An Association of Leishmaniasis and Dyserythropoiesis in Children

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Abstract Visceral leishmaniasis results in hematological problems such as cytopenias and coagulopathies. This disorder also has morphological effects on the bone marrow. Dyserythropoiesis is one of the most prominent seen with changes like multilobed nuclear cells and the appearance of bridges between nuclei and cytoplasm. Approximately half of the children with leishmaniasis showed dyserythropoietic findings in bone marrow aspirate slides. Because this is endemic regions, physicians of these countries must be alert to correctly diagnose disease and discriminate from other dyserythropoietic disorders.

Keywords Leishmaniasis · Dyserythropoiesis · Children

Introduction

Kala azar is a zoonotic disease characterized by fever, pancytopenia, hepatosplenomegaly and hypergammaglobulinemia [1]. It affects people mostly in the Mediterranean countries as well as Turkey beside other endemic countries like Bangladesh, Brazil, India, Nepal and Sudan. It has some distinct hematologic features related with its bone marrow effects and results in some bone marrow cellular changes. Visceral Leishmaniasis related marrow changes are mostly related with prominent dyserythropoiesis even similar with congenital dyserythropoietic anemia [2].

Dyserythropoiesis findings include anisocytosis, poikilocytosis, polychromasia, tear-drop cells in peripheral blood smear and cytoplasmic or nuclear bridges between and bi- and trinucleated erythroblasts in bone marrow smears. The reticulocyte count is inappropriately low, with erythroid hyperplasia, ineffective erythropoiesis is also seen with morphological dysplasia [3]. Dyserythropoiesis can be seen in a variety of disorders affecting bone marrow like congenital dyserythropoietic anemia, myelodysplastic syndrome, some inherited hemolytic anemia or bone marrow failure syndromes, B₁₂ and folate deficiency [4]. Because some kala azar cases lack obvious parasite in bone marrow and dyserythropoiesis is one of the main findings of some disorders above it is important to discriminate all of them.

Here we report our kala azar cases and discuss dyserythropoiesis findings of their bone marrow smears to clarify from those clinical overlaps.

Case Series

Thirteen children with visceral leishmaniasis were re-evaluated retrospectively with their bone marrow smears for dyserythropoiesis findings. They were between 7 months and 17 years-old and all have hepatosplenomegaly with cytopenias in a varying degree. They were diagnosed as having visceral leishmaniasis with leishmania amastigote detection on bone marrow aspiration evaluations. They were treated with antimonite agents for kala azar for 28 days. The demographic and some clinical data's of patients were given in Table 1. Six of the thirteen patients' bone marrow smears have revealed some dyserythropoietic findings as bi- or trinucleated erythroblasts, cytoplasmic bridging and dysplastic figures (Fig. 1). All of them responded to the antimonite treatment with full recovery without any complication.

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Fig. 1 Binucleated erythroblast seen in bone marrow smear of the kala-azar patient

Discussion

Visceral leishmaniasis (kala-azar) characterized by severe splenomegaly and pancytopenia in varying degrees secondary to splenomegaly that result in increased pooling of blood cells within the spleen, an increase in plasma volume (haemodilution), and some reduction in the life span of blood cells. However, other mechanisms have also been claimed for the anemia. Dyserythropoiesis and ineffective erythropoiesis are included to these mechanisms as a result of effects of toxins generated by the organisms or some other mechanisms [3].

Leishmaniasis; is seen only in endemic regions, is well known but infrequent cause of dyserythropoiesis. This association may be useful in some clinical conditions to reaching its diagnosis and treatment. In patients with cytopenia and dyserythropoiesis it is important to search for disease especially before diagnosing premalignant disorders like myelodysplastic syndrome. Leishmaniasis can be diagnosed by help of kinetoplast, “double dot” appearance of the nucleus and identification of Leishmania organisms extracellular or within macrophages [5].

Dyserythropoiesis in kala azar is well known condition but on review of literature there are few and only older reported cases. [6, 7]. The most recent literature is about an adult case with leishmaniasis and obvious dyserythropoiesis in bone marrow [5]. Because myelodysplastic syndrome is relatively common in adults, there may be some confusion in the diagnosis of leishmaniasis, in those without classical bone marrow appearance of parasites. This clue may present differentiating features but the condition must be taken into consideration while managing diagnosis and treatment.

In the older review reported while 1981 outbreak at Kenya 3 children were diagnosed by splenic aspirates and diagnosed visceral Leishmaniasis [3]. Their bone marrow materials evaluated by light and electron microscopy revealing that hypercellular marrows with decreased myeloid:erythroid (M:E) ratios due to erythroid hyperplasia, and increased numbers of megakaryocytes. Erythroblasts with dyserythropoietic features include cytoplasmic stippling and irregularly shaped nuclei or karyorrhexis.

Table 1 Patient’s characteristics and their bone marrow findings

Pts.	Age	Gender	Treatment	Bone marrow findings
1.C.I.	17 years	Male	Sodium stibogluconate	Binucleated erythroblasts [3], nuclear bridging [2], cytoplasmic bridging (5 %)
2.S.A.	1.5 years	Male	Meglumine antimoniate	Dyserythropoiesis (–)
3.F.A.	12 years	Female	Meglumine antimoniate	Dyserythropoiesis (–)
4.Z.Y.	4 years	Female	Meglumine antimoniate	Binucleated erythroblasts [4], nuclear bridging [1], cytoplasmic bridging (4 %)
5.S.Y.	2 years	Female	Meglumine antimoniate	Dyserythropoiesis (–)
6.E.Ö.	17 years	Male	Meglumine antimoniate	Binucleated erythroblast, cytoplasmic bridging, nuclear dysplasia (5 %).
7.Ö.C. K	3 years	Male	Meglumine antimoniate	Dyserythropoiesis (–)
8.B.A.E.	9 years	Male	Meglumine antimoniate	Dyserythropoiesis (–)
9.E.A.	20 months	Female	Meglumine antimoniate	Dyserythropoiesis (–)
10.C.C	13 years	Female	Meglumine antimoniate	Dyserythropoiesis (–)
11.H.B.	16 years	Female	Sodium stibogluconate	Cytoplasmic bridging and irregular membrane, nuclear and cytoplasmic dissociation (4–5 %)
12.M.P.	7 months	Female	Meglumine antimoniate	Cytoplasmic bridging and irregular membrane, nuclear and cytoplasmic dissociation (3 %)
13.H.A.	9 years	Male	Meglumine antimoniate	Cytoplasmic bridging and irregular membrane, nuclear membrane irregularity and dysplasia (5 %)

Cytoplasmic stippling- was seen in 6–14 % and irregularly shaped nuclei or karyorrhexis in 7–13 % of the erythroblasts. There were 1–4 % of binucleate or multinucleate erythroblasts.

In our cases we also found cytoplasmic stippling, binucleate and dysplastic erythroblasts with approximately same ratios (Table 1).

Dyserythropoiesis and ineffective erythropoiesis is one of the main reasons for anemia and it is supposed to be related with macrophage invasion by parasites and deranged relation between erythroblasts and macrophage for erythroid cell normal differentiation. This derangement results in abnormal erythropoiesis [3].

In conclusion leishmaniasis may be hidden behind dyserythropoiesis, and this finding may be useful for diagnosing kala azar and avoiding over diagnose of other dysplastic disorders when taken into consideration.

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