Congenital Dyserythropoietic Anemia Type I: Report of a Case

A. Kumar · R. Kushwaha · U. S. Singh

Received: 13 February 2012 / Accepted: 6 August 2012 / Published online: 28 August 2012
© Indian Society of Haematology & Transfusion Medicine 2012

Abstract The congenital dyserythropoietic anemias (CDAs) comprise a group of rare hereditary disorders of erythropoiesis that is characterized by ineffective erythropoiesis as the predominant cause of anemia and by distinct morphologic abnormalities of the majority of erythroblasts in the bone marrow. Congenital dyserythropoietic anemia type I (CDA I) is an autosomal recessive disorder with ineffective erythropoiesis and iron overloading. More than 100 cases have been described, but with the exception of a report on a large Bedouin tribe, these reports include only small numbers of cases. 1,2 CDA-I is uncommonly reported from Indian subcontinent hence we are discussing a case of CDA I. Our case also highlights the fact that diagnosis of CDAI can be made with high reliability by careful examination of bone marrow aspirate.

Keywords Anemia · Congenital Dyserythropoietic-type 1 · Bone marrow

Introduction

The congenital dyserythropoietic anemias (CDAs) comprise a group of rare hereditary disorders of erythropoiesis that is characterized by ineffective erythropoiesis as the

predominant cause of anemia and by distinct morphologic abnormalities of the majority of erythroblasts in the bone marrow. CDA I is an autosomal recessive disorder with ineffective erythropoiesis and iron overloading. More than 100 cases have been described, but with the exception of a report on a large Bedouin tribe, these reports include only small numbers of cases [1, 2].

CDA-I is uncommonly reported from Indian subcontinent hence we are discussing a case of CDA I. Our case also highlights the fact that diagnosis of CDAI can be made with high reliability by careful examination of bone marrow aspirate.

Case

A 12 year child presented with pain and lump in abdomen. He had history of repeated blood transfusion since childhood. On examination he had pallor and his spleen was palpable till umbilicus. His hemoglobin was 2.0 g%. Total bilirubin and indirect bilirubin was raised. His peripheral smear examination and bone marrow aspiration was done.

In peripheral smear RBC's showed anisocytosis and poikilocytosis with presence of macrocytes and tear drop cells. Few of the RBC's showed basophilic stippling (Fig. 1a, b).

Total leukocyte count, differential leukocyte count and platelet count were within normal range. Reticulocyte count was 0.5 %. MCV was 108 fl.

Bone marrow smears showed distinct hypercellularity due to erythroid hyperplasia. The erythropoietic to granulopoietic ratio was 6:1. The erythroid precursors showed megaloblastic appearance (Fig. 2a, b). They also showed dysmorphic features like lobulated nuclei, multiple nuclei, internuclear chromatin bridges and irregular nuclear

A. Kumar · R. Kushwaha (✉) · U. S. Singh
Department of Pathology, C.S.M. Medical University
(erstwhile KGMC), Lucknow, India
e-mail: docrashmi27@yahoo.co.in

A. Kumar
e-mail: kumarashutosh45@hotmail.com

U. S. Singh
e-mail: ussinghjyotsana@yahoo.co.in

Fig. 1 Blood smear **a** Anisopoikilocytosis, macroovalocytes and tear drop cells (Leishman stain $\times 40$). **b** Basophilic stippling (Leishman stain $\times 40$)

Fig. 2 Bone marrow smear **a, b** Megaloblastic erythroid hyperplasia, binucleated and multinucleated erythroblasts (Leishman stain $\times 40$) **c, d**, Internuclear chromatin bridges (Leishman stain $\times 100$)

outline (Fig. 2c, d). Fifty-five percentage of all the erythroblasts were abnormal.

Granulocytic precursors showed normal maturation and megakaryocytes were adequate in number and were functional.

Cytogenetic revealed mutation of CDAN1 gene. Based on above findings diagnosis of CDA-I was made.

Discussion

CDA I is a rare clinical entity that has been reported mainly from the Central and Western European countries and North Africa with very few cases reported from Indian Subcontinent [1].

CDA I should be suspected in any person with a chronic anemia. The presence of ineffective erythropoiesis would be indicated by a low absolute reticulocyte count for the degree of anemia despite erythroid hyperplasia in the marrow. Characteristic morphological aberrations of the erythroblasts on light microscopy in bone marrow aspirate are still the cornerstone of the diagnosis. Bone marrow smears are hypercellular due to erythroid hyperplasia. Major abnormalities seen are: megaloblastoid aberrations of chromatin structure, large polyploidy cells with an irregularly shaped nuclear mass often consisting of two segments, double- or triple-nucleated erythroblasts with nuclei of different sizes and structure. Of particular significance are thin chromatin bridges between pairs of erythroblasts, which may also be seen between two nuclei in one cell (Fig. 2c, d). They are not seen in normal bone marrow, but are occasionally observed in single cells in patients with myelodysplastic syndromes or erythroleukemia [1, 3, 4].

Differential diagnosis included thalassemia, some hemoglobinopathies, hereditary sideroblastic anemia, myelodysplasia, megaloblastic anemia (mainly B12 or folate deficiency) and other forms of CDA. Our patient showed prominent macrocytosis with dyserythropoiesis, commonly not observed in a case of thalassemia or hemoglobinopathy. No ringed sideroblasts as well as absence of microcytic blood picture rules out sideroblastic anemia. No dysplastic features on the granulocytic/megakaryocytic lineage rules out myelodysplastic syndrome. Other causes of macrocytosis (mainly B12 or folate deficiency) are ruled out because of absence of loose and fine chromatin structures of erythroblastic nuclei and giant granulopoietic cells and hyperlobulation of megakaryocytes [4–6]. Acidified serum lysis was normal (rules out CDA II). Peripheral blood

smears at initial presentation and the bone marrow aspirate revealed internuclear chromatin bridges and erythroid hyperplasia with megaloblastoid changes and multinuclearity. No giant erythroblasts were observed (rules out CDA III) [5]. These findings favored a diagnosis of CDA type I.

In conclusion, CDA I should be suspected in children with refractory anemia, hepatosplenomegaly, erythroid hyperplasia and features of dyserythropoiesis in marrow examination. The diagnosis of CDA I can be made with high reliability from diligent analysis of peripheral blood and technically appropriate specimens of aspirated bone marrow.

References

1. 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
2. Marwaha RK, Bansal D, Trehan A, Garewal G, Marwaha N (2003) Congenital dyserythropoietic anemia: clinical and hematological profile. *Indian Pediatr* 40:551–555
3. 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
4. Heimpel H (2004) Congenital dyserythropoietic anemias: epidemiology, clinical significance, and progress in understanding their pathogenesis. *Ann Hematol* 83:613–621
5. Kato K et al (2001) Congenital dyserythropoietic anemia type I with fetal onset of severe anemia. *J Pediatr Hematol Oncol* 23(1):63–66
6. Wickramasinghe SN, Glader B (2009) Congenital dyserythropoietic anemia. In: Greer JP (ed) *Wintrobe's clinical hematology*, 12th edn. Lippincott Williams and Wilkins, Philadelphia, p 1212