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CASE REPORT

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A neonate with thrombocytopenia absent radius presenting with DIC sydrome

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Abstract: Thrombocytopenia with bilateral absent radius (TAR) is a rare entity inherited in autosomal recessive pattern. Its incident in sub-Saharan Africa is not known. These infants can present with severe thrombocytopenia leading to intracranial/intraventricular hemorrhage, disseminated intravascular coagulopathy (DIC) and death. This is a case of a female baby small for gestational age who presented with absent radius bilateral and severe thrombocytopenia. This is the first case in the country to highlight the presence of TAR syndrome in neonates who present with DIC and limb malformations. Early diagnosis antenatally with timely treatment postnatal of neonates with TAR syndrome can reduce the complications brought about by TAR syndrome including death secondary to DIC.

Key words: Thrombocytopenia
Bilateral absent radii DIC
Neonate

Résumé: La thrombopénie avec l'absencence bilatéral du Radius (TAR) est une entité rare héritée selon un schéma autosomique récessif. Son incident en Afrique subsaharienne n'est pas connu. Ces nourrissons peuvent présenter une thrombocytopénie sévère entraînant une hémorragie intracrânienne/intraventriculaire, une coagulopathie intravasculaire disséminée (CIVD) et la mort. Il s'agit d'un bébé de sexe féminin, a faible poids de naissance et un retard de croissance intra-uterine pour son âge gestationnel. Elle s'est présenté avec une thrombocytopénie sévère, et l 'ábsence bilatérale de radius. Il s'agit du premier cas dans le pays mettant en évidence la présence du syndrome TAR chez des nouveau-nés présentant une CIVD et des malformations des membres. Un diagnostic précoce avant la naissance et un traitement postnatal rapide des nouveau-nés atteints du syndrome TAR peuvent réduire les complications provoquées par le syndrome TAR, y compris le décès secondaire à une CIVD.

Mots clés: Thrombocytopénie
Rayons absents bilatéraux
CIVD Nouveau-né

Introduction

Thrombocytopenia absent radius (TAR) is a rare inherited condition presenting with either unilaterally or bilaterally radial aplasia and low platelets count (thrombocytopenia) due to defective or hypoplastic megakaryocytes.[1] Thrombocytopenia can be severe causing intracranial hemorrhage and disseminated intravascular coagulopathy (DIC). These episodes are usually more frequent in the first year of life and tend to decrease as the child grows.[2] Skeletal malformation in TAR can range from an absent radius bilateral to ulna deformity however other abnormalities of the lower limb have also been reported. They have a hypoplastic thumb and can have clinodactility or syndactility. It is inherited in an autosomal recessive pattern. They may have hematologic, cardiac and renal abnormalities.[3] The incidence is 0.42/100,000, however in sub-Saharan Africa its incidence is not known.[4] Diagnosis is usually clinical however genetic studies can be done to locate chromosome abnormality[5] Complete blood count denotes the degree of thrombocytopenia. Management involves platelet transfusion and skeletal correction as the child grows. Mortality rate is high in those who develop DIC.[6]

Case

Female baby born of a 32 years P2L2 woman in a non-consanguineous marriage. Birth weight was 1.3kg at 36 weeks gestational age. She was delivered by emergency Caesarean section due to previous scar in labor and

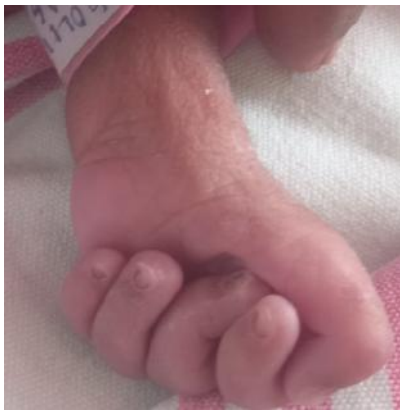
needed resuscitation with bag and mask due to absence of spontaneous breathing followed by low flow oxygen. Apgar scores were five and eight at 1st and 5th minutes respectively. Intramuscular Vitamin K was administered and she was referred to a tertiary hospital at 6hours of life.

Mother booked at 10thweek of GA, had a total of 5 clinic visits. Obstetric ultrasound done at 22 weeks and 34 weeks gestational age were both normal. Screening for human immunodeficiency virus (HIV) negative and syphilis were negative. She received tetanus toxoid immunization, was dewormed and given hematenics. There was no history of pregnancy induced hypertension, gestational diabetes or history of drug abuse reported. She was not on any treatment throughout pregnancy.

Upon arrival, baby was alert, a febrile with a temperature 36.8°C, had significant respiratory distress with grunting, sternal and xyphoid retractions, respiratory rate of 70 breath/min and oxygen saturation of 85% on low flow oxygen. Had dysmorphic features including contracture of the wrist joint with flexion of the both upper limbs (figure 1) and overlapping of fingers (figure 2), micrognathia, prominent forehead, microtia and low set ears (figure 3).Baby was kept on continuous positive airway pressure (CPAP) with moderate settings and saturated above 95%.

Fig 1: Contracture of the right wrist joint with flexion and slight overlapping fingers

Fig 2: Clinodactyly of the lefthand fingers



Complete blood count revealed white blood cell count (WBC) of 22k/ul, hemoglobin (Hb) of 13g/dl and platelets of 25k/ul. TORCHES screen was negative and blood culture had no growth. X-ray of the right upper limb showed absent radius and malformed ulna (figure 4).A bilateral grade 2 intraventricular hemorrhage (figure 6) was seen on cranial ultrasound and a small atrial septal defect (ASD) on ECHO screening. Abdominal ultrasound was normal.

Baby was transfused twice with 10mls/kg of platelets and given injection vitamin K. First line antibiotics (ampicillin and gentamycin) were initiated but stopped after negative blood culture results after 48 hours.

During the hospital stay, the respiratory continued to worsen and she developed pink frothy secretions through nose and mouth at 36 hours of life. Chest x-ray showed diffuse alveolar infiltrates (figure 5).She was also bleeding through the gastrointestinal tract. Seizures were observed at the 40th hour which did not respond to phenobarbitone and Phenytoin. She was kept on mechanical ventilator, received more platelets and fresh frozen plasma with no significant improvement. Her condition continued to deteriorate as hemostasis was not achieved and baby died on 3rd day.

Fig 3: Microtia and low set ear

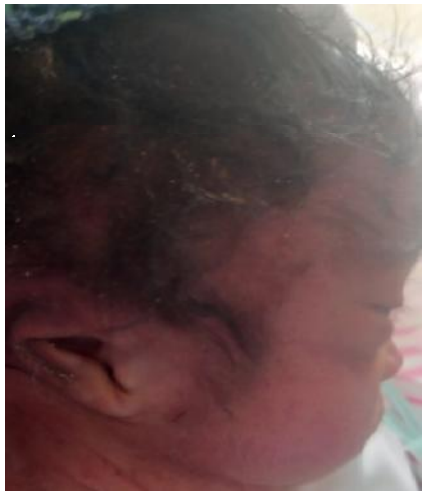


Fig 4: X-ray of the right upper limb showing absent radius and malformed ulna

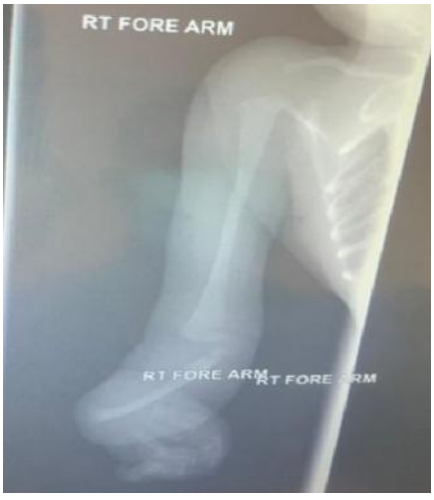


Fig 5: Chest Xray showing patchy alveolar infiltrates

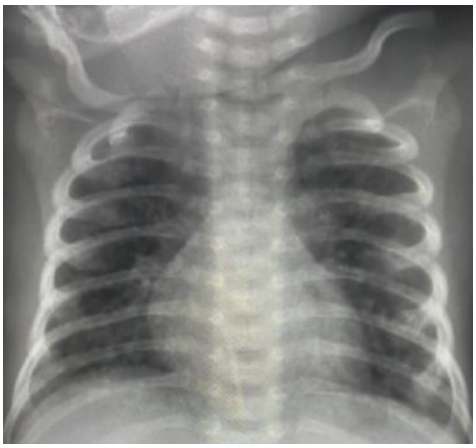
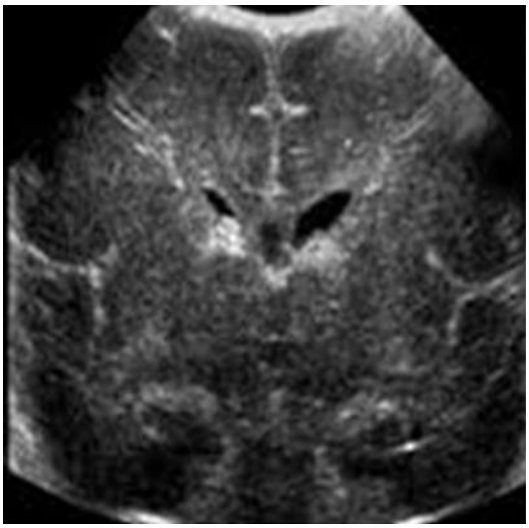


Fig 6: Cranial ultrasound showing Bilateral grade II intraventricular hemorrhage



Discussion

Thrombocytopenia in TAR is symptomatic in up to 90% of infants. It can be moderate to severe, and can present at birth in up to 50% or within the first few weeks of life in 95%. Its severity is thought to decrease with increasing age. [7] Skeletal malformation are variable with bilateral absent radius and deformed ulna and other skeletal malformation of the ribs and vertebrae have been reported. It can also present with extra skeletal anomalies of the genitourinary system and the heart. The case presented had symptoms from time of birth involving severe respiratory distress and later severe bleeding into the lungs, gastrointestinal system and brain due to severe thrombocytopenia. Such severe bleeding in the first 72hours can have a grave prognosis on the outcome of the infant including death if hemostasis is not achieved, as seen in the index case. She also had skeletal malformation that was seen upon physical examination involving the upper limbs presenting with contractures.

Antenatal diagnosis through ultrasound can be seen presenting with limb shortening or phocomelia.[8] This was not the same in this case as both ultrasounds were reported normal, likely due to limited expertise to do anomaly scans in the country. Postnatal diagnosis is usually through combination of physical examination and radiological examination including chromosomal analysis which can reveal micro deletion on chromosome 1q21 which results in a null or hypomorphic allele of the RBM8A gene.[5,9] Due to limited resources and expertise, genetic studies could not be done to have a confirmatory diagnosis and hence physical examination and investigation enabled to have a diagnosis of TAR. Some studies have reported female's predilection.[10] Like this presented case, other three published reports were also females.[4,11,12]

Management is multidisplinary involving pediatrician and orthopedic interventions.[13] These neonates can require multiple transfusion including platelets and packed red blood cells before they can reach their first birthday as this is the most crucial time of their life. The infant required vitamin K, platelet and fresh frozen plasma transfusion in order to achieve hemostasis however there was still ongoing bleeding. The platelets severity is thought to decrease as the child grows.[8] Orthopedic interventions can involve maximizing limb functions as the child grows if baby had survived.

Mortality of those with TAR syndrome, especially in our setting is unknown. Data from a review by Hedberg et al of 100 cases found 21 deaths out of 77 cases.[14] Prognosis in neonates with TAR syndrome can be grave especially in those who present with severe thrombocytopenia and involving intracranial/intraventricular hemorrhage or DIC in the first one month of life.[2] As with this infant hemostasis could not be achieved and this led to the death of the baby in the first 72hours of life due to ongoing bleeding. The first two years are the most devastating period of infants with TAR syndrome. They can present with altered platelets counts due to immature megakaryocytes, easy bruising and bleeding tendencies and can predispose to multiple platelet and PRBC transfusions and even death.[6] Studies show that these episodes tend to diminish as the infant grows beyond two years.[15] Some studies also show a risk to developing leukemia in early childhood. These infants do not seem to have intellectual disability.[2]

Conclusion

TAR syndrome is rare presenting with both skeletal and extra-skeletal malformations. To our knowledge, this is the first case reported in the country. Mortality is usually high in the first one year due to severe thrombocytopenia that can present with intracranial/intraventricular hemorrhage and DIC. Thrombocytopenia is transient and resolves with increasing age. These infants require multiple platelet transfusion and orthopedic intervention to improve limb functions if they survive. Though a rare entity this case highlights that antenatally diagnosis if

made the mother should be referred to tertiary center for delivery and thereafter timely management postnatal could decrease morbidity and mortality.

Authors' contributions
All authors contributed equally to the write up of this article.
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