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Congenital dyserythropoietic anemia type 1: about a case at the Avicenna military hospital Marrakech

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Abstract

Congenital dyserythropoietic anemias (CDA) are a group of rare hereditary anemias that share inefficient erythropoiesis and common morphological abnormalities of mature red blood cells and their precursors (1). Three major types of CDA and a number of variants have been described (1, 2), The classification is based on morphological findings in the bone marrow with serological studies (2) .Although the etiology of CDA I has apparently has been defined at the molecular level (2), little is known about the mechanisms underlying other forms, the diagnosis of CDA type I is based on the set of clinical, cytologic and cytogenetic cytological criteria.

Keywords: ,Congenital dyserythropoietic anemias ,CDA-1, Marrakech

Introduction

Congenital dyserythropoietic anemias (CDA) are a heterogeneous group of rare hereditary anemias, with no other cytopenias and no tendency to malignant transformation. (2,3) The cause of peripheral anemia is a blockage of maturation of the erythroid lineage In late stages, associated with varying degrees of dyserythropoiesis, ADCs were divided into three main types, CDA types 1, 2 and 3, and other forms designated CDA groups IV-VII (3,4). Congenital dyserythropoietic anemia, type 1 (CDA-1) CDA-1 has a variable presentation, as it can appear during the neonatal period or at any time during the first five decades of life. It can also occur in utero, and its diagnosis is based on a set of clinical, biological cytological and cytogenetic criteria

Observation

This is a 26-year-old patient with a history of chronic anemia unaffected by treatment with a family history of an older sister also followed by chronic anemia.
Patient admitted to hospital for haemolytic anemia of sudden onset
Clinical examination revealed asthenia, conjunctival subcutaneous, splenomegaly
With the notion of dystrophic syndrome represented by skeletal abnormalities, the rest of the clinical examination is without particularity

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I/Biological assessment

A/Hematological data

1/Hemogram:

a/blood count:
severe anemia at 4.7g / dl hypochromic microcytic VGM at 44fl and MCHC at 19%; Regenerative Reticulocyte: 3.5% 132 000 / mm3. And thrombocytopenia PLQ = 117,000 / mm3.

b-The Bloodsmear :
Anisopoikilocytoe red blood cells and without platelet aggregates (Figure1)

2-The myelogram:

Average marrow of richness, showing very many megakaryocytes,

Moderate hyperplasia of the erythroblastic line at 56% (normal: 10-30) (Figure 2)

Signs of dyserythropoiesis: interchromatinic bridges +++++++ (Figure 3)

3-immuno-hematological test:

• Coombs test: negative

4- Biochemical examinations:

• Total Bilirubin: 34.2 µmol / L (VN <18 µmol / L)

• Conjugated bilirubin: 56 µmol / L (VN <4µmol / L)

• Ferritinemia: 162 ng / ml (normal: 15-150)

• LDH: 650 IU / L (200-400 IU / L)

• Serum iron: 2.6mg / l (0.6-1.9mg / l)

• Hemoglobin electrophoresis: in favor of a normal hemoglobin profile (Hb A 97.7% Hb A2 2.3%)

II/Abdominal ultrasound:

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• found a moderate, homogeneous splenomegaly.

A family survey; was started in the family (sister, parents).

The diagnosis of CDA type 1: retained on (according to the description of CDA Wendt and Heimpel [3]):

• Epidemiological criteria (young adult age, family and personal history of treatment-resistant anemia),

• Clinical criteria (dysmorphic syndrome),

• Biological criteria (severe hemolytic anemia with dyserythropoiesis specific to CDA type 1: interchromatinic bridges affecting the more mature basophilic and acidophilic erythroblasts)

DISCUSSIONS:

Congenital dyserythropoietic anemias (CDA) are a rare group of hereditary hemopathies characterized by inefficient erythropoiesis, hemolysis, and morphological abnormalities of erythroblasts (3). The inefficiency of erythropoiesis leads to an ineffective response of reticulocytes to the degree of anemia despite the presence of hyperplasia of the markedly marked erythroid line (3). Based primarily on the signs of dysplasia observed by light and electron microscopy, ADCs were divided into three main types, designated CDA types 1, 2 and 3, and other forms designated CDA groups IV-VII (2, 3).
Some patients with CDA have congenital anomalies such as syndactyly, bone abnormalities of the hands and feet (absence or hypoplasia of certain phalanges, additional phalanges), dysplastic nails, short stature and abnormal pigmentation of the skin areas (1, 2), other patients have an increased tendency to develop marked iron overload despite a limited number of transfusions and a lack of transfusion dependence (1, 3)
The severity of anemia observed in DCOs varies considerably: some patients are completely asymptomatic, while others may require a blood transfusion. Most often, however, anemia is mild to moderate, with hemoglobin (Hb) concentrations between 8 and 11 g / dl. Normocytic or macrocytic indices are typical
CDA type I is an autosomal recessive disorder, although the variation in clinical expression has been well documented, most patients have splenomegaly and mild to moderate macrocytic anemia ([1, 2]). Observed in circulating erythrocytes, appear to be unique to ADC I. [2,3] In optical microscopy, the peripheral blood smear shows macrocytes and basophilic dots (3,4) and the reticulocyte count is normal or only slightly increased. erythroid hyperplasia is present in the bone marrow Some of the more mature basophilic erythroblasts and many early and late polychromatophilic erythroblasts exhibit dyserythropoietic features The characteristic morphological abnormality is internuclear bypass, where the chromatin strands link polychromatophilic erythroblast pairs completely separated (0.6-2.8 strands per 100 erythroblasts) (3,4,6), also a small percentage of erythrocytes (usually 5-10%) are binucleate or

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contain an irregular nuclear mass resulting from incomplete nuclear division (4). These cores can be of different size

the CDAN1 gene was identified through 12 different mutations in 9 families with CDAI. This 28-exon gene, which is ubiquitously transcribed in mRNA, encodes codanine-1, a putative o-glycosylated protein of 1 226 amino acids, with no obvious transmembrane domain. Codanin-1 has an amino-terminal domain of 150 residues with sequence similarity to collagens and two shorter segments that have low similarities to microtubule-associated proteins (neuraxin) and synapsin. These findings, and the cellular phenotype, suggest that codanin-1 may be involved in the integrity of the nuclear envelope, probably related to microtubule attachments. (4,7)

regarding the role of hyperexpression of growth differentiation factor (GDF15) in inefficient erythropoiesis and in CDA I-type iron overload complications, results suggest that CDA I patients express very high levels of Serum GDF15, and that GDF15 contributes to the inappropriate suppression of hepcidin with subsequent secondary hemochromatosis. (5,8)

CONCLUSION

CDA I is an autosomal recessive disorder. Although the variation in clinical expression has been well documented, most patients have splenomegaly and mild to moderate macrocytic anemia (2). Cabot's rings, seen in circulating erythrocytes, appear to be unique to ADC I [23]. Recently, CDA I has been associated with skeletal abnormalities of limbs [24].

the diagnosis of CDA type I is based on the set of clinical, cytologic and cytogenetic criteria (1)

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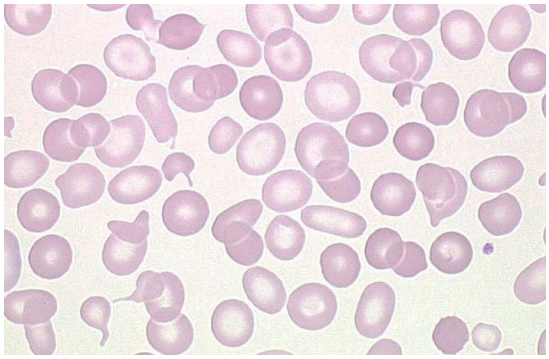

Figure 1: Peripheral blood (May-Grünwald-Giemsa stain): Anisopikilocytose

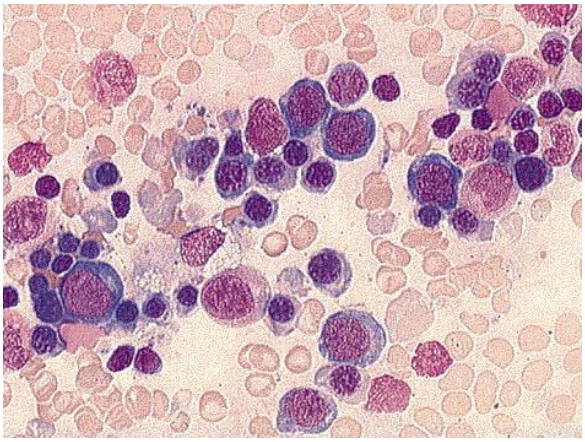

Figure 2. Marrow (May-Grünwald-Giemsa stain): erythroblastic hyperplasia objective x40:

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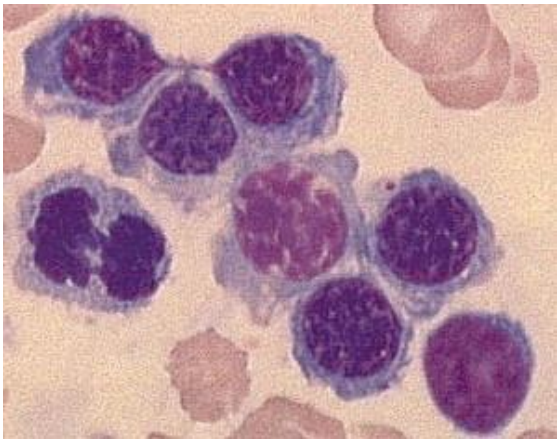

Figure 3: Marrow (May-Grünwald-Giemsa stain): inter-chromatin bridge