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CIRCULATING RINGED SIDEROBLASTS IN THE COURSE OF THE INITIAL ERYTHREMIC PHASE OF ERYTHROLEUKEMIA

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A 57-year-old man was admitted to our Institute with a two-week history fever up to 39°C, hepatomegaly and splenomegaly. Hematological findings were as follows: Hb 8.8 g/dL, platelet count 193×10^9/L, WBC 54×10^9/L with neutrophils 12%, lymphocytes 8%, blasts 80%, nucleated red blood cells 65/100 WBC. The immunological studies carried out by flow cytometry showed that circulating blasts were CD2, CD7, CD33, CD13, CD14, CD19 and CD10 negative.

Examination of bone marrow aspirate smears revealed the presence of 70% erythroblasts, with a prevalence of proerythroblasts, early erythroblasts and blasts, a few of which contained cytoplasmic granules. The karyotype was normal. Erythroleukemia (EL) in the initial erythremic phase[1] was diagnosed. The patient underwent induction chemotherapy but died two months later with a hematological picture of acute myeloblastic leukemia.

Morphology and cytochemistry

At May-Grünwald-Giemsa staining circulating blasts appeared as medium-sized cells with a round nucleus, a delicate nuclear chromatin pattern, and one or two nucleoli. With Prussian Blue staining, a significant percentage of circulating erythroblasts showed the typical appearance of ringed sideroblasts (Figure 1a). PAS was positive in a high percentage of blasts, with either diffuse or block-like positive material (Figure 1b). Myeloperoxidase, Sudan Black B and α-naphthyl-butyrate esterase reactions were negative. The same morphological and cytochemical features were displayed by bone marrow blasts, with 40% of erythroblasts having the appearence of ringed sideroblasts. Circulating

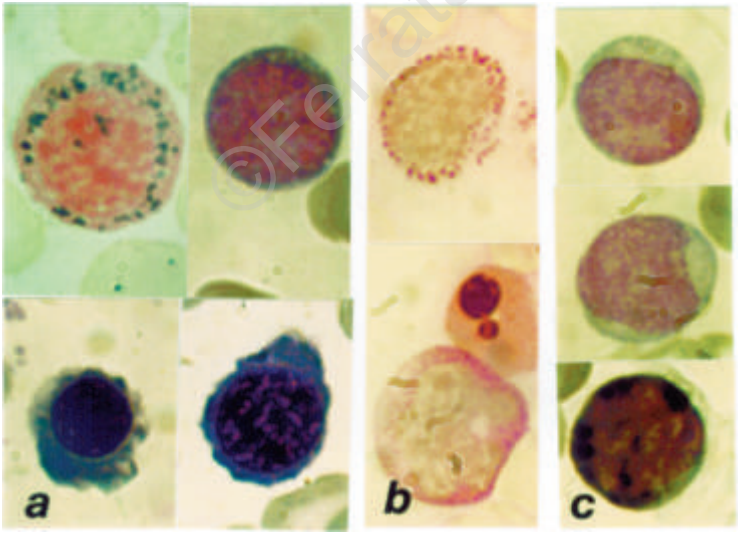

Figure 1. Morphologic and cytochemical features of circulating blasts at presentation and during the final phase of disease;
a: May-Grünwald-Giemsa staining and Prussian Blue staining (early phase of disease). *Upper panel, left*: ringed sideroblast; *right:* proerythroblast; *lower panel*: two erythroblasts at different stages of maturation;
b: PAS staining (early phase of disease). Two basophilic erythroblasts with intense PAS reactivity are shown. In the lower panel, an orthochromic erythroblast shows nuclear abnormalities;
c: circulating blasts during the final phase of disease. A myeloperoxidase-positive myeloblast is shown in the lower panel; two blasts with myeloid morphologic features after May-Grünwald Giemsa staining are also shown (1,100×).

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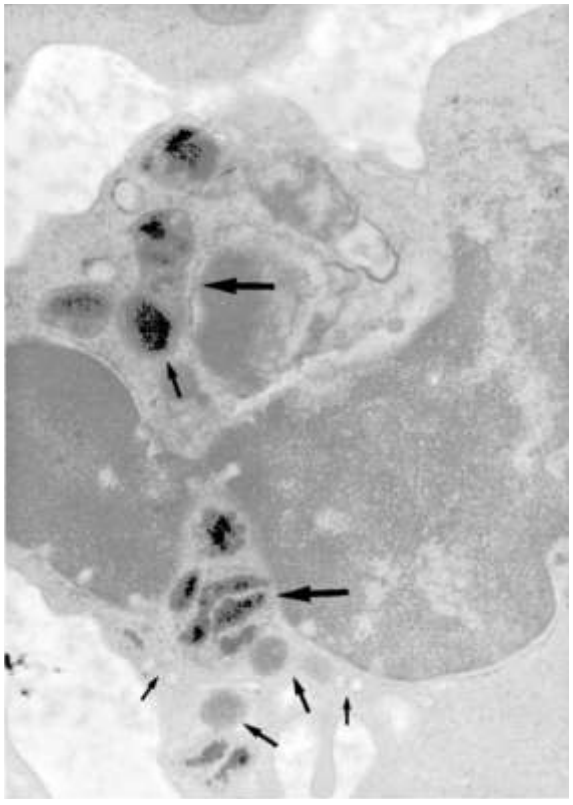

Figure 2. Electron microscopy, peripheral blood (early phase of disease). A basophilic erythroblast with features of a ringed sideroblast is shown. The cytoplasm contains dispersed polyribosomes, pale vesicles (small-sized arrows), siderosomes (medium-sized arrows), and mitochondria (large-sized arrows) with high amounts of ferruginous micelles (36,000×).

siderocytes were frequently observed.

During the final, myeloid phase circulating and bone marrow blasts showed typical myeloid morphologic, immunologic (CD33$^+$, CD13$^+$), and cytochemical features (Figure 1c).

Electron microscopy

During the initial erythroid phase the majority of circulating and bone marrow blasts were found to contain a high amount of ferruginous micelles within the mitochondrial lamellae and cristae (Figure 2). In more mature circulating erythroblasts and in circulating siderocytes, large block-like deposits of ferruginous micelles were still present within the cristae of persisting mitochondria.

Conclusions

The use of ultrastructural techniques has proven to be very useful in identifying blast cells that belong to the erythroblastic line, even though they appear undifferentiated morphologically.[2,3] Some cytochemical features, such as the PAS reaction and Prussian Blue staining, are useful aids to electron microscopy.[4,5]

Our case was characterized by some peculiar features. In fact, a high number of circulating erythroid precursors showed the typical features of ringed sideroblasts and, to the best of our knowledge, this finding has never been reported until now. Circulating siderocytes with a great amount of ferruginous micelles in persisting mitochondria were also found, suggesting impaired hemocatheretic function of the spleen in the presence of a high erythroblastic output from the bone marrow.

In conclusion, EL is rare and the chances of observing the initial, pure erythremic phase of this type of leukemia is more rare. As a consequence, clinical, morphologic, cytochemical, ultrastructural and immunologic data from each single case deserve careful evaluation. Our case shows that interesting results can be provided by an adequate electron microscopy investigation of circulating erythroid precursors in the early phase of the disease.

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