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A NEW DIAGNOSTIC TEST FOR ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS*

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THE value of the bone marrow examination as a diagnostic aid in acute disseminated lupus erythematosus has been previously reported.[1] Subsequent experience has confirmed the worth of this procedure, but difficulties have been encountered in patients with hypoplastic marrows, and in patients who are considered too sick for even the relatively minor trauma of a sternal puncture. It therefore seems appropriate to report a new diagnostic method, utilizing only the plasma of the patient acutely ill with suspected lupus erythematosus, and the cellular bone marrow of normal persons.

As originally noted by Hargraves, Richmond and Morton,[2] the striking feature of the bone marrow in acute disseminated L.E. is the L.E. cell, usually a polymorphonuclear leukocyte which has engulfed a large homogenized smoky blue material. In addition, polymorphonuclear leukocytes are occasionally seen clustered around masses of bluish staining material, forming "rosettes." These two observations have been considered as essentially the same phenomenon, with the L.E. cell as the end result (fig. 1a and b).

In a preliminary paper,[3] we reported the induction of the L.E. cell and clumping of polymorphonuclear leukocytes in normal bone marrow preparations by the simple addition of plasma from patients with acute disseminated lupus erythematosus. The phenomenon so induced was indistinguishable from those noticed in L.E. bone marrow preparations. Follow-up studies have emphasized the consistency of this response. This procedure has proved its value as a diagnostic test and as an indicator of severity of infection.

Technic

Plasma from a suspected case of acute disseminated lupus erythematosus is prepared by centrifuging oxylated blood. One half cubic centimeter of this plasma is added to the heparinized bone marrow material, freshly aspirated from a normal person.

The heparinized bone marrow and the suspected L.E. plasma are placed in a Wintrobe hematocrit tube, filling the tube as full as possible. The tube is centrifuged at 1000 RPM for five minutes, which separates the cells into a clearly defined myeloid-erythroid layer. This layer is drawn off by a pipette and smeared by the two cover slip method. Wright's stain is used.

The entire procedure after mixing takes approximately one half hour.

In our studies three hematocrit tubes were used for each bone marrow

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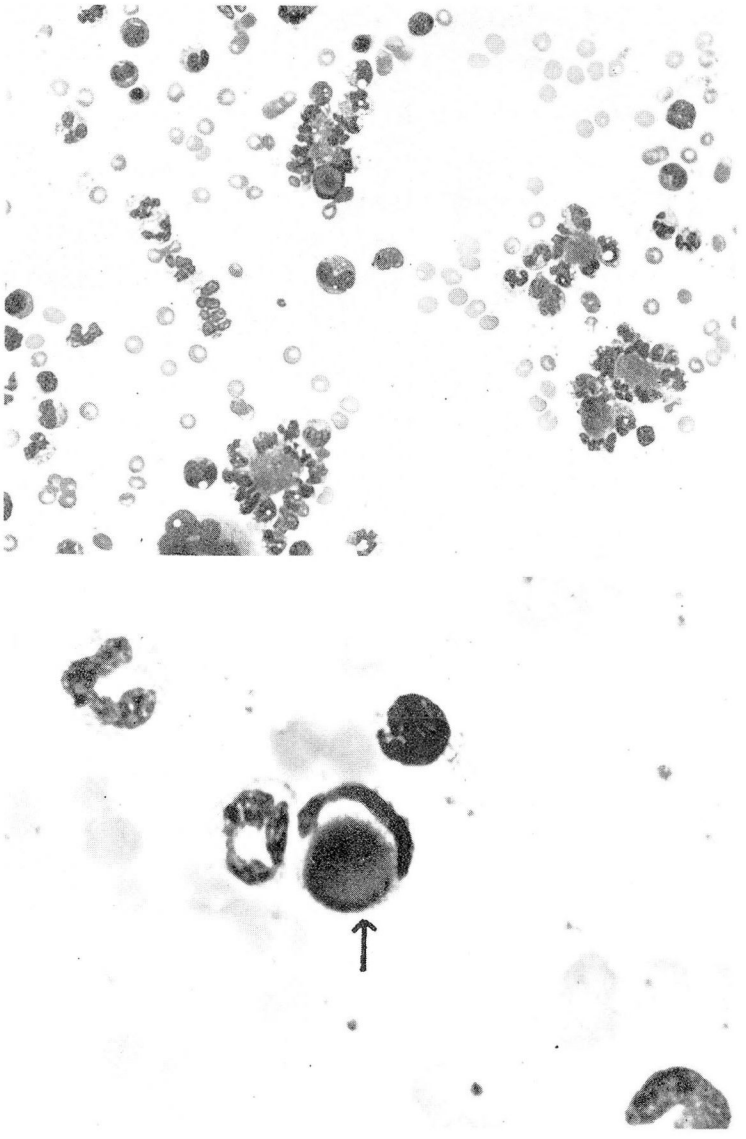
preparation. The first tube contained the normal heparinized bone marrow to which nothing had been added. The second tube contained bone marrow material plus the plasma of a patient suspected of having acute disseminated

(a)



(b)

Fig. 1. Phenomenon induced in a normal bone marrow preparation by L. E. plasma; (a) clumping of leukocytes; (b) the L. E. cell.

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lupus erythematosus. The third tube contained the normal bone marrow preparation mixed with the plasma of a clear-cut case of acute disseminated lupus erythematosus. Comparisons were made of smears from each tube to determine the number of L.E. cells and the number of "rosettes" of polymorphonuclear leukocytes.

Our laboratory for special hematology has provided us with bone marrow material from patients as they appeared consecutively. Most of such preparations are normal, or only slightly altered. Of the many patients with diseased bone marrow examinations, only those with the highly cellular marrows of leukemia have impeded the phenomenon. All bone marrow preparations are concentrated according to Limarzi's technic.[4]

Results

Plasma from each of 14 patients with acute disseminated lupus erythematosus induced L.E. cells and the clumping of leukocytes in at least two different bone marrow preparations. The phenomenon was induced in 27 consecutive normal bone marrow preparations by the plasma from a patient with acute disseminated lupus erythematosus. It was produced in six consecutive bone marrow preparations by plasma from another patient, and in 4 others by plasma from a third patient. Some of the L.E. plasma tended to produce more of the "rosettes" of polymorphonuclear leukocytes than L.E. cells, whereas others produced L.E. cells almost exclusively. Both were observed in every case. L.E. plasma was potent after three weeks of ordinary refrigeration.

The phagocytosis was not observed in bone marrow preparations from 36 patients who did not have acute disseminated lupus erythematosus. We failed to induce the phagocytic phenomenon with plasma from patients with chronic discoid lupus erythematosus, scleroderma, rheumatoid arthritis, or from 1 patient with cirrhosis who had an extremely high total gamma globulin.

The bone marrow of 3 of 7 patients with acute disseminated lupus erythematosus did not show L.E. cells. However when the plasma from these patients was mixed with normal bone marrow L.E. cells and clumping of leukocytes were produced.

Comment

From these observations it is felt that plasma from patients with acute disseminated lupus erythematosus can be of definite diagnostic value when added to normal bone marrow preparations. This test is also of merit in determining the severity of the disease, for only the plasma of acute disseminated lupus erythematosus has thus far induced the phenomena. Plasma from patients with chronic discoid lupus erythematosus produced no appreciable variation from the normal. One patient, a 20-year-old white woman, was considered to have chronic discoid lupus erythematosus in January, 1949. Her own bone marrow preparation at that time did not reveal the L.E. cell. She returned in April, 1949, complaining of increased severity of joint pains, general malaise and high fever. Her plasma then induced large numbers of the L.E. cell in

normal bone marrow preparations. The sedimentation rate and the urine albumin were also greatly increased.

There was no correlation between the induction of L.E. cells and blood group incompatibilities.

The principal value of the test seems to be in clarifying obscure diagnostic problems. The hypothesis that the fraction of the plasma which induces the phagocytic phenomenon may be related to, or actually be, the etiologic agent in acute disseminated lupus erythematosus merits serious consideration. The ability to prevent this phenomenon through the alteration of the plasma by physical or chemical means, gives rise to interesting speculation: it is possible that a drug which would prevent the L.E. phenomenon would be of actual therapeutic value. Further studies are proceeding along these lines of investigation.

Summary

Plasma from 14 patients with acute disseminated lupus erythematosus induced the L.E. cell and clumping of polymorphonuclear leukocytes in the bone marrow of 48 normal patients.

Plasma from patients with chronic discoid lupus erythematosus, cirrhosis, scleroderma, or with rheumatoid arthritis failed to induce the phenomenon.

From these observations, we believe that the following conclusions may be drawn:

1. Plasma from patients with acute disseminated lupus erythematosus contains a substance which regularly induces the L.E. cell and clumping of leukocytes in normal marrows.
2. The L.E. cell observed in the bone marrow of patients with lupus erythematosus is therefore a secondary rather than a primary phenomenon.
3. The L.E. plasma—normal bone marrow preparation is a valuable diagnostic test in acute disseminated lupus erythematosus.
4. The plasma-marrow test is an indicator of severe systemic involvement in lupus erythematosus.
5. The L.E. plasma—normal bone marrow mixture merits consideration as a useful investigative tool.

References

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