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Congenital dyserythropoietic anemia type I: Rare case report

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Abstract
Introduction: Congenital dyserythropoietic anemia type 1 is characterized by autosomal recessive inheritance and a macrocytic anemia with dyserythropoietic features such as megaloblastoid changes, multinuclearity, and internuclear chromatin bridges.
Case report: Here, we reporting a case of Congenital dyserythropoietic anemia type 1(CDA 1) in 4 years old girl who presented with fever and abdominal pain.
Conclusion: Our case highlights the fact that diagnosis of CDA 1 can be made with high reliability by careful examination of bone marrow aspirate and Biochemical study.

Keywords: Dyserythropoietic, anemia, characterized, megaloblastoid

Introduction

Congenital dyserythropoietic anemia (CDA) is a rare hematologic disorder characterized by dyserythropoietic features, ineffective erythropoiesis, and secondary hemochromatosis. It is classified into types 1, 2, and 3, along with some variants [1, 2]. Congenital dyserythropoietic anemia type I (CDA I) is characterized by autosomal recessive inheritance and a macrocytic anemia with dyserythropoietic features such as megaloblastoid changes, multinuclearity, and internuclear chromatin bridges [1–4]. CDA-I is uncommonly reported from Indian subcontinent hence we are discussing a case of CDA I. Due to the rarity of this disorder the diagnosis can be missed. Our case also highlights the fact that diagnosis of CDAI can be made with high reliability by careful examination of bone marrow aspirate and Biochemical study.

Case Report

A four year old girl presented to the paediatric clinic with fever and pain in abdomen. She had history of blood transfusion 2 days back. She was not a known sickle cell anaemia or thalassaemia patient. History of prenatal period, birth and delivery were normal (birth weight 2.5kg). There was no history of neonatal jaundice or family history of similar illness.

At presentation, she was acutely ill-looking, conscious but weak. She was severely pale, icteric, tachypneic and in respiratory distress. The liver was 6 cm below the right costal margin and tender, with splenomegaly, 5cm below the costal margin. There was no lymphadenopathy. Her chest was clear, heart rate 140 beats/minute, and blood pressure of 100/50mmHg. A preliminary clinical diagnosis of recurrent severe haemolytic anaemia was made.

Full blood count showed anaemia with haemoglobin (Hb) concentration of 5.6g/dL, normal red cell indices, white cell count- 18.9 X 10^9/L, platelets- 370 X 10^9/L and reticulocyte count- 5%. Direct and indirect antiglobulin test were negative. Liver functions tests showed high total bilirubin (104mmol/L) and unconjugated bilirubin- 17.4umol/L. LDH 704.2IU/L. Serum urea 30mg% and serum creatinine 0.8mg%. HIV, hepatitis B and C were negative.

Peripheral blood film revealed anisopoikilocytosis, some macrocytes, tear drop cells, polychromasia, basophilic stippling, fragmented red cells and presence of nucleated red cells (5-6/100 white cells)- a few of which were multinucleated (Fig 1). HPLC showed HbF (17.1%) and HbA_2 (2.9%). Bone marrow (BM) aspiration showed a hypercellular marrow, erythroid hyperplasia (myeloid/erythroid ratio 1:2), dyserythropoiesis with megaloblastic change, spongy appearance and significant karyorrhexis. (Fig 2) Myelopoiesis and megakaryopoiesis were essentially normal (Fig 2). Serum ferritin was elevated (427ng/ml). Her serum Iron (223ug/dl) and TIBC (68.4%) also elevated. In the absence of availability of electron microscopy or molecular studies, a diagnosis of CDA type I was made based on clinical, laboratory and characteristic bone marrow findings. Depending upon biochemical study and bone marrow examination diagnosis of CDA1 was confirmed. She was transfused, placed on iron chelation therapy, her parents counseled on treatment options and she is being followed up.

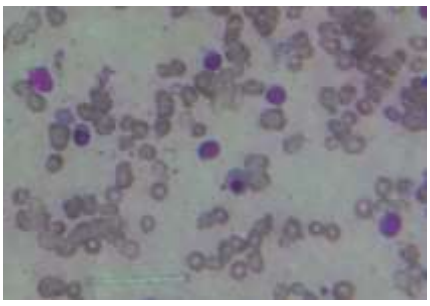

Fig 1: Peripheral smear shows anisopoikilocytosis, some macrocytes, polychromasia, fragmented red cells and presence of nucleated red cells.

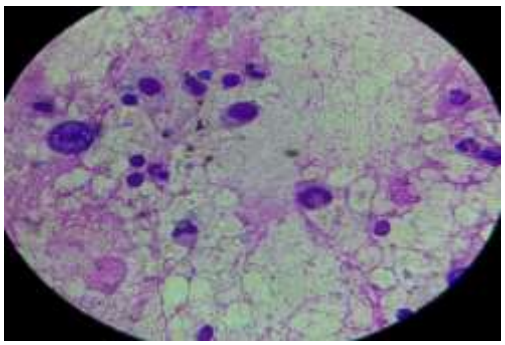

Fig 2: Hypercellular marrow shows dyserythropoiesis, megaloblastic change with spongy appearance and highly significant binucleated cell.

Discussion

The CDAs are classically grouped into 3 types based on bone marrow morphology. Type I has erythroblasts joined by an internuclear bridge. Type II erythroblasts have multinuclearity of late erythroblasts while type III has gigantoblasts (erythroblasts with ≥8 nuclei). Inheritance is autosomal recessive and diagnosis is usually in childhood or early adult life. Common clinical findings are anaemia, jaundice and splenomegaly; however these are seen in other more common inherited haemolytic anaemias. Patients with CDA usually have high serum ferritin that may require iron chelation therapy.

CDA I is seen in all age groups, although, in the majority of cases, symptoms begin in early infancy [5, 6]. Prenatal presentation of the disease has also been described, with severe fetal anemia requiring in utero exchange transfusion [7]. The genetic abnormality is located on 15q [8]. CDA although rare must be considered in a child who has recurrent anaemia in whom other causes have been excluded. BM examination remains a key diagnostic tool in identification of the CDAs. The anemia is macrocytic, with anisocytosis, poikilocytosis, and basophilic stippling. Iron stores in the bone marrow are increased. Dyserythropoiesis, usually suspected when there is reticulocytopenia relative to the anemia and marrow overactivity, is characterized by megaloblastic erythroid hyperplasia, and erythroblastic binuclearity, multinuclearity, karyorrhexis and internuclear chromatin bridges. (swiss cheese pattern) Differential diagnosis included thalassemia, some hemoglobinopathies, hereditary sideroblastic anemia, congenital myelodysplasia, and other forms of CDA [1]. Congenital anemia such as Blackfan–Diamond anemia and Fanconi anemia also should be considered. Our patient showed prominent macrocytosis with dyserythropoiesis, commonly not observed in a case of thalassemia or hemoglobinopathy. No ringed sideroblasts or dysplastic features on the granulocytic/megakaryocytic lineage were seen. Acidified serum lysis was normal. Peripheral blood smears at initial presentation and the bone marrow histology at autopsy revealed internuclear chromatin bridges and erythroid hyperplasia with megaloblastoid changes and multinuclearity. No giant erythroblasts were observed. These findings all favored a diagnosis of CDA type 1 [1, 4, 9].

Conclusion

Our case highlights the fact that diagnosis of CDA 1 can be made with high reliability by careful examination of bone marrow aspirate and Biochemical study. Although CDA1 is rare, we should be aware of this possibility and includes it in differential diagnosis whenever appropriate.

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