Rare Congenital Dyserythropoietic Anemia of Childhood: A Case report

Hamzeh Al Hussien[1], Basil Al-Ekeer [1], Hashem Abu Serhan[2], Issam Haddadin[1], and Abdulqadir Nashwan[2]

[1]Islamic Hospital
[2]Hamad Medical Corporation

October 14, 2022

Abstract

Congenital dyserythropoietic anemias (CDA) is a heterogeneous class of anemia of varying degrees of ineffective erythropoiesis and secondary hemochromatosis. We reported a case of CDA and showed our approach to reaching a diagnosis, highlighting the importance of the typical morphological appearance of bone marrow erythroblasts to reach the diagnosis.

Rare Congenital Dyserythropoietic Anemia of Childhood: A Case report

Hamzeh F. Al Hussien[1], Basil N. Al-Ekeer[1], Hashem Abu Serhan[2], Issam Haddadin[1], Abdulqadir J. Nashwan[3*]

1. Department of Pediatrics, Islamic Hospital, Amman, Jordan
2. Department of Ophthalmology, Hamad Medical Corporation, Doha, Qatar
3. Department of Nursing, Hamad Medical Corporation, Doha, Qatar

*Corresponding author:

Abdulqadir J. Nashwan

anashwan@hamad.qa

Tel: (+974) 40240487

Mob: (+974) 66473549

P.O. Box 3050

Hamad Medical Corporation, Doha, Qatar

ORCID: https://orcid.org/0000-0003-4845-4119

Informed Consent

Written informed consent was obtained from the patient's legal guardian to publish this report in accordance with the journal's patient consent policy.

Abstract

Congenital dyserythropoietic anemias (CDA) is a heterogeneous class of anemia of varying degrees of ineffective erythropoiesis and secondary hemochromatosis. We reported a case of CDA and showed our approach

to reaching a diagnosis, highlighting the importance of the typical morphological appearance of bone marrow erythroblasts to reach the diagnosis.

Key Clinical Message

To avoid delay in diagnosing CDA and provide early care and better management, we urge clinicians to have a high degree of suspicion for congenital anemias when there is evidence of ineffective erythropoiesis in a child.

Keywords: anemia; pediatrics; bone marrow; erythropoiesis; case report

Introduction

Congenital dyserythropoietic anemia (CDA) is an uncommon hematological condition reported primarily in Central and Western Europe and North Africa [1-3]. The hallmark of the disease is ineffective erythropoiesis as the main feature, and there are distinct morphological abnormalities of the bone marrow's erythroblasts. Therefore, it should be considered in any patient with chronic anemia. It is divided into three categories (CDA I, CDA II, and CDA III), with the most common type II and CDA III, whose nonfamilial type is the rarest. A majority of CDA cases are autosomal recessive in nature [4]. In our case, we showed the way we used to reach our diagnosis and that the typical morphological appearance of bone marrow erythroblasts is considered the cornerstone of the diagnosis. Still, a blood smear might give us a hint.

Case Presentation

A 6-year-old female patient presented with chronic anemia for evaluation. She was doing well until the age of 3 years when the mother started to notice gradual and progressive pallor. It was associated with lethargy and intolerance to exercise with attacks of palpitation. Since then, the patient has been treated as a case of hemolytic anemia with regular blood transfusion every 3 months.

The patient is the product of vaginal delivery, term, and no NICU admission. The patient had two previous admissions for chest infections before the age of 3 years. The patient had DDH.

The parents are consanguineous (first-degree). The patient has one younger healthy sister. No family history of chronic illnesses or splenectomy.

On examination, the patient had frontal bossing and mild maxillary hypertrophy with depression of the nasal bridge. The spleen was felt 6 cm below the costal margin.

Peripheral blood film showed normochromic macrocytic RBCs, marked polychromasia and binucleated erythroid, mild poikilocytosis (ovalocyte, teardrop, microspherocyte), few atypical lymphocytes with normal platelets (**Fig. 1)** .

Bone marrow smears showed distinct hypercellularity due to erythroid hyperplasia **(Fig.3)** . The myeloid/erythroid ratio was 6:1, and the erythroid precursors were quantitatively markedly increased; also, erythroid maturation was megaloblastic and dyserythropoietic with many binucleated forms **(Fig.2)** . Blasts was not increased, and there was no evidence of fibrosis.

These findings of bone marrow aspirate and laboratory results fit the diagnosis of congenital dyserythropoietic anemia type II.

Discussion

An uncommon hematological condition known as congenital dyserythropoietic anemia (CDA) has primarily been documented in Central and Western Europe and North Africa [1, 3]. The hallmark of the disease is ineffective erythropoiesis as the main feature, and there are distinct morphological abnormalities of the bone marrow's erythroblasts. It should be considered in any patient with chronic anemia. It is classified into three types (CDA I, CDA II, and CDA III), with the most common being type II and CDA III and its nonfamilial type being the rarest. A majority of CDA cases are autosomal recessive in nature. [4].

To reach the precise diagnosis of congenital anemias is often delayed. Congenital anemia, jaundice, or hereditary evidence are necessary for diagnosing CDAs. Also, evidence of ineffective erythropoiesis should be present. In addition, the erythroblasts' characteristic morphology is thought to be the key to making the diagnosis, and it is important to rule out congenital anemias, including thalassemia syndromes, hemoglobinopathies, and hereditary sideroblastic anemias. Ineffective erythropoiesis should be suspected if there is inadequate reticulocytosis to the degree of anemia despite erythroid hyperplasia; indirect hyperbilirubinemia and low haptoglobin indicates ongoing intramedullary and extramedullary hemolysis [4].

Moreover, if appropriate preparation techniques are applicable in bone marrow aspirate, hypercellularity and distinct erythropoietic hyperplasia is always seen in histobiopsies. By morphological study using light microscopy, CDA I can be diagnosed with great specificity. The most specific finding is the abnormality of chromatin structure with fine chromatin bridges. However, the most specific finding in CDA II is the existence of binucleated cells with two equal-sized nuclei in each cell. Pseudo-Gaucher cells that contain birefringent needles can be seen in types I and II [2]. Furthermore, iron loading and cholelithiasis are found in all forms of CDA [4]. Peripheral blood smear in most cases of CDA shows anisopoikilocytosis, mature erythroblasts, basophilic stippling, and poikilocytes [2].

Differential CDA diagnoses include thalassemia syndromes, some hemoglobinopathies, hereditary sideroblastic anemia, congenital myelodysplasia, and congenital anemia such as Blackfan-Diamond anemia and Fanconi anemia. Also, other forms of CDA should be taken into account [1]. Our patient has chronic anemia with chronic blood transfusion. Also, she has splenomegaly with features of extramedullary hematopoiesis. Moreover, a blood smear showed normochromic macrocytic RBCs with mild poikilocytosis and anisopoikilocytosis. The binucleated erythroid was found even in the peripheral blood, there was reticulocytosis with a negative direct coombs test. These laboratory results are commonly not observed in hemoglobinopathies or thalassemia syndromes. Hereditary sideroblastic anemia was ruled out because neither ringed sideroblasts nor dysplastic characteristics on the granulocytic/megakaryocytic lineage were discovered. Bone marrow aspirate showed hypercellularity, with the erythroid precursors quantitatively markedly increased; also, erythroid maturation was megaloblastic and dyserythropoietic with many binucleated forms. Blasts were not increased, and there was no evidence of fibrosis. These findings of bone marrow aspirate and laboratory results fit the diagnosis of congenital dyserythropoietic anemia type II.

In conclusion, any kid with chronic anemia, hepatosplenomegaly, evidence of extramedullary hematopoiesis, and characteristics of erythroid hyperplasia and dyserythropoiesis in bone marrow aspirate studies should be evaluated for congenital dyserythropoietic anemia. The diagnosis can be made with high accuracy using bone marrow aspirate analysis and peripheral blood smear analysis.

Declarations

Ethics approval and consent to participate

The article describes a case report. Therefore, no additional permission from our Ethics Committee was required.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was not funded.

Authors' contributions

Hamzeh F. Al Hussien, Basil N. Al-Ekeer, Hashem Abu Serhan, Issam Haddadin, Abdulqadir J. Nashwan: Data Collection, Literature Search, Manuscript Preparation

All authors read and approved the final manuscript

Acknowledgments

Open Access funding provided by the Qatar National Library.

References

1. Kato K et al (2001) Congenital dyserythropoietic anemia type 1 with fetal onset of severe anemia. J Pediatr Hematol Oncol

23(1):63–66

2. Heimpel H, Kellermann K, Neuschwander N, Hogel J, Schwarz K (2010) The morphological diagnosis of congenital dyserythropoietic anemia: results of a quantitative analysis of peripheral blood and bone marrow cells. Haematologica 95(6):1034–1036

3. Heimpel H et al (2006) Congenital dyserythropoietic anemia type I (CDA I): molecular genetics, clinical appearance, and prognosis based on long-term observation. Blood 107:334–340

4. Heimpel H (2004) Congenital dyserythropoietic anemias: epidemiology, clinical significance, and progress in understanding their pathogenesis. Ann Hematol 83:613–621

Figure Legends

Fig. 1 Peripheral blood smear, poikilocytosis, polychromasia, binucleated erythroid (leishman stain 400X).

Fig. 2 Bone marrow aspirate from our patient, erythroid hypercellularity and binucleated forms (leishman stain 400X).

Fig. 3 Bone marrow biopsy, from our patient showing erythroid hypercellularity (H&E stain 400X).