Esterase Activity in Erythroleukemia

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Kass, Lawrence: Esterase activity in erythroleukemia. Am J Clin Pathol 67: 368-370, 1977. Specific esterase activity, a property generally ascribed to cells of granulocytic origin, was found in abnormal erythroid precursors obtained from the bone marrows of six patients with untreated erythroleukemia. These erythroblasts also showed nonspecific esterase activity. Neither specific nor nonspecific esterase activity was detected in erythroid precursors obtained from the bone marrows of ten presumed normal individuals. The implications of finding specific esterase activity in the erythroblasts of erythroleukemia are discussed. (Key words: Esterase; Erythroleukemia; Erythroblasts.)

Various cytochemical reactions, such as myeloperoxidase, Sudan black B, and periodic acid-Schiff (PAS) have been utilized to differentiate the various acute leukemias. Recently, reactions devised to demonstrate nonspecific and specific esterase activity have been added to the tests mentioned, and to the growing list of cytochemical tests available for complementing morphologic diagnoses made on the basis of standard panoptic stains. Nonspecific esterase utilizing alpha-naphthyl acetate as substrate has been regarded as specific for cells of the monocytic series, whereas specific esterase using naphthol ASD-chloroacetate as the substrate is believed to be specific for cells of the granulocytic series. The usefulness of the esterase reactions in the evaluation of leukemic blasts and in their more precise identification as lymphocytic, monocytic, or myeloblastic has been steadily appreciated over the past several years. In the present studies, esterase reactions have been applied to patients with erythroleukemia, in an effort to ascertain information regarding properties of the atypical erythroid precursors in this disorder.

Materials and Methods

Bone marrow was obtained from sternum or iliac crest by needle aspiration from ten presumed normal individuals undergoing evaluations that did not disclose any hematologic abnormality, and from six patients with untreated erythroleukemia. The diagnosis of this disorder was made according to morphologic criteria proposed by various investigators. Films of marrow flecks were made between methanol-cleaned coverslips and stained with Wright's stain for conventional morphologic examination. Separate coverslips were stained for iron, using the Prussian blue reagent, for glycogen using the PAS reagent, and for peroxidase. Additional coverslips were stained for specific and nonspecific esterases within the same cell. All of the patients died shortly after diagnosis despite chemotherapy, and in one instance, acute myelomonocytic leukemia developed in a patient four days after the diagnosis of erythroleukemia was made.

Results

In erythroid precursors obtained from the marrows of normal individuals, occasional siderotic granules were obtained after Prussian blue staining. The normal erythroblasts were PAS-negative and showed no evidence of specific esterase, nonspecific esterase, or peroxidase positivity. Using the Prussian blue reagent, numerous ringed sideroblasts were seen in the marrows of patients with erythroleukemia, and the PAS reaction was strongly positive in erythroid precursors, as found in cases of erythroleukemia by other investigators.
In some instances, the PAS reaction was diffuse, and in other instances it was coarse and punctate. In all cases of erythroleukemia, the reaction for nonspecific esterase was strongly positive in erythroid precursors at all stages of maturation. Nonspecific esterase activity was not seen in myeloblasts. In addition, as illustrated in Figures 1 and 2, specific esterase activity could also be detected in the majority of erythroid precursors at all stages of maturation, and in myeloblasts. Occasional peroxidase-positive granules were also observed in most of the erythroid precursors.

Discussion

Since its initial description by DiGuglielmo in 1917, erythroleukemia has aroused controversy, particularly in regard to the morphologic criteria requisite for making the diagnosis of this disorder, to the assignment of erythroleukemia as a part of the myeloproliferative syndrome, and in some instances, to the existence of erythroleukemia as an entity per se. Dameshek and others have attempted to investigate some of these issues, and have concluded that erythroleukemia is a part of the "DiGuglielmo syndrome," which includes acute and chronic erythremic myelosis and erythroleukemia. This school of thought postulates that erythroleukemia is probably a transitory phase in the evolution of acute myeloblastic or myelomonocytic leukemia. In some instances, erythroleukemia may be very brief in duration, and in other situations, it has been reported as having a more chronic course. In the present studies, the intriguing mixture of neoplastic-appearing erythroid precursors and myeloblasts, and the propensity of erythroleukemia apparently to evolve into acute myeloblastic or myelomonocytic leukemia (as it did in one of the patients in the present series) prompted the study of esterase reactions in the erythroid precursors.

In a previous study, specific esterase activity was observed in atypical erythroblasts from the bone mar-
rows of patients with acute erythremic myelosis, a disorder regarded as the first stage of the DiGuglielmo syndrome. Others have also found evidence for granulocytic differentiation in the neoplastic erythroid precursors of acute erythremic myelosis, as exemplified by the presence of occasional peroxidase granules in these cells and the finding of granules in the Golgi apparatus of the abnormal erythroblasts.

The present study demonstrates that in erythroleukemia, regarded as the second stage of the DiGuglielmo syndrome, specific esterase activity was also found in the neoplastic erythroid precursors at all stages of maturation, suggesting that, as in acute erythremic myelosis, the abnormal erythroblasts in erythroleukemia possess properties of granulocytes. Although these cells contain specific esterase activity, on the basis of the present observations it is not possible to state that the neoplastic erythroid precursors containing properties of granulocytes are actually capable of transforming into myeloblasts or neoplastic granulocytes. The findings are more consistent with the viewpoint that in erythroleukemia, there may be a stem cell or clone of stem cells, probably myeloblastic, common to granulocytic and erythroid precursors alike, as in the case of the Ph1-positive chronic granulocytic leukemia where both myeloid and erythroid precursors contain the abnormal Ph1 chromosome.

Erythroleukemia erythroid precursors also contain nonspecific esterase activity, a property generally ascribed to monocytic cells but also found in other erythroid cells having disturbed metabolism, such as pernicious anemia megaloblasts, and in atypical erythroblasts of acute erythremic myelosis. The results of the present study, in which specific esterase activity was found in the erythroblasts of patients with erythroleukemia, provide additional support for the viewpoint that this "mixed" disorder of erythroid precursors and myeloblasts is part of the framework of the DiGuglielmo syndrome, in which the eventual outcome is often acute myeloblastic or myelomonocytic leukemia.

References