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LETTER TO THE EDITOR

Erythrophagocytosis of Peripheral Blood Smear in Antiphospholipid Syndrome Associated with B-Cell Lymphoma

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A 54-year-old woman was referred to our hospital because of intermittent fever for one month. She had a history of spleen marginal zone B-cell lymphoma and antiphospholipid syndrome (APS) for three years and four months, which was untreated by chemotherapy after the first chemotherapy. Physical examination revealed anemia and no jaundice and petechiae. No superficial lymphadenopathy was palpable. Liver was not palpable, and spleen is missing. Her full blood count revealed WBC 9.30 x 10^9/L (neutrophil absolute value of 6.30 x 10^9/L); Hb 100 g/L (normal value 115 - 150 g/L); PLT 415 x 10^9/L (normal value 125 - 350 x 10^9/L). Biochemistry tests of the serum revealed elevated levels of lactate dehydrogenase 352 U/L (normal value 120 - 250 U/L), α-hydroxybutyrate dehydrogenase 269 U/L, creatine kinase 34 U/L, β2-macroglobulin 3.9 mg/L, vitamin B12 204 pg/mL, precursor of type B natriuretic peptide 303 pg/mL, total protein 62.2 g/L, albumin 37.3 g/L, prealbumin 0.15 g/L, γ-glutamate transpeptidase 52 U/L, adenosine deaminase 22 U/L, total cholesterol 2.91 mmol/L, high density lipoprotein cholesterol (HDL-c) 0.68 mmol/L, low density lipoprotein cholesterol (LDL-c) 1.88 mmol/L, apolipoprotein A 0.85 g/L, PT 15.1 s, PTA 64%, INR 1.32, APTT 53.7 s, FDP 31.8 mg/L, D-dimer 6.14 μg/mL, procalcitonin 0.07 ng/mL, c-reactive protein 89.9 mg/L, transferrin 1.57 IU/mL, anticardiolipin antibody 285.54 RU/mL, complement 3 0.46 g/L, and complement 4 0.05 g/L. In

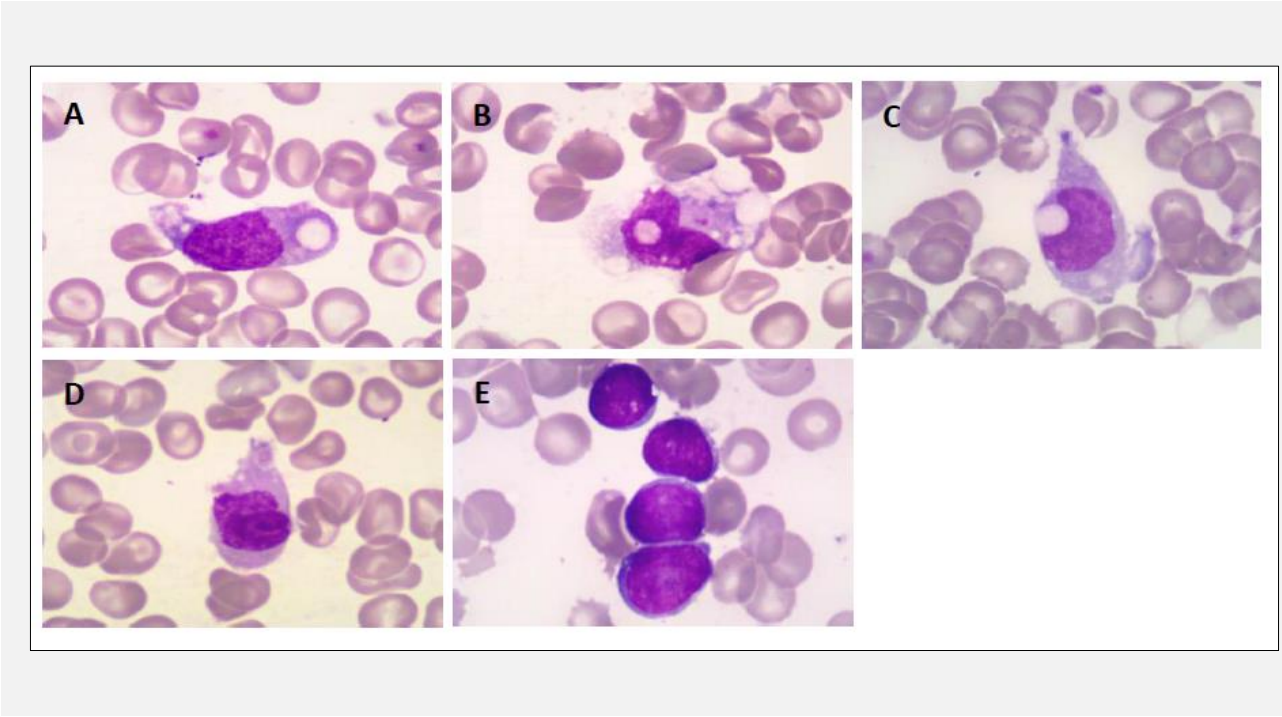

Figure 1. Erythrophagocytosis by monocytes (A - C) and monocyte engulfment of platelets (D) were shown in peripheral blood smear; primitive lymphocytes and immature lymphocytes (E) were shown in bone marrow smear (Wright-Giemsa stain, 1,000 x).

addition, she had positive direct Coombs' tests. Systemic CT scan demonstrated numerous lymph nodes in the left carotid artery space, left supraclavicular fossa, head of the pancreas, retroperitoneal space, and bilateral iliac vessel involvement.

Microscopic examination of a blood film presented primitive lymphocytes and immature lymphocytes (of atypical lymphocytes) accounting for 7% of the white blood cells. Remarkably, erythrophagocytosis by monocytes (Figure 1A - C) and rare monocyte engulfment of platelets (Figure 1D) can be found. The bone marrow aspiration showed active proliferation of bone marrow cells showing primitive lymphocytes and immature lymphocytes (atypical lymphocytes) accounting for 12% of the nucleated cells (Figure 1E). A bone marrow biopsy shows B-cell invasion of the bone marrow. Bone marrow flow cytometry results suggested $CD5^{-}CD10^{-}$ B cell lymphoma. Overall, the findings were consistent with bone marrow involvement by a peripheral splenic B-cell lymphoma (stage IV Group B) with APS. The patient was administered R-CHOP regimens, rituximab 0.6 g for 5 days, vindesine 2 mg for 1 day, cyclophosphamide 400 mg for 1 - 2 days, doxorubicin 20 mg for 1 - 2 days, dexamethasone acetate 20 mg for 1 - 4 days and supplemented by acid inhibition, antiemesis and supplementation of hematopoietic elements. After the end of one course, the patient was discharged with complete remission.

Erythrocytes can be phagocytized by a variety of cells, such as neutrophils, monocytes, and tumor cells, in myelodysplastic syndromes (MDS), acute leukemia, and lymphoma [1,2]. Erythrophagocytosis in peripheral blood is a rare phenomenon which has been significantly related with an autoimmune hemolytic anemia (AHA), most notably the paroxysmal cold hemoglobinuria (PCH) with autoimmune deficiency disease [1,3,4]. In general, erythrophagocytosis by neutrophils in peripheral blood is relatively common with apparent infection or preceding infection represented the clearance of abnormal erythrocytes due to autoimmune dysregulation [1,5]. In this case, erythrophagocytosis by peripheral monocytes is in the context of lymphoma and APS. Pedrote et al. reported a case of diffuse large B cell lymphoma with erythrophagocytosis by peripheral monocytes and histiocytes, and the patient was hepatosplenomegaly, with numerous mediastinal and abdominal lymph nodes and pulmonary involvement, however, negative for comprehensive autoimmune and infectious evaluation [6]. Olaiya et al. and Park et al. separately presented a 14-year-old girl and 3-year-old boy with erythrophagocytosis by leukemic blasts in B-cell acute lymphoblastic leukemia, and *ETV6/RUNX1* gene rearrangement and good prognosis [7,8]. Frame et al. presented a bone marrow involvement by peripheral T-cell lymphoma in a patient with hereditary spherocytosis post-splenectomy, and erythrophagocytosis by T-cell

lymphoma cells both in peripheral blood film and bone marrow biopsy touch imprint [9]. We have also reported a case with Evans syndrome whose peripheral blood smear showing erythrophagocytosis by monocytes. APS is a rare autoimmune disease, and the mechanism underlying hemophagocytic phenomenon related to APS remains unclear.

In conclusion, when a patient's peripheral hemophagocytic phenomena is recognized, the clinician should consider the possibility of the leading primary disease, especially in the absence of typical clinical features.

Ethical Approval:

An approval by the ethics committee was not necessary for the reason that all the data were acquired through tests conducted for clinical purposes. The patient signed an institutional informed consent for receiving treatments.

Declaration of Interest:

The authors report no conflict of interest.

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