Rare Myelodysplastic Neoplasm of Children: Childhood Myelodysplastic Syndrome with Low Blasts. A Case Report

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Abstract
Myelodysplastic syndromes are rare in children, with refractory cytopenia of childhood (RCC) being the most common subtype. We present the case of a 22-month-old boy diagnosed with RCC, initially suspected of having recurrent infections. The child exhibited anemia, thrombocytopenia, leukocytosis, and splenomegaly, with a bone marrow aspiration revealing poor cellularity, dysplasia, and hematogones, but no blasts. Further analysis excluded hereditary and clonal leukemic abnormalities. Despite ongoing mild cytopenia, the child's condition remained stable without transfusions, and hematopoietic stem cell transplantation was not recommended. This case highlights the diagnostic challenges of RCC and the importance of early detection for improved outcomes.

Introduction

Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell disorders resulting in a heterogeneous presentation of cytopenias due to ineffective hematopoiesis, dysplasia, and risk of transformation to acute myeloid leukemia (AML).

This entity is well documented in the adult population but affects only 1 to 2 children per million . Presentation in childhood differs significantly, and adapting classification is essential for adequate disease management.

Refractory cytopenia of childhood (RCC) is the most common subtype of MDS in children; however, diagnosis remains difficult, often due to the poor cellularity of the bone marrow (1-3).

We report the case of a child initially suspected of having idiopathic cytopenia, ultimately diagnosed witch childhood MDS with low blasts (cMDS-LB) according to the WHO 2022 classification.

Case description

A 22-month-old boy was hospitalized for a second episode of fever and bilateral upper limb lymphangitis secondary to an insect bite. He was treated with intravenous antibiotics. He had history of uncomplicated episodes of cellulitis, which had resolved after seven days of intravenous flucloxacillin. This child demonstrated normal growth and development without any relevant past medical history.

On examination, he appeared pale but was not dyspneic. Notably, he had very light blond, almost white hair. Physical examination showed clear visible bilateral lymphangitic streaks on both arms. Hepatomegaly (2 cm below costal margin) and splenomegaly (3 cm below costal margin) were observed, along with multiple subcentimetric cervical, axillary, and inguinal lymph nodes and a hyperpigmented spot on the abdomen.

Laboratory tests revealed anemia (hemoglobin 8.6 g/dL; normal 10.5–13.5 g/dL), thrombocytopenia (platelets 79 x 109/L; normal 150-440 x 109/L), and leukopenia (WBC 1.82 × 10^9/L; normal 6–17.5 x 109/L), without reticulocyte regeneration (49 × 10^9/L; normal 22.5–147 × 10^9/L) (4).

The low white cell count likely explained his recurrent cutaneous infections.

Peripheral smear examination showed no abnormal cells or blasts. Iron, vitamin B12, and folate levels were within normal limits. Serologies for Epstein–Barr virus (EBV), cytomegalovirus (CMV), and parvovirus B19 were negative.

Given the unexplained bicytopenia, a bone marrow aspiration was performed. The initial aspiration showed poor cellularity and an apparent 10% blast count, later identified as benign lymphoid precursors (hematogones). Erythroid dysplasia was observed (Figures 1 and 2). A second bone marrow aspiration performed two weeks later revealed similar findings: abundant hematogones, dysplastic erythropoiesis, and dysmyelopoiesis. Myeloblasts accounted for 2% of nucleated cells (normal < 3%).

FIGURE 1: Bone marrow biopsy of the patient.
A, Dyserythropoiesis (smears stained with Giemsa).
B, Dysmegakaryopoiesis (round non-lobulated megakaryocyte, smears stained with Giemsa). C, Myelofibrosis stage two (smears stained reticulin).

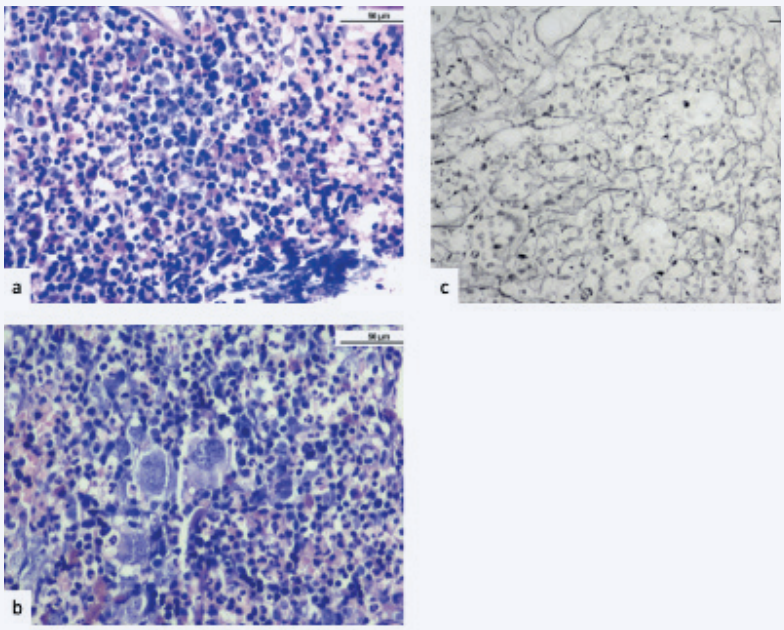
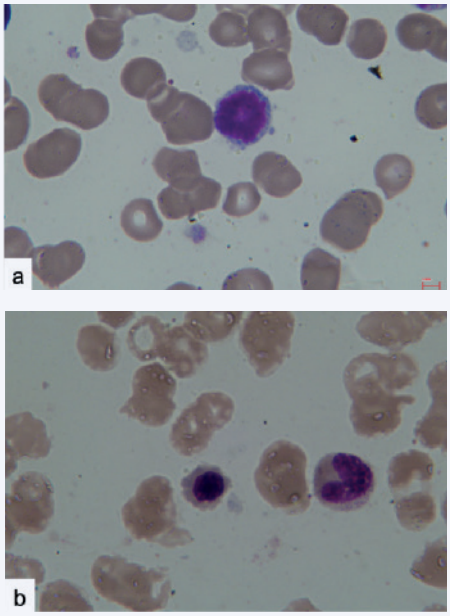


FIGURE 2: Blood smear of the patient.
A, Dysplastic eryhtroblast showing a nucleus in karyorrhexis.
B, Dysplastic polynuclear neutrophil (Pelger-Huet) and a hematogon that can be confused with a blast.



Conventional karyotyping and targeted molecular analysis (*ASXL1, CALR, CEBPA, CSF3R, DNMT3A, ETNK1, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, PTPN11, NRAS, RHOA, RUNX1, SETBP1, SRSF2, TET2, TP53, U2AF1,* and *WT1)* showed no clonal abnormalities associated with MDS or leukemia. Genetic testing ruled out inherited bone marrow failure syndromes, including Fanconi anemia. Immunophenotyping by flow cytometry revealed a normal distribution of lymphocyte subsets with no aberrant markers.

Due to the diagnostic uncertainty, a bone marrow biopsy was performed, which showed erythroid hyperplasia with dysplasia, dysmegakaryopoiesis and grade 2 myelofibrosis without significant blast excess (Figure 1).

These findings led to the diagnosis of childhood MDS with low blasts (cMDS-LB) in according with the 2022 WHO classification, which replaces the former term « refractory cytopenia of childhood » (RCC) (5).

The patient was enrolled in the EWOG-MDS registry, which provides diagnosis guidelines, research protocols, and treatment recommendations for pediatric MDS across Europe. Monthly clinical and laboratory follow-up was initiated, and bone marrow assessments were scheduled every three months. Since diagnosis, the patient has remained clinically stable and transfusion-free. Based on the EWOG-MDS recommendations, hematopoietic stem cell transplantation (HSCT) was not indicated in the absence of transfusion dependence, blast increase, or clonal progression.

As the latest follow up, 31 months after diagnosis, the patient remains clinically stable. Mild anemia (hemoglobin 9,1g/dL) and thrombocytopenia (121 × 10^9/L) persist, along with subtle splenomegaly. No further bacterial infections have occurred.

Discussion

Myelodysplastic syndromes (MDS) represent a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral cytopenias, and a variable risk of transformation to acute myeloid leukemia (AML). Although MDS are well recognized in adults, they are exceedingly rare in children, with an incidence of only 1–2 cases per million annually.

The initial MDS classification proposed in 1982, was based solely on morphological criteria and included five categories: refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), refractory anemia with excess blasts (RAEB), RAEB in transformation (RAEB-t), and chronic myelomonocytic leukemia (CMML) (6).

In 2008, refractory cytopenia of childhood (RCC) was recognized as a distinct pediatric entity. However, it remained underestimated for years due to the challenge of distinguishing it from aplastic anemia in hypo cellular marrow (7). RCC is defined by persistent cytopenias, bone marrow blasts <5%, and peripheral blood blasts <2% (8).

In the 2022 WHO classification, RCC was replaced by childhood MDS with low blasts (cMDS-LB), reflecting a broader, genetically informed understanding of the disease(6).

This entity is a diagnosis of exclusion: non-malignant causes of cytopenia such as viral infections, nutritional deficiencies, metabolic disorders, drug toxicity, and inherited bone marrow failure syndromes must all be ruled out.

Clinically, cMDS-LB most often presents with neutropenia, frequently leading to recurrent or atypical infections. Thrombocytopenia may result in easy bruising or mucocutaneous bleeding, while anemia may cause fatigue or pallor. Elevated fetal hemoglobin levels are also commonly observed.

Cytogenetic analysis is crucial for risk stratification. More than half of cMDS-LB cases present with a normal karyotype; however, abnormalities such as monosomy 7, 7q-deletion, or complex karyotypes are associated with a higher risk of progression to AML and typically warrant HSCT. Conversely, patients with a normal karyotype or trisomy 8 tend to have a more indolent clinical course (8, 9).

Patients should ideally be enrolled in collaborative registries such as EWOG-MDS, which ensure standardized diagnostic criteria, centralized review, and evidence-based therapeutic guidance. The therapeutic approach to pediatric MDS is risk-adapted: observation and supportive care are appropriate for stable patients with cMDS-LB, while HSCT is indicated for disease progression, transfusion dependence, or high-risk cytogenetics (9).

In our case, the diagnosis was particularly challenging due to the presence of hematogones, initially mistaken for blasts. The child's very light hair raised suspicion for Chediak–Higashi syndrome; however, genetic testing (*AP3B1, BLOC1S6, CLCN7, DTNBP1, EDN3, EDNRB, EPG5, HPS1, HPS3, HPS4, HPS5, HPS6, LYST, MC1R, MITF, MLPH, MYO5A, OCA2, PAX3, RAB27A, SLC24A5, SNAI2, SOX10, TYR,* and *TYRP1*) excluded this diagnosis, and no characteristic features such as giant granules in granulocytes were present.

The presence of grade 2 myelofibrosis is unusual in pediatric cMDS-LB. Although marrow fibrosis may occur in adult MDS, its prognostic significance in children remains unclear. The absence of clonal cytogenetic abnormalities, combined with ongoing clinical stability and transfusion independence, supports a favorable prognosis in this patient (10). Long-term monitoring remains essential, although the frequency of marrow evaluations may gradually be reduced to annual assessments if stability is maintained.

Conclusion

Childhood MDS with low blasts (cMDS-LB) accounts for only a small proportion of pediatric hematologic malignancies, with a worldwide incidence of 1–2 per million children annually. Despite advances in diagnostic classification, distinguishing cMDS-LB from other marrow disorders or misleading findings such as hematogones remains challenging. This case underscores the importance of comprehensive diagnostic workup, serial bone marrow analyses, and exclusion of non-neoplastic causes to ensure accurate classification. Early recognition and management guided by international protocols and registries such as EWOG-MDS are crucial to optimize prognosis and prevent both overtreatment and delayed intervention.

The authors have no conflicts of interest to declare.

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