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Case Report

Intrauterine upper limb thrombosis: an unusual presentation

Baraturam B. Bhaisara, Charusheela S. Korday*, Minal R. Wade, Vikram V. Yaragatti, Anjali M. Bhatawdekar, Anupama V. Mauskar

Department of Pediatrics, College Building, HBT Medical College & Dr R N Cooper Municipal General Hospital, Juhu, Mumbai, Maharashtra, India

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***Correspondence:**
Dr. Charusheela S. Korday,
E-mail: c_warke2000@hotmail.com

ABSTRACT

Intrauterine thrombosis with extremity ischemia presenting at birth in a newborn is a rare event. A 29 year old mother, 2nd gravida with one first trimester spontaneous abortion delivered a 33week gestation male preterm baby. On Examination, the entire left upper limb was ischemic and edematous with an absent flow on Doppler USG. Low molecular weight heparin (LMWH) was started after which gradually the limb turned pink with good volume pulsations. Thrombophilia mutation studies revealed the heterozygous state for the MTHFR (C677T) mutation only in the mother. Prompt diagnosis and early treatment has a favourable outcome in cases of intra-uterine thrombo-embolism.

Keywords: Hypercaogulable state, Intrauterine thrombosis, Low molecular weight heparin, Methylenetetrahydrofolate reductase, Neonate, Upper limb ischemia

INTRODUCTION

Intrauterine thrombosis with extremity ischemia presenting at birth in a newborn is a rare event a limited number of cases described in the literature.[1] Intrauterine thrombosis should be distinguished from neonatal thrombosis, which occurs after birth. Neonatal thrombosis is often caused by catherization of the umbilical artery in a sick neonate or seen as complication to sepsis or coagulation disorders.[1,2]

The pathogenesis of intrauterine gangrene can be divided into intrauterine compression or thromboembolic phenomena.[3] Compression is generally caused by uterine anomalies, fetal malpresentation with limb prolapse, oligohydramnios, amniotic bands, or umbilical cord entanglement.[4]

Intrauterine fetal ischemia caused by thrombosis or emboli has been linked to maternal diabetes, preterm delivery, dehydration, polycythaemia, and twin to- twin transfusion syndrome.[1,5,6] Neonates are in a transient thrombophilic state with low activity of protein C, protein S, antithrombin, plasminogen, and tissue plasminogen activator.[1,7]

The risk of thrombosis is even higher if any of the above conditions arepresent. Recently, three case reports have linked intrauterine arterial thrombosis with methylenetetrahydrofolate reductase (MTHFR) mutations and factor V Leiden mutation.[8-10]

However, in many of the reported cases, the precise pathogenesis of the thrombosis has not been found. It requires thorough attention and collaboration between obstetricians, neonatologists, orthopedics, and plastic surgeons. The treatment varies from case to case.

We present a rare case of intrauterine fetal limb ischemia in a neonate born in our hospital.

CASE REPORT

A 29 year old mother, 2nd gravida with one first trimester spontaneous abortion and pre-gestational BMI of 32kg/m2 presented to our hospital with decreased fetal movements since 2 days, failure to progress and severe pregnancy induced hypertension (PIH). She delivered a 33 week gestation male preterm baby, birth weight being 1919grams. On examination, the entire left upper limb was edematous, pulseless, cold and cyanotic along with peeling of skin with undetectable oxygen saturation. Clinically left upper limb ischemia was suspected.

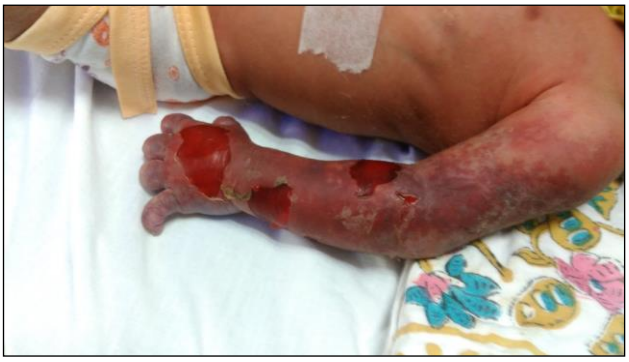

Figure 1: Day of life 1: Ischemic, edematous, cyanotic left upper limb with peeling of skin.

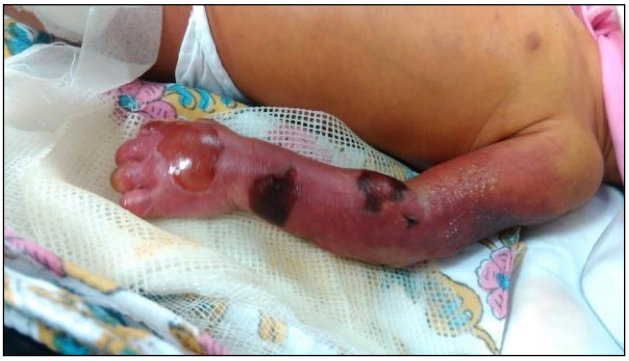

Figure 2: Day of life 5: Pink left upper limb with eschar formation in necrotic areas.

Dopplerultrasonography (USG) revealed an absent flow in the left brachial and subclavian artery which was later confirmed by magnetic resonance angiography (MRA) to be a thrombus. Subcutaneous low molecular weight heparin (LMWH) was started after which gradually the limb turned pink with good volume pulsations. LMWH given for 3months and then stopped. Both parents were examined in order to rule out thrombophilia as an associated risk factor. Screening tests including platelet count, mean platelet volume (MPV), free protein S concentration, total protein S concentration, total protein C concentration, antithrombin III concentration, done in both parents and baby were negative. Factor V Leiden mutation, prothrombin mutation (G20210A) and activated protein C (APC) resistance done in baby and mother were also negative. However, the heterozygous state for the MTHFR (C677T) mutation was positive in the mother, baby and father being negative for the mutation. Baby gradually improved and was discharged at 3 months of age. Currently he is 40months old growing well without any deficit.

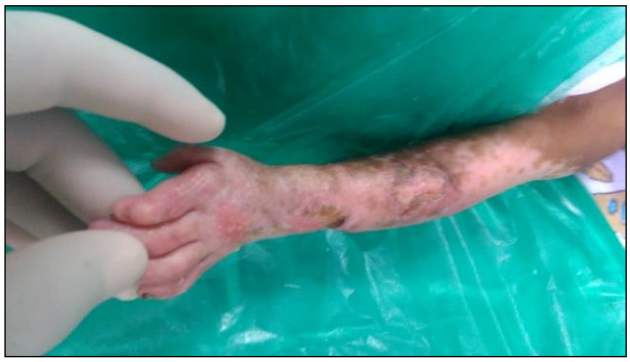

Figure 3: Day of life 30: Left upper limb showing healthy granulation with healing.

DISCUSSION

Various pathological conditions can cause intrauterine thrombosis. The most common are amniotic bands, umbilical cord compression, oligohydramnios, intrauterine thrombosis, and placental emboli.[11] Maternal diabetes or lupus, preeclampsia, polycythemia, asphyxia, sepsis, intrauterine growth retardation, severe dehydration, long obstructed labour and inherited thrombophilia are the major risk factors for intrauterine thrombosis.[12]

Indwelling intra-arterial catheters account for approximately 90% of the iatrogenic causes of thrombosis.[13] Literature search revealed a scarcity of case reports on spontaneous neonatal arterial thrombosis presenting at birth.[12,14] Moreover, upper limb vascular occlusion as a cause of intrauterine thrombosis is even rarer. Neonatal thrombosis occurs primarily in large vessels, commonly, in the aorta presenting like a cyanotic heart disease and as renal vein thrombosis.[12,13,15,16]

Anticoagulation therapy was started immediately in our baby after the arterial thrombosis was confirmed. We used low-molecular-weight Heparin (LMWH), the safest and most commonly used anticoagulant in neonatal thrombosis.[17,18] The role of heparin is mainly in clinically significant thrombosis to prevent clot expansion or embolism LMWH showed significant improvement without the need for thrombolytic therapy in our patient.[17] Our patient probably had a “forming thrombus” rather than a “well-formed thrombus” because there were no collaterals found on ultrasound doppler, and the patient had rapid improvement on anticoagulation alone.

LMWH is predominantly indicated for the primary treatment of neonatal thromboembolism with a proven safety profile.[18] The efficacy of LMWH in NICU setting has been proven in various articles by either partial or complete resolution of thromboembolic events in 59-100% of cases.[19-22] Our patient was given LMWH for 3 months. No consensus is present yet for the duration of treatment after resolution of symptoms.

Clinical features of peripheral arterial occlusion are a combination of 6Ps, which include pallor, pulselessness, paralysis, pain, parasthesia, and perishing cold of involved extremity, out of which atleast four were present in our patient. The clinical presentation varies depending on the site and time of occlusion.[23]

Treatment of neonatal spontaneous arterial thrombosis is controversial. According to the recommendation of an expert panel on the management of arterial thromboembolic events in neonates, treatment should be individualized based on the extent of thrombosis and the urgency of the clinical situation. It also suggested the use of anticoagulation agents as the recommended initial treatment for neonatal thromboembolism, whereas thrombolytic agents to be reserved for selected cases where there is a limb, organ, or any life threatening event.[17,18] Some cases are associated with a favorable outcome due to early diagnosis and prompt management which are thus the essential components for preserving limb function and perfusion.[23]

Since an inherited prothrombotic state of the mother, or in some case the father, increases the risk of thrombosis in the neonate, it is advisable to screen the parents for deficiencies and/or thrombophilic factors in the coagulation system.[24]

The upper limb thrombosis, in our case may have occurred most probably due to an emboli dislodged prenatally from the placenta.

First trimester spontaneous abortion, severe PIH, preterm delivery along with the pre-gestational pre-diabetic condition seemed to have aggravated the hypercoagulable state in the mother having MTHFR (C677T) mutation. The direct cause of the thrombosis was never found in our case. It has previously been described that emboli from the placenta can pass through the foramen ovale and lodge in the arterial system, usually causing upper-limb necrosis.[1,11] Hence, one can speculate that this was the reason for the upper-limb involvement even though we did not find any evidence of thromboses in the placenta. The positive heterozygous state for the MTHFR (C677T) mutation leading to an underlying hypercoaguable state in the mother could be the probable explanation for the origin of the emboli. Now the boy is 3 year old with normal and equal growth as well as neuromuscular functioning of both upper limb on both side.

CONCLUSION

All neonates with risk factors for thromboembolic disease should be evaluated for hypercoagulation, particularly those with spontaneous thrombosis in the absence of indwelling catheter. Prompt diagnosis and of early treatment has a favourable outcome.

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