abdominal examination, the left lobe of liver was enlarged (3.5 cm below the costal margin) and tip of spleen was also palpable. No bruits were audible over the right upper quadrant. Central nervous system examination revealed no abnormality with intact cranial nerves and motor system.

Complete blood picture showed mild hypochromic, microcytic anemia with haemoglobin of 10.3 g/dl, white blood cell count of 5400/µL with normal differentials and platelet count of 137000/µL. Liver function tests revealed multiple abnormalities including mild transaminitis (Alanine transaminase, 156 U/L, Aspartate amino-transferase, 190 U/L and Gamma-glutamyl transferase,

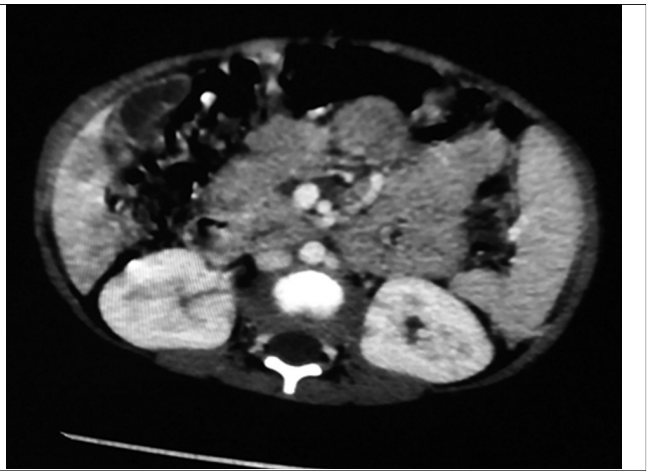

Figure 1: Computed tomography scan abdomen with contrast showing enlarged liver studded with multiple ill-defined hypodense focal lesions.

99 U/L) with slightly elevated total bilirubin (2.0 mg/dl) and significantly elevated alkaline phosphatase (1058 U/L) with international normalised ratio INR of 2.5. Partial thromboplastin time (PT) and activated partial thromboplastin time (APTT) were prolonged at 20.9 sec (control 13 sec) and 45 sec (control 31 sec), respectively. Alfa fetoprotein (AFP) and serum albumin were normal.

Computed tomography (CT) scan abdomen with contrast (Figure 1) showed enlarged liver which was studded with multiple ill-defined hypodense focal lesions without any significant mass effect with largest lesion involving segment 1 and measured 6.4 cm in size. Portal venous system was intact with no filling defect. On delayed phase imaging, there was evidence of filling in with lack of differentiation. The scan was otherwise normal.

Dynamic liver CT showed heterogeneous parenchyma with multiple hypoenhancing areas, likely perfusion-related abnormalities, with sparing of a small amount of normal parenchyma. There was no arterially enhancing lesion or areas of washout on delayed venous phase images. Hepatic and portal veins were normally contrast opacified. There was no evidence of thrombosis and no ascities was seen. No focal lesion was seen in any viscera.

Echocardiography was normal. Chest CT appeared normal, except for a few areas of nodular opacity in the left lingual and in the right base. Catheter-directed pulmonary angiogram revealed multiple pulmonary AVMs consistent with HHT, but not amenable to closure. Genetic testing could not be done as it was not available in our set-up.

During the hospital stay, we managed the patient conservatively with antibiotics, intravenous fluids, and fresh frozen plasma transfusions. He was discharged on prophylactic antibiotics as there was history of recurrent chest infections; although, clinically chest was clear. Nutritional counselling was also done with additional vitamin and mineral supplementation. This decreased the recurrence of chest infections and improved the overall health on follow-up. Parents were fully counselled about the course and prognosis of disease. Nothing much could be done medically for liver involvement; and liver transplantation also could not be offered because of systemic involvement.

DISCUSSION

HHT is a multi-organ disorder resulting in vascular dysplasias. At least 5 genetic mutations are involved but two are responsible for more than 85% of cases.[3] Hepatic HHT is scarce, two cases reported had different age of onset and presentation. The first described a 15-year boy with hepatic AVMs, complicated by portal hypertension; while the other reported a 21-month child with gastrointestinal bleeding thought to be secondary to hemorrhage from the hepatic vascular malformation into the biliary tract. The present case had much more extensive involvement of the liver as compared to the more focal nature described in these cases.[4,5]

The present case indicates that HHT-related AVMs can cause decompensation of liver at an early age. This is contrary to the previously reported data in which 35 children with HHT were systematically screened and a relatively higher incidence of hepatic AVMs (47%) in children was reported. However, no clinical hepatic signs or abnormal liver tests were noted in any child.[6]

Another long duration study screened 14 children with HHT for visceral AVMs; and found only one 12-year child with HHT with a rather extensive disease pattern including cerebral, pulmonary and symptomatic hepatic AVMs manifested by elevated transaminases and coagulopathy.[7] This child had developmental delay as well, contrary to this case.

However, another recent case series reported earlier presentation and cardiovascular manifestation of HHT-related hepatic AVMs. The three infants presented during the first 24 hours of life with high-output congestive cardiac failure caused by intrahepatic arteriovenous shunting. Single-embolization procedure resulted in immediate improvement in the condition of the two surviving infants and eventually involution of AVMs in both cases.[8] This reflects on the congenital origin of hepatic AVMs that can manifest as early as first day of life and probably have better outcome in case of earlier intervention.

Different radiological patterns have been described in hepatic AVMs. The hepatological pattern in our case was more consistent with HHT-cirrhosis described in adults.[9]

Around 20% cases with HHT have no family history.[8] HHT with early and extensive liver involvement in pediatric age group is not reported in our literature. However, it is reported in an adult where liver was

predominantly occupied by vascular structures and there was scarce residual hepatic parenchyma showing that hepatic involvement may rarely result in hepatic failure.[10]

Pediatric data is lacking regarding the liver transplantation in hepatic HHT as is the natural history of pediatric hepatic AVMs. Moreover, there is no consensus regarding early screening for liver involvement, as is recommended for pulmonary and cerebral AVMs in asymptomatic patients specially in children. We suggest that in pediatric HHT, early hepatic screening should be a part of multi-visceral screening to avoid impending life-threatening complications.

In conclusion, we recommend that early hepatic screening, in addition to pulmonary and cerebral screening, should be considered in children with definite or possible HHT.

REFERENCES

1. McDonald J, Wooderchak-Donahue W, VanSant Webb C, Whitehead K, Stevenson DA, Bayrak-Toydemir P. Hereditary hemorrhagic telangiectasia: genetics and molecular diagnostics in a new era. *Front Genet* 2015; **6**:1-8.
2. Faughnan ME, Palda VA, Garcia-Tsao G, Geisthoff UW, McDonald J, Proctor DD, *et al*. International guidelines for the diagnosis and management of hereditary hemorrhagic telangiectasia. *J Med Genet* 2011; **48**:73-87.
3. McDonald J, Bayrak-Toydemir P, Pyeritz RE. Hereditary hemorrhagic telangiectasia: An overview of diagnosis, management, and pathogenesis. *Genet med* 2011; **13**:607-16.
4. Arfa MN, Bouzaiene H, Ben Farhat L, Gharbi L, Ghariani B, Mestiri H, *et al.* Intrahepatic Osler's disease: Report of two cases and review of the literature. *Hepatogastroenterology* 2003; **50** (Suppl 2):ccx-ccxiii.
5. Bross DA, Perez-Atayde A, Mandell VS, Hyams JS, Jonas MM. Hereditary hemorrhagic telangiectasia presenting in early childhood. *J Pediatr Gastroenterol Nutr* 1994; **18**:497-500.
6. Giordano PS, Nigro A, Lenato GM, Guanti G, Suppressa P, Lastella P, *et al.* Screening for children from families with Rendu-Osler-Weber disease: from geneticist to clinician. *J Thromb Haemost* 2006; **4**:1237-45.
7. Mei-Zahav M, Letarte M, Faughnan ME, Abdalla SA, Cymerman U, MacLusky IB. Symptomatic children with hereditary hemorrhagic telangiectasia. A pediatric center experience. *Arch Pediatr Adolesc Med* 2006; **160**:596-601.
8. Al-Saleh S, John PR, Letarte M, Faughnan ME, Belik J, Ratjen F. Symptomatic liver involvement in neonatal hereditary hemorrhagic telangiectasia. *Pediatrics* 2011; **127**:1615-20.
9. Juaresl AJ, Dell'AringaII AR, NardiIII JC, KobariI K, Gradim Moron Rodrigues VL, Perches Filho RM. Rendu-Osler-Weber Syndrome: Case report and literature review. *Braz J Otorhinolaryngol* 2008; **74**:452-7.
10. Mukasa C, Nakamura K, Chijiiwa Y, Sakai H, Nawata H. Liver failure caused by hepatic angiodysplasia in hereditary hemorrhagic telangiectasia. *Am J Gastroenterol* 1998; **93**:471-3.