ORIGINAL RESEARCH PAPER

Pediatrics

SPECTRUM OF INDICATIONS AND FINDINGS OF BONE MARROW EXAMINATION IN NEONATES AT A TERTIARY CARE CENTER FROM INDIA

KEY WORDS: Neonate, Bone marrow, sepsis, HLH

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ABSTRACT

OBJECTIVES: Bone marrow examination is one of the most valuable procedures in the evaluation of haematological disorders. There is a shortage of published literature regarding the indications, procedure, and outcome of BME in neonates. The aim of the present study is to analyse the common indications of performing BME, to assess the findings and spectrum of disorders diagnosed by it in neonates.

METHODS: A retrospective analysis of BMEs performed in neonates over a period of 24 months, between 2015 and 2017 was done.

RESULTS AND DISCUSSION: A total of 12 BME were performed on 12 neonates, which constitutes 10.3% of pediatric BME procedures during the same period. In our institute, BME is routinely performed by trained haemato-oncologist from posterior superior iliac spine in neonates with an overall sample adequacy of 97%. Evaluation of cytopenias was the most common indication for BME procedure, while normal marrow and myeloid hypoplasia due to sepsis were the most common diagnoses offered in neonatal BM.

CONCLUSIONS: Posterior superior iliac spine is a good site of BME in neonates in trained hands. BME not only helps to make specific diagnoses but should also be used as an extremely valuable and economically viable procedure to exclude major haematological disorders and malignancies in this age group.

INTRODUCTION:

Bone marrow examination (BME) is an important procedure for the diagnosis of haematological diseases in neonates and children. During BME, bone marrow particles are obtained for analysis including microscopic morphologic evaluations and differential counts. This invasive procedure should only be performed by a trained individual. There is a shortage of published literature regarding the indications, procedure, site and outcome of bone marrow examination (BME) in neonates.

COMMON CLINICAL INDICATIONS FOR BONE MARROW ASPIRATION

1. To investigate neonates with abnormal peripheral blood findings (eg, atypical cells [or blasts], pancytopenia, unexplained anemia, leukopenia or thrombocytopenia) [1,2,3];
2. To obtain microbiological cultures in neonates with fever of unknown origin.

TECHNIQUE

The preferred site for obtaining bone marrow in children is the posterior superior iliac crest because it contains the most cellular marrow, there are no vital organs in close proximity and it is a nonweight-bearing structure [3]. In neonates, the anteromedial face of the tibia can be used for marrow aspiration [3]; however, this site may fail to yield adequate samples when the procedure is performed by an inexperienced technician; there is also a risk of fracturing the bone thus making posterior superior iliac spine a safe option [4,5,6]. Bone marrow aspiration (BMA) must be performed only by experienced health care providers who have been well-trained in the technique.

BME are performed by trained Pediatric Hematooncologist in our institute by using 18G needle from posterior superior iliac spine under sedation effect of Midazolam. There were no dry taps or failed attempts.

METHODS

A retrospective analysis of BMEs performed in neonates over a period of 24 months, between March 2015 and February 2017 was done.

RESULTS

In our study, out of 12 BME (table 1), 6 of them are for persistent thrombocytopenia, 3 of them are for persistent pancytopenia, 2 of them are for persistent anemia and one for abnormal cell morphology on peripheral smear. The one done for abnormal cell morphology on peripheral smear in a diagnosed neonate of Downs syndrome turned out to be Transient abnormal myelopoisis. Among those BME done for persistent thrombocytopenia, 3 of them showed no abnormality which later had growth in blood cultures, 1 showed myeloid hyperplasia with clinical sepsis, 1 showed features suggestive of marrow hypoplasia in a case of Neonatal Lupus, 1 showed features suggestive of increased megakaryocytes in a case of mother with Idiopathic Thrombocytopenic Purpura. Among those done for pancytopenia, all of them showed features of HLH of which one was positive for dengue serology (IgM positive). Those done for anemia showed erythroid suppression.

DISCUSSION

Cytopenias are common among neonates who require intensive care. More than 20% of neonates admitted to intensive care units develop thrombocytopenia and 5±8% develop neutropenia at some time prior to hospital discharge [7]. Of recent, cytopenic neonates are managed without bone marrow studies. However, in certain cases of prolonged cytopenias or culture negative suspected sepsis cases BME study can be useful, and in such cases marrow aspirates have generally been used [7]. Congenital (erythroid) hypoplastic anemia occuring primarily in young infants due to subnormal erythropoiesis produces profound anemia with no alteration in the white blood cells or platelets; and no response for known hematinics [8].

The incidence of HLH is 1:50,000 births, with an equal gender distribution [9]. It can be divided into two categories: primary (familial) hemophagocytic lymphohistiocytosis (FHL) and secondary HLH. In contrast to secondary HLH, which may affect any age and may resolve spontaneously, FHL is seen primarily in children and is fatal if untreated [9]. Because neonatal HLH can be rapidly fatal without specific intervention, it is recommended to start a treatment when a high clinical suspicion exists and results of diagnostic studies are still pending. Stem cell transplant is the standard treatment for FHL, once remission is achieved on immuno-modulatory therapy [10,11]. Over a recent past years there is an increased reporting of cases of neonatal HLH with dengue [12].

The causes of thrombocytopenia in neonates are diverse and include immune, inherited and acquired disorders and evaluation is challenging [13]. It is a significant cause of morbidity and mortality in the sick pre and full term infant and accounts up to 20 to 40% of the newborns admitted to Neonatal Intensive Care Unit (NICU). Most of the ill and premature infants have low platelet count [14], thrombocytopenia may be considered as an important and early tool in diagnosis of septicemia in neonates [15]. Neonatal

autoimmune thrombocytopenia accounts for only 3% of all cases of thrombocytopenia at delivery and is present in about 10–15% of infants born to mothers with ITP [16]. Haematologic disease, consisting of thrombocytopenia, neutropenia, or anemia, occurs in about 10% of cases of neonatal lupus [17].

The diagnosis of congenital leukemia is more stringent than the adult counterpart due to the labiality of infants hemopoiectic system, which on exposure to stressors can mimic leukemia [18]. The differential diagnosis of congenital leukemia includes leukemoid reactions, congenital infections, severe erythroblastosis and neonatal neuroblastoma [18]. Neonates with Downs syndrome are at risk for Transient abnormal myelopoisis and congenital leukemia [19].

CONCLUSIONS:

Posterior superior iliac spine is a good site of BME in neonates in trained hands. Trephine biopsy is a difficult procedure in this age group, however remains indispensable in situations where an infiltrative pathology is suspected. BME not only helps to make specific diagnoses but should also be used as an extremely valuable, quick, and economically viable procedure to exclude major haematological disorders including certain forms of storage disorder and haematological malignancy in this age group. Evaluation of cytopenias was the most common indication for BME procedure, while normal marrow and myeloid hypoplasia due to sepsis were the most common diagnoses offered.

What is already known: BME is useful for diagnostic workup of refractory anemia and bleeding disorders in children. But there is not much literature available for indications, site and outcome of BME in neonates.

What this study adds: BME can be of immense use in diagnosing refractory pancytopenias, peripheral blood culture negative sepsis, congenital dyserythropoiesis and fatal conditions like HLH even in neonatal age group. Needs more further studies in neonatal age group.

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