Appearance of Bone Marrow Smears With Necrotic Tumor Cells

By GEOFFREY M. BRITTIN AND GEORGE BRECHER

Bone marrow smears of necrotic tumor cells stained with Romanowsky dyes frequently have a definite reddish color that contrasts so strikingly with the blue color of normal marrow that necrosis may be suspected from gross examination. The bone marrow cells appear "smudged" and are difficult to identify on microscopic examination. Commonly, only a small amount of material is obtainable by ordinary needle aspiration of bone marrow containing necrotic tumor, and all of it is used to make smears. It is therefore important to recognize that bone marrow smears with a reddish gross appearance and in which the cells appear distorted and are difficult to identify may represent necrotic tumor and not an artifact produced by poor techniques.

RETICULIN FIBROSIS and necrosis of bone marrow have been described as frequent complications of acute leukemia.[1] In addition, we have encountered similar findings in a number of cases of lymphosarcoma metastatic to the bone marrow. Necrosis is easily recognized in paraffin sections of specimens obtained with a Westerman-Jensen biopsy needle,[2] or with the Agress aspirate section technique.[3] However, we have found that most hematologists and pathologists are unfamiliar with the appearance of bone marrow smears of necrotic tumor cells and erroneously attribute the unusual color of the smears and the moth-eaten appearance of cells to artifacts caused by anticoagulants used in the aspiration or to faulty technic in the preparation and staining of smears. A brief description of the characteristic appearance may therefore be useful.

Bone marrow smears of necrotic tumor cells stained with Romanowsky dyes can frequently be diagnosed correctly from gross examination. Cover-slip smears without necrotic tissue contain central dark blue particles surrounded by areas that stain a lighter blue. By contrast, smears of necrotic tumor cells contain particles that stain dark blue to purple and the surrounding areas stain a definite reddish color. This tinctorial difference is easily seen when smears of necrotic and nonnecrotic bone marrow are placed side by side. Gross examination of the smear of necrotic tumor cells may show that the particles have a "stringy" appearance, but this is not always the case (Fig. 1).

From the Department of Clinical Pathology, The University of Texas, M. D. Anderson Hospital and Tumor Institute at Houston, Tex., and The Department of Clinical Pathology and Laboratory Medicine, University of California Medical Center, San Francisco, Calif.

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GEOFFREY M. BRITTIN, M.D.: *Head, Department of Clinical Pathology, University of Texas, M. D. Anderson Hospital and Tumor Institute at Houston, Tex.* GEORGE BRECHER, M.D.: *Professor and Chairman, Department of Clinical Pathology and Laboratory Medicine, University of California Medical Center, San Francisco, Calif.*

Fig. 1.—"Stringy" appearance of cover slip smear of necrotic tumor in bone marrow. Wright-Giemsa. × 6.5.

Microscopic examination of the stained smears shows a variable number of cells, most of which are difficult or impossible to identify (Fig. 2). They appear to be "smudged," and the nuclei may have ragged outlines and thus assume a stellate appearance. Although the nucleus may stain deeply basophilic, morphological detail is poor. The cytoplasmic margins are ill-defined, and the cytoplasm may appear to be absent. Often the cells are surrounded by masses of slightly acidophilic, granular material. Careful examination usually permits identification of this material as the ghosts of necrotic cells. The acidophilic staining may cause confusion with poorly smeared erythrocytes, but red cells have better defined outlines and stain more pink.

Presumably, the affinity of the necrotic cells for the acidic component of the Romanowsky stains is responsible for the reddish gross appearance of the stained smears. Excessive acidity of the buffer, stain, or water may produce a similar red appearance; however, excessive acidity causes the nuclei to stain pale blue and the erythrocytes to stain bright red or orange,[4] which is not the case with necrotic tumor. We have not found that the presence of small amounts of heparin or EDTA in the syringe used for aspiration produces the appearance described above.

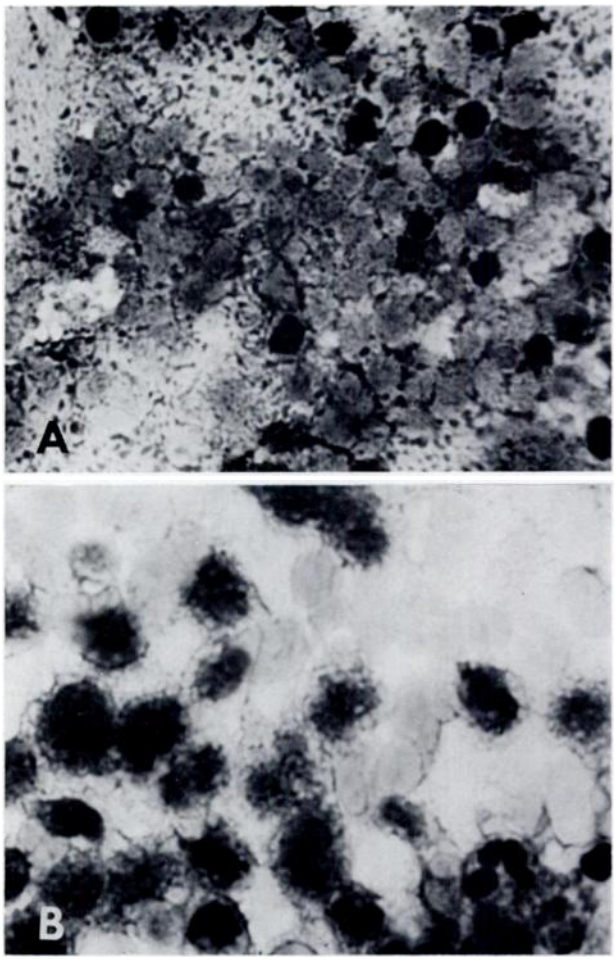

Fig. 2.—Necrotic leukemic cells in bone marrow. (A) The field is filled with necrotic (acidophilic) cells. In only a few are the nuclear outlines distinct. × 400. (B) High magnification of similar field. Note moth-eaten appearance of leukemic cells. × 1000.

Commonly, only a small amount of material is obtainable by ordinary needle aspiration of necrotic bone marrow and all of this material is used to make smears. It is therefore important to recognize that bone marrow smears with a reddish gross appearance and in which the cells are distorted and difficult to identify may represent necrotic tumor in the bone marrow and not an artifact produced by poor techniques.

References

1. Kundel, D. W., Brecher, G., Bodey, G. P., and Brittin, G. M.: Reticulin fibrosis and bone infarction in acute leukemia. Implications for prognosis. Blood 23:526, 1964.

2. Ellis, L. D., Jensen, W. N., and Westerman, M. P.: Needle biopsy of bone and bone marrow. Arch. Intern. Med. (Chicago) 114: 213, 1964.

3. Agress, H.: Comparative study of spreads and sections of bone marrow. Amer. J. Clin. Path. 27:282, 1957.

4. Cartwright, G. E.: Diagnostic Laboratory Hematology (ed. 3). New York, Grune & Stratton, 1963, p. 99.