

# Erythrophagocytosis by Myeloid Cells in a Patient with Myeloproliferative Disorder

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This report documents a case of myeloid erythrophagocytosis in a patient with myeloproliferative disorder. The patient had pancytopenia and his marrow was hyperplastic with erythrophagocytosis by myeloid cells of various stages, including myeloblasts. He was diagnosed to have a prefibrotic stage of chronic idiopathic myelofibrosis. The erythrophagocytosis by myeloid cells persisted even after 2 months of treatment for the primary disorder.

**Key Words:** Myeloid erythrophagocytosis, myeloproliferative disorder, pancytopenia

## INTRODUCTION

Erythrophagocytosis by myeloblasts has been reported in only a few patients with acute myeloid leukemia,<sup>1-5</sup> chronic myelogenous leukemia in blast crisis,<sup>6</sup> and myelodysplastic syndrome.<sup>7</sup> Immature myeloid cells such as promyelocytes, myelocytes, metamyelocytes, as well as band neutrophils showing erythrophagocytosis, have also been reported in a patient with refractory anemia with an excess of blasts in transformation.<sup>7</sup>

We report here a case of erythrophagocytosis by myeloid cells in a patient with a prefibrotic stage of chronic idiopathic myelofibrosis and with secondary myelodysplasia. To our knowledge, this is the first such case of erythrophagocytosis by myeloid cells in Korea.

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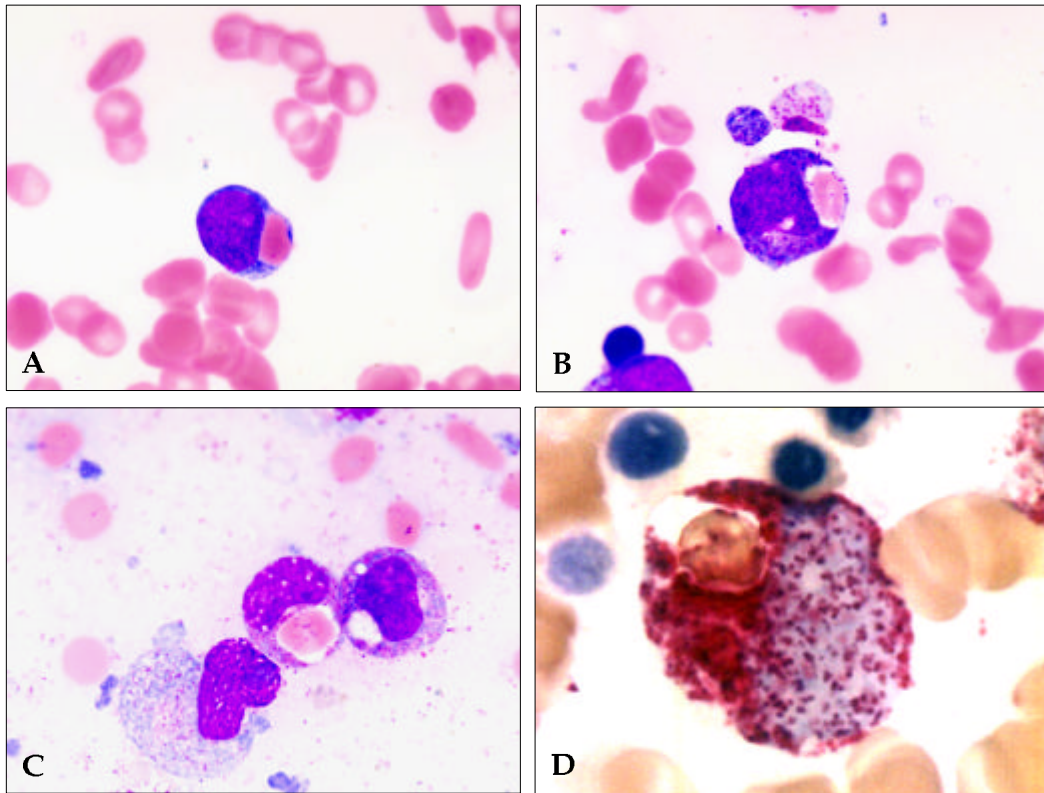
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## CASE REPORT

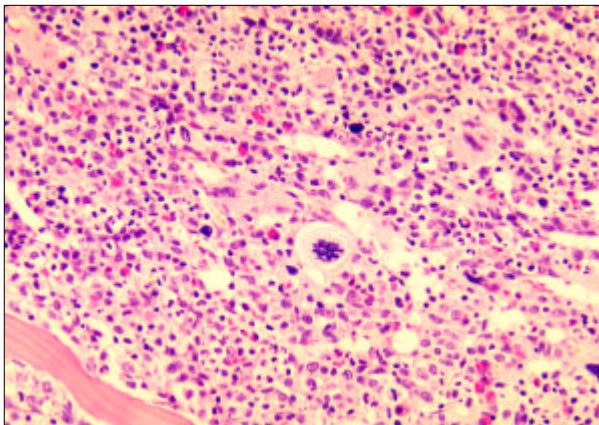
A 57-year-old man was admitted to the Ajou University Hospital in January 2001, complaining of persistent anal bleeding after an operation for an anal fissure at a local clinic. On admission, his palpebral conjunctivae were slightly pale but no other physical abnormality was observed.

Peripheral blood count revealed pancytopenia (white blood cell [WBC] count  $1.5 \times 10^3/\mu\text{L}$ , hemoglobin [Hb] 7.9 g/dL, and platelet count  $12 \times 10^3/\mu\text{L}$ ). A bone marrow study revealed a shift to the left of the myeloid series, several foci of abnormal localization of immature precursors (ALIP), and dysplastic changes of the myeloid and megakaryocytic series. All maturation stages of myeloid precursors showed erythrophagocytosis (Fig. 1). Monocytes and lymphocytes engulfing red blood cells were also present, although rarely. No cells engulfing normoblasts, myeloid cells, or platelets were observed. The cellularity of bone marrow was 90% with panmyelosis (Fig. 2). Plasmacytosis (2%) with several Russell bodies was also observed. Reticulin and Masson trichrome stains revealed a mild increase in reticulin and collagen fibers. The patient was diagnosed to have a cellular phase of idiopathic myelofibrosis with secondary myelodysplasia.

In addition, the patient showed seropositivity for Epstein-Barr virus (EBV)-early antigen (EA) IgM, EBV-EA IgG, Epstein-Barr virus nuclear antigen (EBNA) IgG, viral capsid antigen (VCA) IgG, and cytomegalovirus (CMV) IgM. Cytogenetic analysis was performed using a routine G-banding method which revealed 46, XY. He was treated conservatively with granulocyte-colony stimulating factor (G-CSF), blood transfusion, and



**Fig. 1.** Bone marrow aspirate (A to C, Wright-Giemsa stain; D, specific esterase stain) showing erythrophagocytosis in a variety of the myeloid cells. A, myeloblast; B, promyelocyte; C, myelocyte; D, specific esterase positivity in an erythrophagocytic myeloid cell.



**Fig. 2.** Bone marrow biopsy (H&E stain) showing hypercellular marrow with panmyelosis.

antibiotics, for a period of 60 days.

Seventy days after the initial admission his anemia was aggravated and he was readmitted. Pancytopenia (WBC count  $1.8 \times 10^3/\mu\text{L}$ , Hb 4.9 g/dL, and platelet count  $21 \times 10^3/\mu\text{L}$ ) with an

increase in the number of normoblasts (20/100WBCs) was noted. Examination of the bone marrow at this time revealed 100% cellularity, marked erythroid hyperplasia (myeloid : erythroid ratio=1 : 10), and secondary dysplastic changes in the erythroid and myeloid series. Erythrophagocytosis by myeloid cells was again observed. The patient was treated with low-dose Ara-C, G-CSF, and blood transfusion. After discharge he was administered with erythropoietin, G-CSF, folic acid, and vitamin B complex as an outpatient for 15 months.

Two years after the first admission, follow-up bone marrow aspiration and biopsy were performed. The aspiration failed and the biopsy revealed a marked increase of reticulin fibers with osteosclerosis, indicating progression to a fibrotic stage of chronic idiopathic myelofibrosis. No evidence of progression to overt leukemia was detected in samples of the peripheral blood obtained throughout his clinical course.

## DISCUSSION

Phagocytosis involves two steps: "binding" and "ingestion". The receptors involved in "binding" include CR1 (binding C3b) and CR3 which are receptors for complement; receptors for IgG, Fc receptors (FcR); and the receptor for fimbriae, gp150. CR1 initially appears in band-form neutrophils, CR3 and FcR are first detected at the promyelocyte stage, and gp150 is first detected at the myelocyte stage.<sup>8</sup> The C3 receptor tightly binds C3b but not native C3. On the other hand, it is well known that the complement system is activated and C3b is therefore readily available in disseminated intravascular coagulation. Lobreglio and Valacca reported a case of immune hemolytic anemia showing peripheral blood granulocytes that had phagocytized erythrocytes.<sup>9</sup>

It is not clear why erythrophagocytosis appears in the myeloid cells. It has been reported that certain leukemic blasts show normal phagocytic response, although the digestion of the engulfed erythrocytes may be slow.<sup>10</sup> Kuyama, et al. reported a case of myelodysplastic syndrome associated with erythrophagocytosis by blasts and myeloid cells, but not in monocytes or macrophages.<sup>7</sup> They assumed either an aberrant expression of Fc or C3b receptor or a lack of an adequate amount of lysosomes to digest the engulfed erythrocytes in the myeloid cells. Some investigators suggest an association of several cytokines such as IL-2, IFN- $\gamma$ , and TNF- $\alpha$ .<sup>11,12</sup> Mori, et al. reported that the expression of mRNA of TNF- $\alpha$  was greatly increased as detected by semi-quantitative RT-PCR on the bone marrow mononuclear cells in a patient with minimally differentiated, acute myeloid leukemia showing erythrophagocytosis.<sup>2</sup> Unfortunately, we could not perform any tests that could confirm the possible mechanisms of the erythrophagocytosis mentioned above.

All patients that have been reported to show erythrophagocytosis by myeloblasts and/or other myeloid cells, including the present case, had clonal disorders, such as acute or chronic leukemia, myelodysplastic syndrome, and myeloproliferative disorders as in our case. We suggest that the abnormalities which induce erythrophagocytosis might occur at a stem cell level. However, further study may be necessary to prove the clonality of

the myeloid cells showing erythrophagocytosis.

The patient described showed seropositivity for EBV IgM and CMV IgM, and the possibility of virus associated hemophagocytic syndrome was also considered. However, the latter possibility involves histiocytes and/or macrophages, which engulf normoblasts, erythrocytes, myeloid cells of various stages, and/or platelets. The bone marrow cells showing erythrophagocytosis in this case were proved by simple morphology and specific esterase stain to be myeloid cells (Fig. 1).

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