Bone Marrow Trephine Biopsies from Posterior Superior Iliac Crest in Living Neonates.

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Abstract

Cytopenias are common among neonates in neonatal intensive care units (NICU). Although, bone marrow aspirations (BMA) are often performed as part of diagnostic work up but trephine marrow biopsies (BMB) have not been reported from living neonates. BMB is indispensable to accurately assess the cellularity and architecture. There is paucity of literature regarding the technique of BMB in neonates. In this report, for the first time, we describe trephine BMB from Posterior superior iliac crest (PSIC) using 18 guage BMA needle in six living neonates admitted to NICU where bone marrow biopsy findings helped in understanding the underlying mechanism and diagnosis of cytopenias.

Title Page

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Abbreviation Table

NICU	Neonatal Intensive Care Unit
BMA	Bone marrow aspiration
BMB	Bone marrow biopsy
PSIC	Posterior Superior Iliac Crest
CAMT	Congenital Amegakaryocytic Thrombocytopenia

ABSTRACT

Cytopenias are common among neonates in neonatal intensive care units (NICU). Although, bone marrow aspirations (BMAs) are often performed as part of diagnostic work up but trephine marrow biopsies (BMBs) have not been reported from living neonates. BMB is indispensable to accurately assess the cellularity and architecture. There is paucity of literature regarding the technique of BMB in neonates. In this report, for the first time, we describe trephine BMB from Posterior superior iliac crest (PSIC) using 18 guage BMA needle in six living neonates admitted to NICU where bone marrow biopsy findings helped in understanding the underlying mechanism and diagnosis of cytopenias.

INTRODUCTION

In neonates bone marrow aspirations (BMAs) are occasionally carried out to evaluate cytopenias particularly thrombocytopenia and neutropenia.[1,] However, BMA in neonate is often diluted with peripheral blood and BMA is less optimal for evaluation of cellularity and architecture of bone marrow which is best assessed by bone marrow biopsy (BMB). Indeed, BMB is complementary to BMA in diagnostic evaluation of various hematological disorders.[3]In adults and older children BMB is performed from posterior superior iliac crest (PSIC) as it is safe and yields adequate sample.[4]BMB is usually performed by using Jamshidi-type needle, smallest available size of which is 14 guage.[5]Moreover, it is advised to insert the needle 1 to 2 cm inside the bone to get adequate BMB specimen.[6]This makes carrying out BMB in neonates impractical. Although a technique of bone marrow clot section from tibia has been described in neonates, BMBs from PSIC in living-neonates have not been reported so far.[7]In this communication, we describe BMBs from PSIC in six neonates using 18 guage BMA needle.

METHODS

BMA and BMB were performed from PSIC to evaluate cytopenias in neonates after obtaining informed consent from parents. A Salah bone marrow aspiration needle (18 gauge, 35 mm in length) was introduced into the marrow space after using local anaesthetic (1% lidocaine) for skin and periosteum of PSIC. Once it was felt that the needle has firmly penetrated the bone, the stylet was withdrawn, and a 5 ml syringe was attached to the needle and 0.5 ml of bone marrow was aspirated and aspiration smears were made.

The needle was withdrawn from bone and reintroduced with stylet into adjacent bone surface 0.5 cm to 1 cm away from BMA site until it is firmly placed into the bone. The stylet was completely withdrawn and hollow needle was advanced into the marrow space for 3 to 5 mm. The needle was rotated 5 times clockwise and then anticlockwise direction. It was confirmed with the help of stylet that the needle contained a small piece of bone/cartilage at its tip. The needle was finally removed slowly from bone and skin. The biopsy specimen at the tip of the needle was dislodged with the help of stylet and put in fixative solution, processed, and stained like typical bone marrow biopsy.

RESULTS

From June 2016 through December 2019, we performed BMA and BMB in six neonates admitted to neonatal

intensive care unit (NICU). Gestational age of infants, day of life and weight at the time of procedure, indications and findings of BMBs are depicted in Table 1 and Figure 1. All the patients tolerated the procedure well and none of the patients had any complications of the procedure like bleeding, infection or excessive discomfort. The size of obtained BMB specimens varied between 2 mm to 4 mm.

For patients P1 and P2 with persistent thrombocytopenia, BMA was dilute and megakaryocytes were not seen; however, BMB clearly showed presence of normal megakaryocytes (Fig 1, Panel P1and P2) suggesting peripheral destruction as mechanism of thrombocytopenia. In both P1 and P2 neonates platelet counts normalised after appropriate management. P3 had thrombocytopenia at birth and history of death of elder sibling due to pancytopenia at 2 years of age. BMB showed absence of megakaryocytes suggesting hypofunctioning marrow (Fig 1, Panel P3). A diagnosis of congenital amegakaryocytic thrombocytopenia (CAMT) was confirmed by next generation sequencing which showed homozygous mutation in MPLgene. P4 had isolated severe anemia requiring transfusion. BMA and BMB showed pure red cell aplasia (Fig 1, Panel P4) and a diagnosis of Diamond Blackfan Anemia (DBA) was confirmed on genetic testing.

P5 and P6 had pancytopenia for which BMB was carried out, which showed trilineage hematopoiesis ruling out infiltrative process or bone marrow failure state (Fig 1, Panel P5 and P6). Blood cultures of P5 and P6 grew Klebsiella pneumoniae and Burkholderia cepacia respectively. Pancytopenia resolved after appropriate antibiotic treatment.

DISCUSSION

The incidence of thrombocytopenia among neonates admitted to NICU is as high as 18% to 35% reaching approximately to 70% among neonates born with weight < 1000g.[1] Despite high frequency of thrombocytopenia among sick neonates, not much is known regarding the underlying mechanisms. There is paucity of literature regarding megakaryopoiesis in neonates[2], and this can be attributed to difficulties in obtaining adequate bone marrow samples from neonates, the rarity of megakaryocytes in the bone marrow aspirates and the inability to accurately differentiate small megakaryocytes from cells of other lineages. Majority of the cases are managed without bone marrow examination; however, this test is useful in the management of some persistent cytopenias. Most often, BMA is performed in neonates and small infants from tibia.BMA smears are often dilute and do not reflect true cellularity of bone marrow and are inadequate to assess rare cells in the marrow like megakaryocytes or histiocytes. A technique of bone marrow clot section from tibia has been described to assess the cellularity and rare cells in the marrow.[7] However, this site may fail to yield adequate sample when the procedure is performed by an inexperienced person; there is also risk of fracture of tibia.[8] Moreover, many physicians are experienced and comfortable with PSIC as a site for bone marrow examination. Indeed, many centres prefer PSIC site for BMA even in small infants and neonates.[8,9]

There are reports of trephine needle biopsies to obtain post-mortem specimens of fetal cartilage and bone to study their bone marrow; however, trephine BMB from living neonate has not been reported.[10] The reasons for this include non-availability of smaller trephine biposy needle, risk of damaging vital organs and possibility of excessive pain and discomfort to the neonate. In this report we demonstrate that BMB can be successfully obtained from PSIC even in small neonates with the help of Salah BMA needle. Although the tip of the BMA needle is not tapering, unlike trephine biopsy needle, we observed that small piece of cartilage containing bone marrow tissue easily gets trapped in the needle tip with the technique described above. The quality of the biopsy specimens was good in assessment of cellularity, morphology of cells and architecture of the bone marrow as shown in Fig 1. The procedure was safe and did not cause any complication in our cohort. Moreover, it did not increase the pain and discomfort as compared to BMA procedure alone.

Information obtained by BMB as compared to that revealed by BMA alone was helpful in the management of our patients. For example, in patients P1 and P2, BMA did not show megakaryocytes raising the suspicion for bone marrow failure state; however, BMB clearly showed presence of adequate megakaryocytes helping the physician to pursue causes for platelet consumption. Similarly, absence of megakaryocytes on BMB in P3 expedited genetic work up for CAMT.

In conclusion, BMB can be safely carried out from PSIS in neonate with the help of Salah BMA needle by

experienced physicians. It undoubtedly adds value to BMA alone in the evaluation of cytopenias in neonates.

Authorship contribution;

SB carried out the procedures and wrote manuscript.

UL and SS reported the bone marrow findings and provided the photomicrographs for figure and helped in writing the manuscript.

Conflict of Interest: None

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Figure Legend

Figure1. Hematoxylin and eosin (H&E)-stained sections of trephine bone marrow biopsies from patients P1 to P6.

Panel P1 and P2. Bone marrow biopsy with adequate megakaryocytes (original magnification × 100)

Panel P3. Bone marrow with absent megakaryocytes (original magnification × 100)

Panel P4: Bone marrow with near total absence of erythroid precursors (original magnification × 100)

Panel P5 : Bone marrow with active trilineage hematopoiesis (original magnification × 400)

Panel P6: Bone marrow with active trilineage hematopoiesis (original magnification × 100)

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