Open Access Case Report

Childhood Myelodysplastic Syndrome: A Rare Entity

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Abstract

Myelodysplastic syndrome (MDS) encompasses a range of bone marrow disorders caused by a clonal stem cell defect. These disorders present with cytopenias, ineffective hematopoiesis, and dysplasia in all three cell lines. MDS is uncommon in children, accounting for less than 5% of all hematopoietic malignancies in children under 14 years of age. Refractory cytopenia of childhood (RCC) is the most common type of MDS observed in children. In this study, we report the case of a 14-year-old boy who presented with suspected aplastic anemia but was ultimately diagnosed with refractory cytopenia of childhood, a subtype of myelodysplastic syndrome.

Key words: Myelodysplastic syndrome, cytopenias, dysplasia.

Introduction

Myelodysplastic syndromes (MDS) represent a diverse group of clonal stem cell disorders characterized by cytopenias, macrocytosis, and morphological dysplastic features in the bone marrow. These conditions carry an overall 40% risk of transformation into acute leukemia.[1] MDS is typically associated with older age, with the median age of onset occurring in the seventh decade. It is relatively uncommon in children, accounting for less than 5% of all hematopoietic malignancies in patients under 14 years of age.[2,3]

It's important to distinguish between primary MDS, also known as de novo MDS, and secondary MDS, which is associated with bone marrow failure syndromes (either congenital or acquired) and cytotoxic therapy used for the treatment of prior malignant or non-malignant conditions.[3] In the past, MDS associated with Down syndrome constituted approximately one-fourth of pediatric MDS cases.[4]

The term "Refractory Cytopenia of Childhood" is used to describe cases of MDS characterized by persistent cytopenias, bone marrow containing less than 5% blast cells, and peripheral blood with less than 2% blast cells.[5]

Case Report

A 14-year-old boy presented on January 31, 2020, for a bone marrow biopsy procedure at Chughtai Institute of Pathology, Lahore, with suspicion of aplastic anemia. The patient had been experiencing vomiting for the last two weeks, gum bleeding for the past four months, low-grade fever for the past two years, dyspnea on exertion, anorexia, and undocumented weight loss. He had received a total of four transfusions over a period of six months, with the last transfusion given one month prior to the bone marrow biopsy procedure. On examination, the patient was stable but exhibited marked pallor. No visceromegaly or lymphadenopathy was observed, and there were no dysmorphic features, rudimentary or absent thumbs. Radiological findings were unremarkable.

CBC and Peripheral Smear: The complete blood picture showed pancytopenia (TLC: 3.57 x 10^9/L, Hb: 4.7 g/dl, Platelets: 28 x 10^9/L). The absolute neutrophil count was 1.2 x 10^9/L, the reticulocyte count was 1%, and the absolute reticulocyte count was 75%.

RBCs displayed a dimorphic population with normochromic, normocytic, and macrocytic characteristics. WBCs exhibited a Pseudo Pelger-Huet anomaly. Platelets were reduced on the smears, but no platelet clumps were observed, and platelets showed normal morphology.

Bone Marrow Aspiration: The bone marrow aspiration revealed a hypocellular bone marrow aspirate. Although the overall cellularity of the marrow was reduced, a significant number of hematopoietic cells were present on the smears. Erythroid precursors exhibited dysplastic features such as megaloblastoid changes, multinuclearity, and karyorrhexis. Myeloid precursors also displayed dysplastic changes, including giant stab forms and metamyelocytes, Pseudo Pelger Huet anomaly, and hypogranularity. Blast cells constituted approximately 2-3% of nucleated marrow cells. Megakaryocytes were present but showed

dysplasia (hypolobated megakaryocytes). Dysplasia was observed in all three cell lineages.

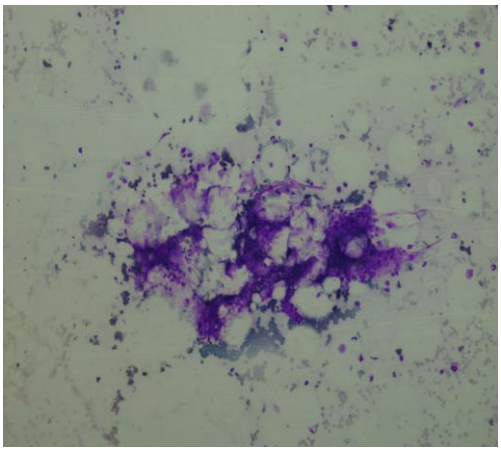


Figure 1. PMG showing hypocellular BMA fragment (20x)

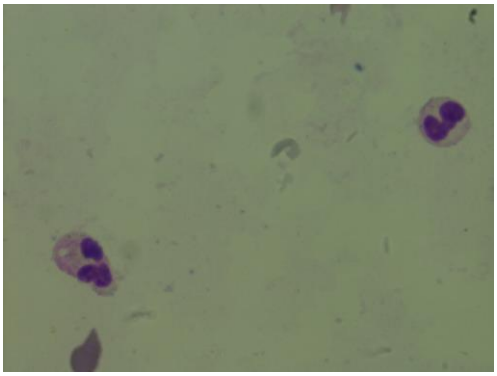


Figure 2. Pseudo Pelger Huet anomaly in neutrophils (100x)

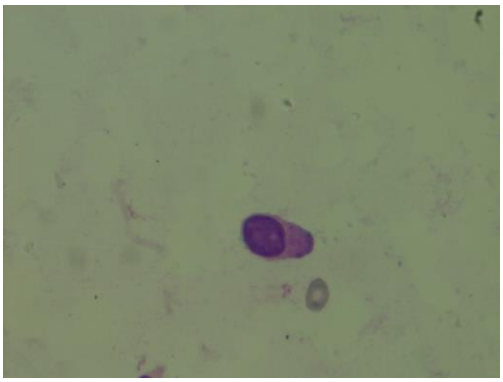


Figure 3. Blast cell in bone marrow aspirate(100x)

Trephine biopsy: 2 trephine biopsies were done from right and left posterior iliac crest which showed normal bony trabaculae and hypocellular bone marrow with patchy distribution i.e hypocellular areas alternating with a few cellular areas. Erythroid and myeloid precursors showed dysplastic changes. Megakaryocytes were prominent in the cellular areas and many micromegakaryocytes were also seen. No area of infiltration was seen at the site of biopsy.

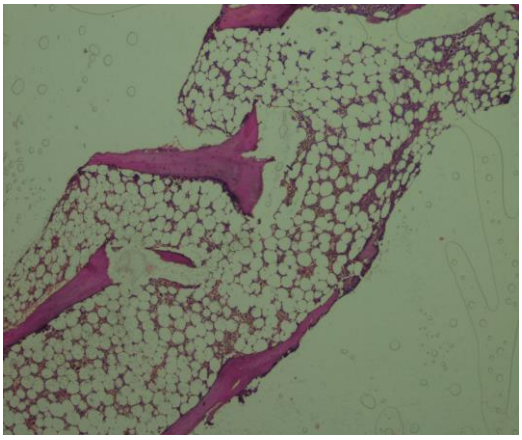


Figure 4. H&E section of trephine biopsy showing patchy cellularity

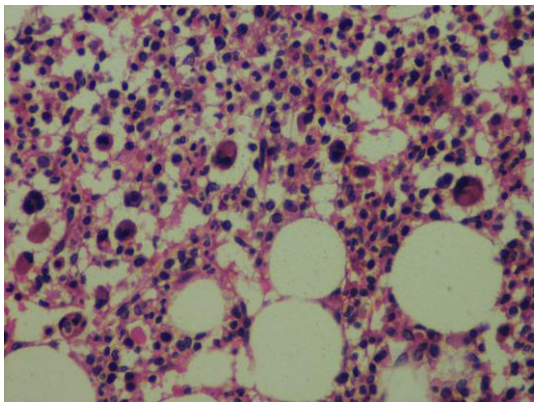


Figure 5. Trephine biopsy showing hypolobated, mononulcear micromegakaryocytes

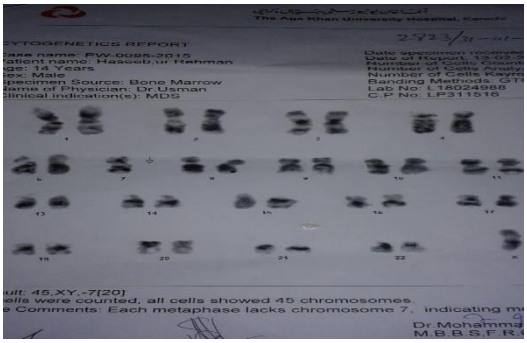
Immunohistochemistry:

CD34: Positive in 3-4% of the nucleated marrow cells

CD61: Positive in micromegakaryocytes

Impression: Bone marrow findings were suggestive of refractory cytopenia of childhood with multilineage dysplasia.

Karyotyping: Monosomy 7 (reported on bone marrow aspirate.)



Chromosomal breakage studies and workup for Paroxysmal Nocturnal Hemoglobinuria (PNH) was not recommended due to morphological and cytogenetic

evidence for RCC. The patient was counseled and referred regarding further treatment. Multiple unsuccessful attempts were made to contact the patient for follow up.

Discussion

"Childhood myelodysplastic syndrome is a rare condition, accounting for only a small percentage of cases. Renal cell carcinoma (RCC) is responsible for approximately 50% of childhood MDS cases, with a median age of presentation at 6.8 years.[6] The most appropriate treatment option is allogeneic stem cell transplantation, which yields a cure rate of approximately 60%.[7]

Distinguishing between refractory cytopenia of childhood, bone marrow failure syndromes, and severe aplastic anemia (SAA) can be challenging, as all of these disorders typically exhibit hypocellular bone marrow.[8] However, a few cases may also present with hypercellular bone marrow.[5] In our case, the bone marrow aspirate showed hypocellular features, while the trephine biopsy revealed patchy cellularity. With the aid of clinical features, morphology, and cytogenetics, we were able to make an accurate diagnosis.

Unlike inherited bone marrow failure syndromes, RCC does not typically exhibit skeletal abnormalities. Specific features that aided in the diagnosis of our case included the presence of patchy marrow cellularity and erythroid islands, along with dysplastic features such as nuclear budding, karyorrhexis, and internuclear bridging. Myelopoiesis displayed dysplastic characteristics like hyposegmentation with pseudo-Pelger-Huet nuclei, and blast cells constituted less than 5% of the bone marrow cells, a feature not typically seen in aplastic anemia or other bone marrow failure syndromes.[1,9] When 5% or more CD34-positive, myeloperoxidase-positive, lysozyme-positive, and CD117-positive blast cells are observed, it suggests disease progression to high-grade MDS. Micromegakaryocytes, which can be identified using CD41 and CD61 staining, are a strong indicator of RCC.[2,5] None of these aforementioned features are typically found in bone marrow failure syndromes, which facilitated our diagnosis of RCC.

Karyotyping is a valuable tool for assessing disease progression. The most common cytogenetic abnormalities in childhood MDS include monosomy 7, followed by trisomy 8 and trisomy 21.[4] The presence of monosomy 7 indicates a higher likelihood of disease progression, whereas patients with trisomy 8 or a normal karyotype may have a more stable disease course.[7,10] The identification of cytogenetic abnormalities plays a crucial role in distinguishing between refractory cytopenia, aplastic anemia, and congenital or acquired bone marrow failure syndromes.[9]

Conclusion

Aplastic Anaemia and Myelodyslastic Syndrome got overlapping presentations, but an accurate diagnosis has important clinical implications, as the prognosis and treatment can be quite different for both of these. Patients with MDS have a risk of neoplastic progression, a short survival time and a lower response to immunosuppressive therapy, compared to Aplastic Anaemia.

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