Rare cases of neonatal thrombosis - case series

Ramesh Khadayat[1], Prenana Kansakar[2], Shreya Thapa[2], Sailesh Shrestha[2], Ramesh Basnet[2], Sagar Rana Magar[1], and Tilak Gautam[2]

[1]Tribhuvan University Institute of Medicine
[2]Patan Academy of Health Sciences

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Ramesh Khadayat[1], Prerana Kansakar[1], Sailesh Shrestha[1], Shreya Thapa[1], Tilak Gautam[1], Ramesh Basnet[1], Sagar Rana Magar[1]

1. Patan Hospital, Patan Academy of Health Science, Lalitpur, Nepal

*Corresponding author:-

Ramesh Khadayat

Patan Hospital, Patan Academy of Health Science, Lalitpur, Nepal

Email:- rameshkhadayat123@gmail.com

Key Clinical Message

In this case series, we report two rare cases of neonatal thrombosis, one in portal vein and another in descending aorta with underlying various risk factors. Here we discuss the risk factors for neonatal thrombosis, clinical presentation, management and outcome of each case.

Keywords:- Neonatal thrombosis, portal vein thrombosis, anticoagulant, sepsis, enoxaparin

1. INTRODUCTION

Neonatal thrombosis, either venous or arterial, are rare complications, however the incidence of thromboembolic events in neonates has increased over the last few decades(1). Critically ill and preterm neonates are at highest risk of such complications. Various Maternal, peri delivery and neonatal risk factors can contribute to development of thrombosis(2). The most common risk factors related to neonate include CVC, umbilical venous catheter and sepsis. Thromboembolic events in neonates can lead to mortality or serious morbidity and disability such as limb loss due to arterial thrombosis, loss of vital vascular access, bleeding risk secondary to anticoagulation therapy, portal hypertension and renal dysfunction(3,4). Standard treatment protocols or guidelines for management are lacking, and whatever available is largely extrapolated from adult data.Here we are going to report two cases, one case of portal vein thrombosis due to sepsis and another case of aortic thrombosis.

2. CASE REPORTS

2.2 Description of Case 1

History and Examination:-

This was a case of a newborn male born to 28 years primigravida at 37+3 WOG,with birth weight 3300 gm, via emergency lower segment caesarean section(Em LSCS) for per vaginal leaking for more than 24

hours. The child cried immediately after birth with an APGAR score of 8/10 and 9/10 at 1 and 5 mins of life. However, the newborn started developing multiple episodes of vomiting within 2 hours of life. No history of fever, irritability, excessive crying. There was no history of any thrombotic disorder running in the family and no history of umbilical vein catheterization. On examination the neonate was active and alert, his cry, color tone and reflexes were normal. Anterior fontanelle was open and at level. Abdomen was soft nondistended and there was no organomegaly, with normal rest of the physical examination.

Methods:-

For those symptoms septic workup which included CBC, CRP, Blood culture and sensitivity, urinalysis and culture, Lumbar puncture was done and broad spectrum antibiotics started(piperacillin-tazobactam and amikacin). Ultrasound of the abdomen and pelvis was also ordered which demonstrated incidental left portal vein thrombosis(figure-1) The laboratory reports showed Total leucocytes count of 12700/µl with 24% Neutrophils and 70 % lymphocytes, platelets was 39500/µl, hemoglobin 11.8 gm/dl, CRP-5.7 mg/dl, PT/iNR- 10/1 sec, APTT- 24 sec, urine analysis showed normal findings and urine culture was sterile. Initial blood was sterile, however repeated blood culture after 1 week showed growth of *Acinetobacter baumannii* , which was sensitive to amikacin, gentamicin, doxycycline, ciprofloxacin, TMP-SMX and colistin and resistant to piperacillin-tazobactam, ceftriaxone, cefepime, so antibiotic changed accordingly. Repeated ultrasound on the 7th day still showed the thrombus in the portal vein. Treatment with enoxaparin started, and weekly Ultrasound was done to see regression of thrombus.

Outcome and Follow-up

There was no evidence of thrombus in the portal vein in the Ultrasound at the end of 4 weeks of enoxaparin treatment and the child was doing well at follow-up(figure-2).

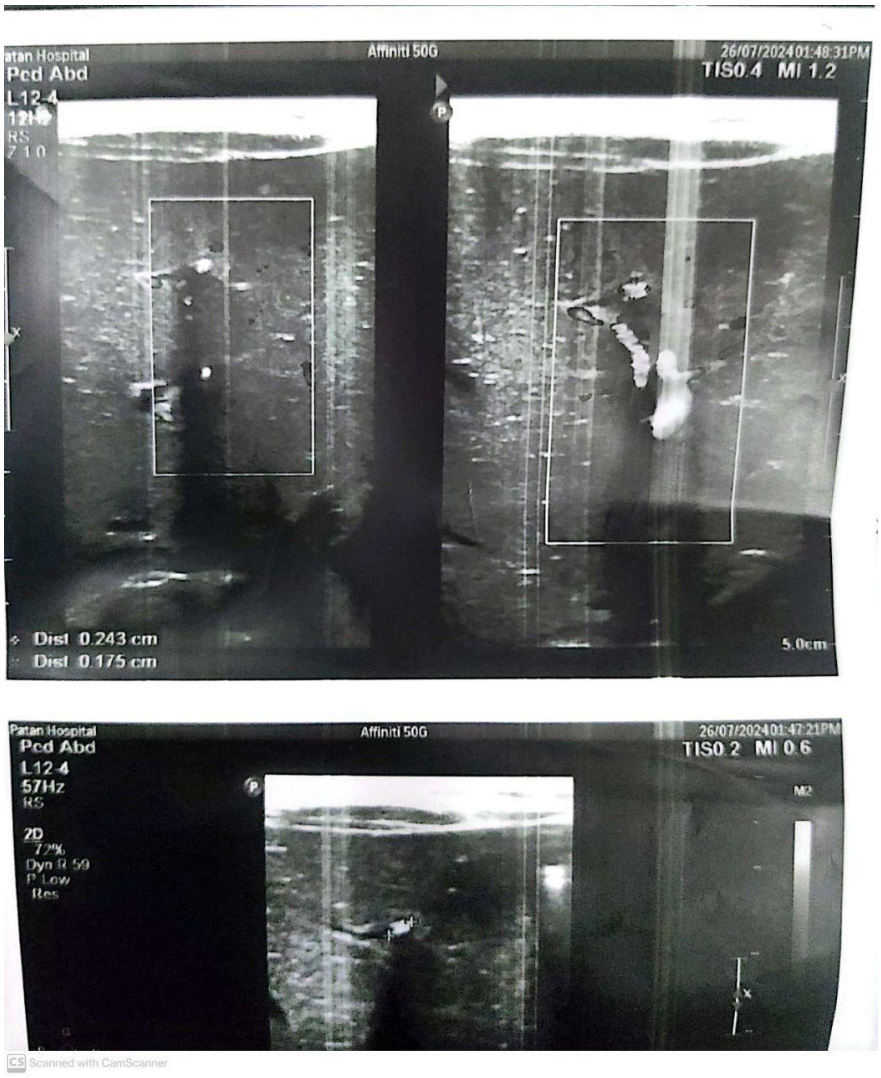

Fig-1: Thrombosis in left portal vein branch.

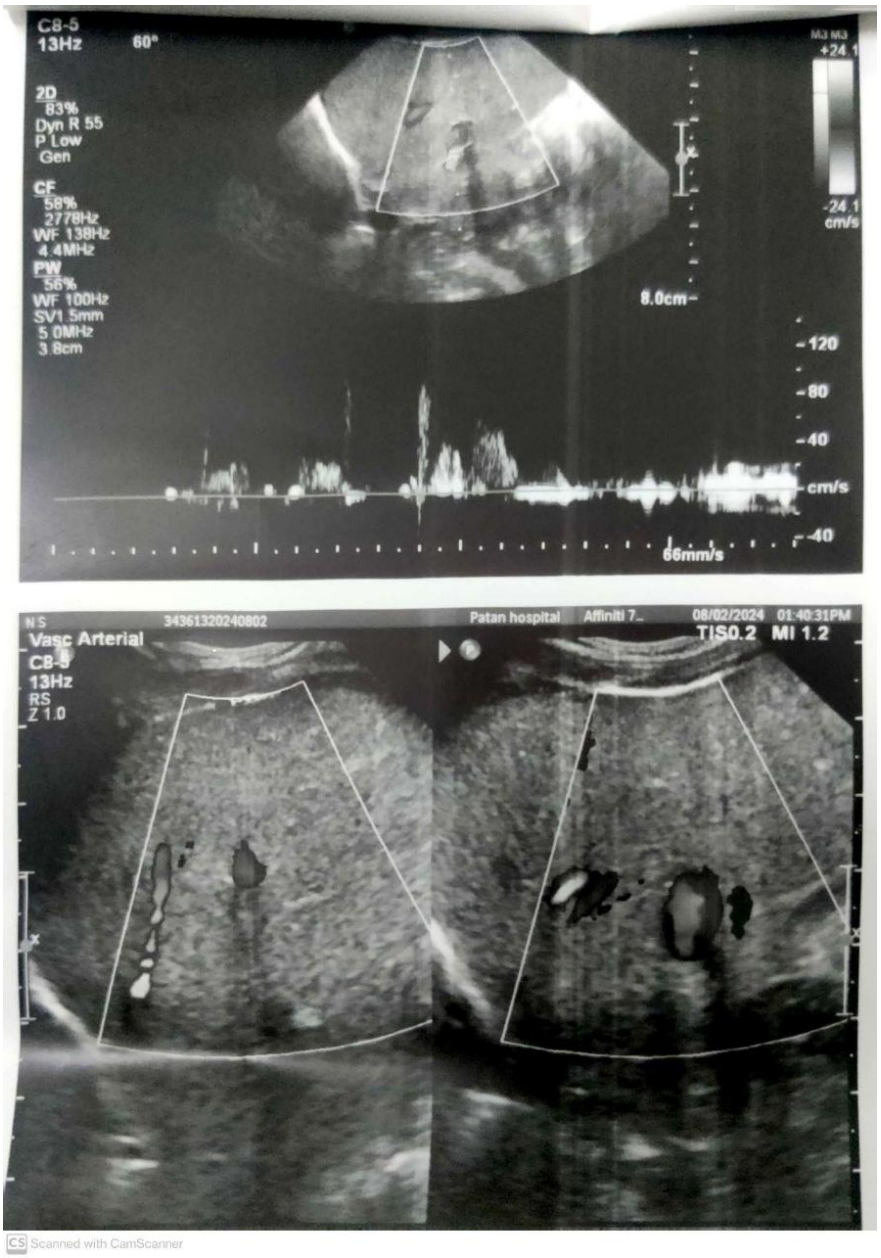

Fig-2: Ultrasound showing no evidence of thrombosis after 4 weeks of anticoagulant therapy.

2.3 Description of Case 2

History and examination:-

This was again a male baby born to 28 years multigravida at 40 WOG,via Em LSCS for moderate meconium stained liquor with BW 3540gm, and APGAR score of 4/10 and 6/10 at 1 min and 5 mins of life, child received resuscitation after birth and was intubated for birth asphyxia and was transferred to NICU for further management.

Methods:-

The child required inotropic support of dobutamine,dopamine and epinephrine for which umbilical vein and artery catheterization was done. The neonate developed features of persistent pulmonary hypertension requiring him milronin and sildenafil. On 5th days of life, the neonate developed pale and cold peripheries and on examination bilateral femoral pulses were not palpable. Immediate ultrasound with doppler of the abdomen was done which showed echogenic focus measuring 0.27cm*0.9 cm in descending thoracic aorta likely thrombosis with 54% occlusion of descending thoracic aorta. Umbilical lines were removed immediately and enoxaparin along with iv antibiotics started. This child received enoxaparin for 4 weeks, inotropes for 8 days and antibiotics for 3 weeks.

Outcome and Follow-up:-

Neonate was taken out from NICU after 4 weeks and was discharged from hospital. Child was doing well in the follow up visit.

3. DISCUSSION

Over the last few decades, the incidence of thromboembolic events in children, particularly among the critically ill neonatal population, has significantly increased(1). Estimates of neonatal thrombosis range from 1 in 100,000 live births1 to 36 per 1000 neonatal intensive care unit admissions(2,4–6). Various studies showed incidence of venous thrombosis more than arterial thrombosis(7–9). The neonatal population has a unique risk factor profile for the development of thrombosis secondary to the contribution of maternal and peri delivery risk factors, not present in other pediatric populations(1,2). The most common neonatal-related factors include the presence of a CVC and the development of infection/sepsis or other inflammatory conditions(10). The maternal risk factor includes, infection, underlying comorbidities such as metabolic syndrome, diabetes, pre-eclampsia or hypertension, inherited or acquired thrombophilias and placental thrombosis or abruption. Emergency c- section, PROM, PPROM, perinatal asphyxia, meconium aspiration, steroid use and bradycardia are peri delivery risk factors associated with neonatal thrombosis(2). Neonatal hemostatic system is different from the one of the older children and adults(11,12). Coagulation proteins do not cross the placenta but are synthesized in the fetus from an early stage and levels of antithrombin, heparin cofactor II and protein C and S are low at birth(1). Additionally, infection and sepsis increases the risk of thrombosis through several mechanisms such as direct endothelial dysfunction, activation of coagulation factor and consumption of anticoagulant proteins and downregulation of the protein c system,(13). Thromboembolic events in neonates are associated with significant morbidity and mortality, including the loss of vital vascular access, increase bleeding risk secondary to the use of anticoagulation therapy, and the development of long-term complications such as limb loss in arterial thrombosis, portal hypertension, renal dysfunction, and the post-thrombotic syndrome in venous thrombosis(1,2,4).

In our first case, prolonged rupture of membrane(more than the probable risk factors for the development of portal vein thrombosis. Similarly in the second case, emergency c-section, meconium stained liquor, birth asphyxia and umbilical vein and artery catheterization were the likely factors for thrombus development.

Clinical presentations of neonatal thrombosis are nonspecific and depends on various factors, including the anatomic location of the thrombosis, the presence of organ damage, the characteristics of the thrombus (occlusive vs nonocclusive), the chronicity of the thrombosis, and the underlying clinical status of the patient(2). Although diagnosis is an incidental finding during imaging, most of the neonates might have some symptoms at the time of diagnosis. In the first case, the neonate had persistent vomiting and in the second case, there were pale and cold peripheries and absent femoral pulses bilaterally.

Different imaging modalities such as doppler ultrasound, echocardiography, venography/angiography, CT or MRI can be used to make a diagnosis of thrombosis, and choice of imaging modalities depends upon the location of the thrombus. Incidental portal vein thrombosis was found during abdominal ultrasound in our first case reports. However, diagnostic doppler ultrasound was considered in the second case after the neonate had symptoms of arterial obstruction.

Several factors such as location of the thrombus, extension of thrombus, clinical status of the patients are

very important to consider while managing neonatal thrombosis. Proper guidelines for the management of thrombosis in neonates are lacking, therefore management of such conditions requires experts' opinions, individualization of each case and guidance from studies done in the adult population(14)]. The primary goal of management using anticoagulants is to prevent short term such as extension of thrombus, organ damage, thrombus embolization, limb loss and long term complications recurrence of thrombus, portal hypertension and gastrointestinal bleeding in case of PVT(15–17). Unfractionated heparin, low molecular weight heparin, vitamin k antagonist, direct thrombin inhibitor(intravenous or oral) and thrombolysis are the choices for the management, however low molecular weight heparin remains the drug of choice for the pediatric population(2). In both cases, we used enoxaparin(LMWH) at the recommended dose of 1.5 mg/kg/dose twice daily(18). Regular completed blood count was performed to rule out heparin induced thrombocytopenia, however due to resource limited setting and financial issues of families we were not able to check anti-Xa level for monitoring(2,19).

4. CONCLUSION

Neonatal thrombosis cases are increasing in recent years, and critically ill and premature neonates carry the highest risk. Since maternal and perinatal risk also contributes in development of thrombosis in neonates, meticulous antenatal and perinatal history is very important for early diagnosis and intervention. Additionally, most of the time symptoms of thrombosis are nonspecific, therefore acknowledging the risk factors is crucial. Immediate management with anticoagulants is necessary to prevent complications, especially in resource limited settings, where management of complication would be more difficult. Cautious umbilical vein or artery catheterization and immediate removal of it once not required, is also important to decrease risk of thrombosis.

AUTHORS CONTRIBUTION

Ramesh Khadayat and Prenana Kansakar are involved in conceptualization, resources, writing–original draft, and writing–review and editing. Shreya Thapa, Sailesh Shrestha, Tilak Gautam are involved in conceptualization, investigation, and writing–review and editing. Ramesh Basnet and Sagar Rana Magar are involved in investigation, resources, and writing–review and editing. The manuscript is reviewed and approved by all the authors.

CONFLICT OF INTEREST

None to declare.

CONSENT

Written informed consent was obtained from parents for the publication of these case reports. A copy of the written consent is available for review by the editor in chief of this journal on request.

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ABBREVIATIONS:-

CBC:- complete blood count

CRP: C-reactive Protein

CT :- computed tomography

CVC:- central venous catheter

LMWH:- low molecular- weight heparin

LSCS: - low segment cesarean section

MRI:- Magnetic resonance imaging

NICU:- neonatal intensive care unit

PROM: prolonged rupture of membrane

PPROM: Premature prolonged rupture of membrane

PVT:- Portal vein thrombosis

WOG: weeks of gestation

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