Erythrophagocytosis in a Case of Plasma Cell Leukemia

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THE PHAGOCYTOSIS of erythrocytes by circulating leukocytes and by
tissue macrophages of the reticuloendothelial system is a well known phe-
nomenon. The first recorded observation of erythrophagocytosis by bone marrow
cells is probably that of Cohnheim3 who noted the phenomenon in postmortem
marrow specimens from a man with pernicious anemia. Shortly thereafter,
Ehrlich6 described erythrophagocytosis by the circulating leukocytes in patients
having paroxysmal cold hemoglobinuria. Many reports have subsequently con-
firmed these initial observations. In most cases erythrophagocytosis in the
peripheral blood has been limited to the monocytes and granulocytes, but there
are reports in which the phenomenon was observed in lymphocytes18 and in large
circulating atypical phagocytes resembling marrow macrophages.20 A review of
the literature and of standard texts reveals no convincing reports of erythro-
phagocytosis by the plasma cell series. Du Bois7 demonstrated the absence of
phagocytosis by the plasma cells of multiple myeloma by the intravenous in-
jection of a suspension of carbon particles. In their review of the blood and bone
marrow from fifty-five patients with multiple myeloma, Diggs and Sirridge4 state that “no cells were observed which contained in their cytoplasm red cells,
pigment, or other identifiable particulate matter.” Rowley14 claims to have ob-
served erythrophagocytosis in plasma cells of peripheral blood, but from the text
descriptions and illustrations, these should probably be regarded as atypical
lymphocytes or monocytes. In 1937, Goodpasture16 reported finding intracellu-
lar E. typhosa in young plasma cells of Peyer's patches in a young man who had
died of typhoid fever. The organisms were also demonstrated within plasma cells
in regional lymph nodes draining the terminal ileum but they were not present
in bone marrow or spleen. He noted that “they [plasma cells] are never seen to
contain phagocytosed material other than the bacillary aggregates.” Recently,
we studied a case of plasma cell leukemia in which a marked degree of erythro-
phagocytosis by plasma cells of the bone marrow was demonstrated five days
before death. In view of the recent renewed interest in the mechanisms of blood
formation and destruction, it is felt that the findings warrant presentation in
some detail.

MATERIALS AND RESULTS

A marrow examination was done as a part of the initial diagnostic study. Sternal puncture
was performed in the usual manner; less than 0.5 cc. of marrow was aspirated into a dry,
sterile syringe and transferred to a clean glass slide, from which small drops containing

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Fig. 1.—Photomicrographs from bone marrow smears. × 950. (A) Plasma cell containing a phagocytized red blood cell; (B) plasma cell containing two phagocytized red blood cells; (C) plasma cell with a partially engulfed red cell within its cytoplasm; (D) plasma cell in mitosis containing an engulfed red cell; (E) the cell to the left appears to contain disintegrating red blood cells and an unidentifiable nuclear fragment. The cell to the right of center contains an engulfed normoblast. This cell is elongated but its cytoplasm is identical with that of the other plasma cells; (F) plasma cell containing an engulfed normoblast; (G) plasma cell containing an engulfed red blood cell; (H) a representative group of cells showing one neutrophilic myelocyte and numerous plasma cells.
Macroscopic marrow particles were taken with a wire loop and smeared immediately. No anticoagulant was used and there was no incubation or concentration of leukocytes. The smears were stained with Wright's stain.

The marrow was of normal cellularity. Megakaryocytes were present in normal numbers and were producing platelets. Cells morphologically characteristic of plasma cells, both mature and immature, constituted 44 per cent of the total leukocytes seen. These cells were from 15 to 30 µ in diameter, had deeply basophilic cytoplasm which was occasionally vacuolated, eccentric nuclei, and a perinuclear clear zone. In some areas nuclei that were slightly understained presented a spoke-wheel appearance. An average of 4.5 per cent of the non-erythroid cells were plasma cells containing one or more red cells (fig. 1). Several phagocytized normoblasts were observed. Erythrophagocytosis by monocytes and neutrophils was not observed. Very rarely a neutrophil engulfed by a plasma cell could be found, although the phenomenon appeared to be directed primarily against cells containing hemoglobin. A few plasma cells containing hemoglobin-like globules suggested that engulfed red cells were occasionally broken up in the process of digestion. None of these cells resembled the Russell body cells which have been adequately described and illustrated elsewhere. Additional laboratory findings were as follows: RBC 1140, WBC 9500, HGB 3.4 Gm., platelets 32,000 per cu. mm. The differential count of the white cells was: plasma cells 12 per cent, lymphocytes 42 per cent, monocytes 13 per cent, segmented neutrophils 15 per cent, stab neutrophils 8 per cent, juvenile neutrophils 1 per cent, neutrophilic myelocytes 7 per cent, eosinophils 1 per cent, and basophils 1 per cent. Three normoblasts per one hundred white cells were present.

The total serum protein was 5.1 Gm. with 3.2 Gm. albumin and 1.9 Gm. globulin. The blood urea nitrogen was 52 mg. per cent. The urine contained albumin but no Bence Jones protein. The sickle cell test was negative. The icterus index was 5.3 and the Coombs test was negative. X-rays revealed marked osteoporosis of the bones in the pelvic girdle, spine, and ribs. Several areas of relative radiolucence were present in the ribs and the right sixth rib revealed a fracture in the axillary line with early callus formation. There were no punched out areas in the skull. There was a compression fracture of the ninth thoracic vertebra.

**DISCUSSION**

Normally, senescent red cells are thought to be removed from the circulation by phagocytes in the bone marrow, spleen, and elsewhere in the body or there is intravascular hemolysis followed by phagocytosis of the end products. In certain diseases, erythrophagocytosis by marrow cells far exceeds that found in the spleen and it has been suggested that this phenomenon may play a role in the production of some cases of anemia, especially when the red marrow expands and occupies spaces which normally contain yellow marrow. Such a mechanism for the anemia associated with the leukemias may account for the results observed by Ross, et al., who showed that in some cases of leukemia there was an increased production of red cells associated with an increased rate of red cell destruction. It has been estimated that a phagocytized red cell can be completely broken down within a period of two hours. While recognizing the occurrence of erythrophagocytosis in the bone marrow at autopsy and in certain diseases, Castle does not believe that this method of blood destruction reaches significant proportions during life. Erythrophagocytosis has been reported in the polymorphonuclear neutrophils and monocytes of peripheral blood and in the macrophages of the bone marrow in a variety of conditions. We have occasionally observed the phenomenon in the myeloblasts of bone marrow in acute leukemia. Red cells engulfed by leukocytes have also been observed in cases of
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transfusion reaction, erythroblastosis fetalis, paroxysmal cold hemoglobinuria, acquired hemolytic anemia, and in various infections. Large numbers of erythroblasts have recently been reported in the incubateduffy coat layer of blood from patients with acquired hemolytic anemia. This finding has been advocated as a helpful laboratory test in establishing the diagnosis of acquired hemolytic anemia. The recent work of Jordan, et al. has shown that in paroxysmal cold hemoglobinuria both antibody and complement are necessary for phagocytosis, whereas the human isoantibodies anti-A and anti-B will bring about erythrophagocytosis in vitro when complement is absent. In the light of evidence that plasma cells produce antibodies it would seem plausible that in the case presented here an antibody rendered the patient’s red cells unusually susceptible to phagocytosis. In order to test this hypothesis normal red and white cells from a donor of homologous type (O, -D-) were suspended in the patient’s plasma and incubated at 37 C. for 1 hour. Buffy coat smears were examined and no erythrophagocytosis was observed. This single negative finding is not considered adequate to rule out autogenous factors enhancing erythrophagocytosis. Unfortunately the patient died the day after the above test was performed and further studies could not be done.

Most authorities believe that plasma cells are derived from reticulum cells. The observations in this case suggest that under certain circumstances plasma cells may retain or acquire the phagocytic properties of their reticulum cell line. It is felt that erythrophagocytosis was an important factor in the production of the severe anemia in this patient. The layman’s concept that in leukemia “the white cells eat up the reds” may not be entirely without basis in fact.

SUMMARY

A case of plasma cell leukemia is presented in which erythrophagocytosis by cells of the plasma cell series occurred. This case serves to add the cells of the plasma cell series to those of the monocytic and granulocytic series as cells capable of erythrophagocytosis under certain conditions.

REFERENCES

6 ---: The type of phagocytic cell and its relative proportions in human bone marrow and spleen as identified by the supravital technique with special reference to pernicious anemia. J. Exper. Med. 43: 289, 1926.
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