Deep Vein Thrombosis Associated with Dengue Fever

AMRITA ROY, JASODHARA CHAUDHURI AND SWAPNA CHAKRABORTY
From Department of Pediatrics, Medical College and Hospitals, Kolkata, India.

Correspondence to:
Dr Jasodhara Chaudhuri,
247 Lake Gardens, Kolkata 700 045, West Bengal, India.
jasodharachaudhuri@gmail.com
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Background: Hemorrhagic manifestations are common with Dengue but thrombotic events are uncommonly reported. ***Case characteristics:*** 11-year-old boy who presented with ileo-femoral deep vein thrombosis associated with serologically confirmed infection with DEN1 dengue virus. ***Observation:*** There was no other history or investigation suggestive of a procoagulant state. ***Outcome:*** Successfully treated with enoxaparin and warfarin. ***Message*:** Thrombotic complications are possible with dengue infection.

Keywords: *Anticoagulation, Complications, Thrombosis, Dengue fever.*

Dengue infection can be either asymptomatic, or progress to involve hemorrhagic manifestations with shock [1]. Thrombotic events have not been extensively reported, despite the wide range of increased procoagulant activity during illness [2,3].

CASE REPORT

An 11-year-old boy presented with high grade fever for past 7 days, headache, arthralgia, myalgia, nausea, abdominal pain and right calf pain. Examination revealed stable vitals, mild pallor, soft tender hepatomegaly, right calf swelling, and tenderness with positive Homan's sign. There was no evidence of capillary leak. His hemogram revealed normocytic normochromic anemia, haematocrit 49%, TLC 9500/cu mm and platelet count of 1,60,000/cu. mm. His liver function tests showed mildly increased transaminases (SGOT 119 IU/mL, SGPT 171 IU/mL); serum urea and creatinine levels were normal. Ultra-sonography (USG) with colour Doppler study of right leg showed extensive thrombosis with no color flow involving right popliteal; right superficial, deep, common femoral vein with proximal extension upto external iliac vein

There was no history of venous catheter placement in his lower limbs or any past history or family history suggestive of venous thromboembolism. D-dimer was increased (6694 ng/mL). Malaria parasite antigen test, blood culture and Widal test were negative. Coagulation studies and routine stool examination yielded normal results.Hepatitis A, B, C virus infections were ruled out serologically. But, he was serologically confirmed positive for anti-DEN 1 IgM by IgM antigen capture enzyme-linked immunosorbent assay on day 6 of illness.

Screening for inherited thrombophilia did not reveal any abnormality. He was screened for Protein C,S deficiency and prothrombin mutation analysis done. Echocardiography and Doppler ultrasonography of portal and mesenteric veins was normal.

Keeping in view the risks of life threatening pulmonary embolism and because his PT, APTT and TT reports and platelet counts were within normal ranges, he was started on subcutaneous enoxaparin 1 mg/kg/day in 2 divided doses with twice weekly monitoring of platelet counts, APTT levels and USG and weekly peak anti-Xa levels maintained between 0.5 and 1.0 IU/mL. After 12 days, USG with color Doppler of ileo-femoral venous system showed decreased extent of the thrombus. After 2 weeks of subcutaneous heparin, he was started on oral warfarin keeping INR between 2-3. After 4 weeks, the veins were completely recanalized and his anticoagulation therapy was discontinued after 3 months.

DISCUSSION

Many factors might increase thrombotic risk in children with dengue fever [2, 3]. Dengue virus may down regulate thrombomodulin-thrombin-protein C complex formation thus reducing activated protein C [4]. Low concentrations of plasma anticoagulant proteins C and S and antithrombin III have been detected in severe dengue but have not been associated with clinical thrombosis [3]. No procoagulant risk factor was identified in this case.

Dengue virus activates endothelial cells and increases the expression of thrombomodulin [5]. Lin, *et al*. [6] described host antibodies formed against dengue non-structural protein that had cross-reactivity with host endothelial cells which can lead to inflammatory responses. Increased PAI-1 plasma levels were also observed [3]. Disseminated intravascular coagulation and consequent microthombi formation may contribute but have not been associated with large vessel thrombosis [2]. Antibodies against phospholipids, cardiolipin and increased lupus anticoagulant have been associated with thrombotic events in peripheral arteries and cerebral vasculature [7]. Venous cerebral vasculature thrombosis and ischemic stroke not associated with any risk factor have been rarely reported in dengue fever [8]. As the thrombosis was clinically detected at admission, loss of

endothelium non-thrombogenic protective factors may have been the cause [2].

There are only a handful of reported cases where deep vein thrombosis have been reported in direct association with dengue fever [2,7]. Thrombotic events in large veins [ileo-femoral deep vein thrombosis (DVT), pulmonary thromboembolism, mesenteric vein thrombosis] in DF patients have been reported from Brazil in 5.4% of all dengue inpatients.

The dilemmas posed in treating a blood clot in a patient who is at risk for excessive bleeding were challenging.

Awareness for these thrombotic complications is recommended to all practitioners who treat dengue in hospital settings

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Neonatal Aortic Thrombosis as a Result of Congenital Homocystinuria

BONNY JASANI AND RUCHI NANAVATI
From Department of Neonatology, KEM Hospital, Parel, Mumbai, India.

Correspondence to:
Dr Bonny Jasani, Department of Neonatology, 10th Floor, New M.S. Building, KEM Hospital, Parel, Mumbai 400 012, India.
docbonny_2000@yahoo.com
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Background: Arterial thrombosis, that too in aorta is rare in neonates. **Case characteristics:** A 4-day-old presented with non-recordable BP in lower limbs. Doppler ultrasonography of abdomen revealed aortic thrombus. **Observation:** Serum homocysteine level was elevated (25.5 µmol/L). **Outcome:** Thrombus resolved with subcutaneous LMW heparin therapy for 2 weeks. **Message:** Congenital classic homocystinuria can rarely cause aortic thrombosis in neonatal period.

Keywords: Congenital aortic thrombosis, Congenital classic Homocystinuria, Neonate.

Thrombotic diseases are rare in neonates. The main known risk factors at this age are perinatal asphyxia, dehydration [1], umbilical arterial catheterization [2] and inherited thrombophilia [3,4]. Inherited thrombotic disorders become manifest in <5% of affected children [5]. Arterial thrombosis, even more rare than venous thrombosis, rarely occurs in the aorta. Most of the described cases of aortic thrombosis are associated with the catheterization of an umbilical artery. We hereby describe a case of abdominal aortic thrombosis due to congenital classic homocystinuria.

CASE REPORT

A four-days-old full term female infant, born vaginally through meconium stained amniotic fluid, presented to us with respiratory distress, lethargy and poor feeding. Infant had cried immediately after birth. There was no history of umbilical arterial catheterization. The mother had pregnancy induced hypertension and two spontaneous second trimester abortions in the past. There was no family history of thrombotic events. Examination revealed mild respiratory distress with Downe's score of