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Transient Spontaneous Remission in Acute Promyelocytic Leukemia

— Two Case Reports —

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Two cases of spontaneous remission in acute promyelocytic leukemia are reported. They had precedent febrile episodes and subsequent resolution of all clinical and hematological abnormalities occurred after supportive care including administration of various antibiotics. Their remissions lasted for 12 and five months respectively, when they relapsed.

Key Words: *Spontaneous remission, Acute leukemia*

INTRODUCTION

Spontaneous remissions are very rare in acute myelocytic leukemia in adults. Although a number of cases before 1955 were reported with poor documentation of the diagnosis and remission, only a few cases have been reported after that, reflecting the use of more precise criteria for complete remission (Rai et al., 1981), and the onset of active chemotherapeutic treatment. In Korea, there is no reported case of spontaneous remission in acute myelocytic leukemia. We report two cases of spontaneous complete remission of acute promyelocytic leukemia in adults.

REPORT OF CASES

Case 1:

A 19-year-old woman was transferred to Seoul National University Hospital on April 16, 1990 with a diagnosis of pneumonia and acute leukemia. Her body temperature was 38.2°C, pulse 115/min, and blood pressure 120/80mmHg. Hepatomegaly was found. Chest X-ray showed pneumonic infiltration of the right lower lobe. Hemoglobin was 6.2g/dL, leukocyte count 3.8×10^9/L. Bone marrow aspirates and biopsy showed hypercellularity with 70% of myeloblasts and promyelocytes containing multiple Auer rods, which were the findings of an acute promyelocytic leukemia (Fig. 1). The parenteral treatment of antibiotics was started. Blood and urine cultures were negative. Her fever waxed and waned but her platelet count had risen without any transfusion (Fig. 2). The second bone marrow study was performed on May 14, 1990. It showed hypercellular marrow with an increase of normal hemopoietic cells and a decrease of leukemic cells. Myeloblasts were counted to 2% and abnormal cells containing Auer rods were rarely observed. The marrow was considered to represent a phase of recovery from leukemia. Thereafter, the hemoglobin level, leukocyte and platelet count continued to rise without the aid of transfusion. The marrow taken on May 24, showed myeloid hyperplasia with normal maturation. No Auer rods were encountered (Fig. 1). Acid fast bacilli were found in transtracheal aspirates taken with a fiberoptic bronchoscopy on May 30. Treatment against tuberculosis was started. The patient continued to improve throughout the rest of her hospitalization and was discharged on June 1. Bone marrow studies were done twice, on June 11 and 24, which were interpreted to be normal.

On June 16, 1991, she was admitted via the emergency room with alteration of consciousness and blindness in both eyes. At that time, hemoglobin was 5.1g/dL, leukocytes 55.3×10^9/L and platelets

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21×10^9/L. The differential count of peripheral blood leukocytes showed 94% of myeloblasts and atypical promyelocytes with a similar morphology to the first occasion. Four days later, she died despite a blood transfusion and other supportive care.

Case 2:

A 19-old male was admitted to Seoul National University Hospital on August 23, 1991 with fever and an abscess on the left gluteal region. There was gener-

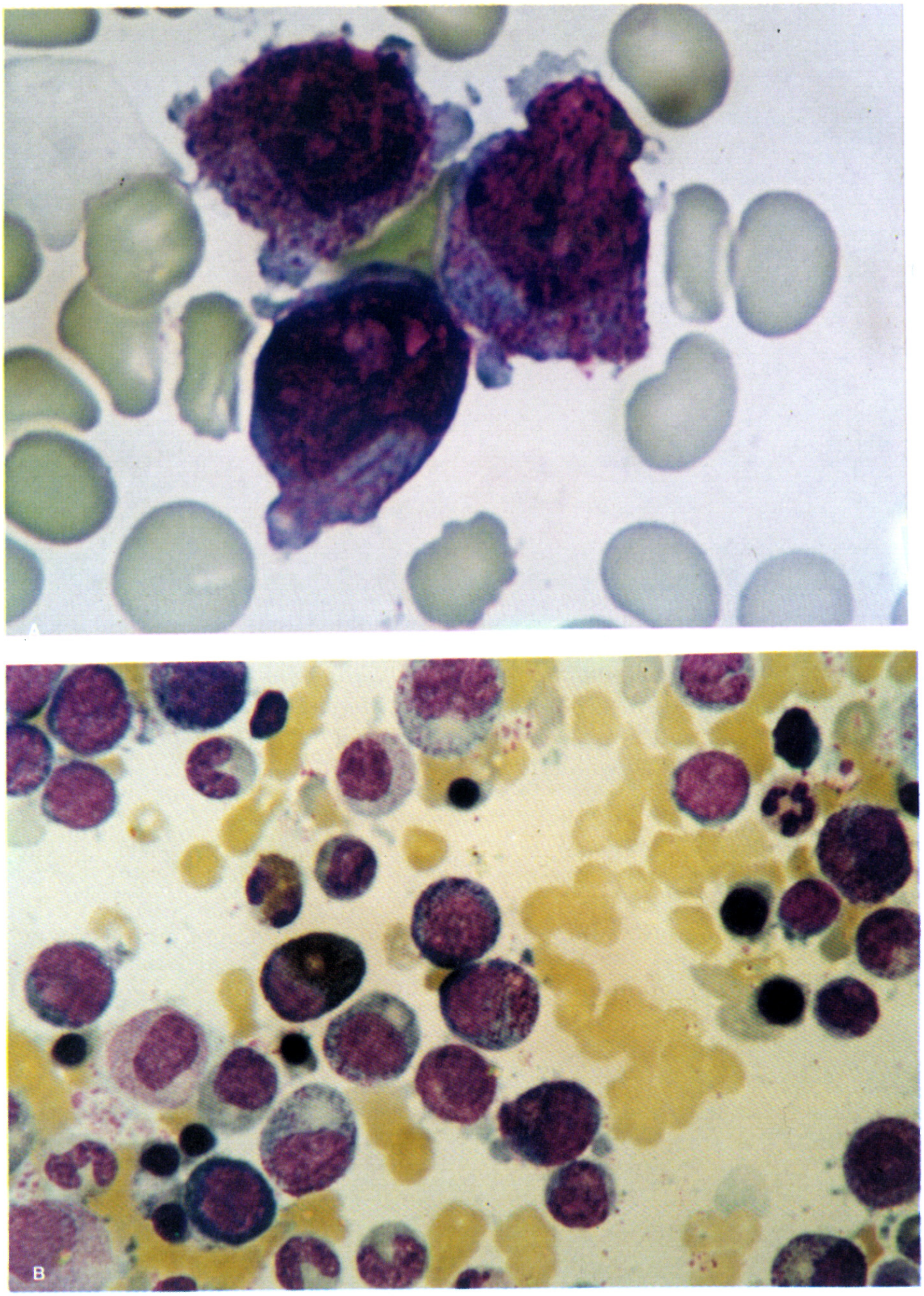

Fig. 1. (case 1). (A) Bone marrow aspirate obtained at the time of initial presentation showing leukemic promyelocytes containing multiple Auer rods. (Wright-Giemsa stain, ×1000). (B) Bone marrow at spontaneous remission showing mild granulocytic hyperplasia. (Wright-Giemsa stain, ×400)

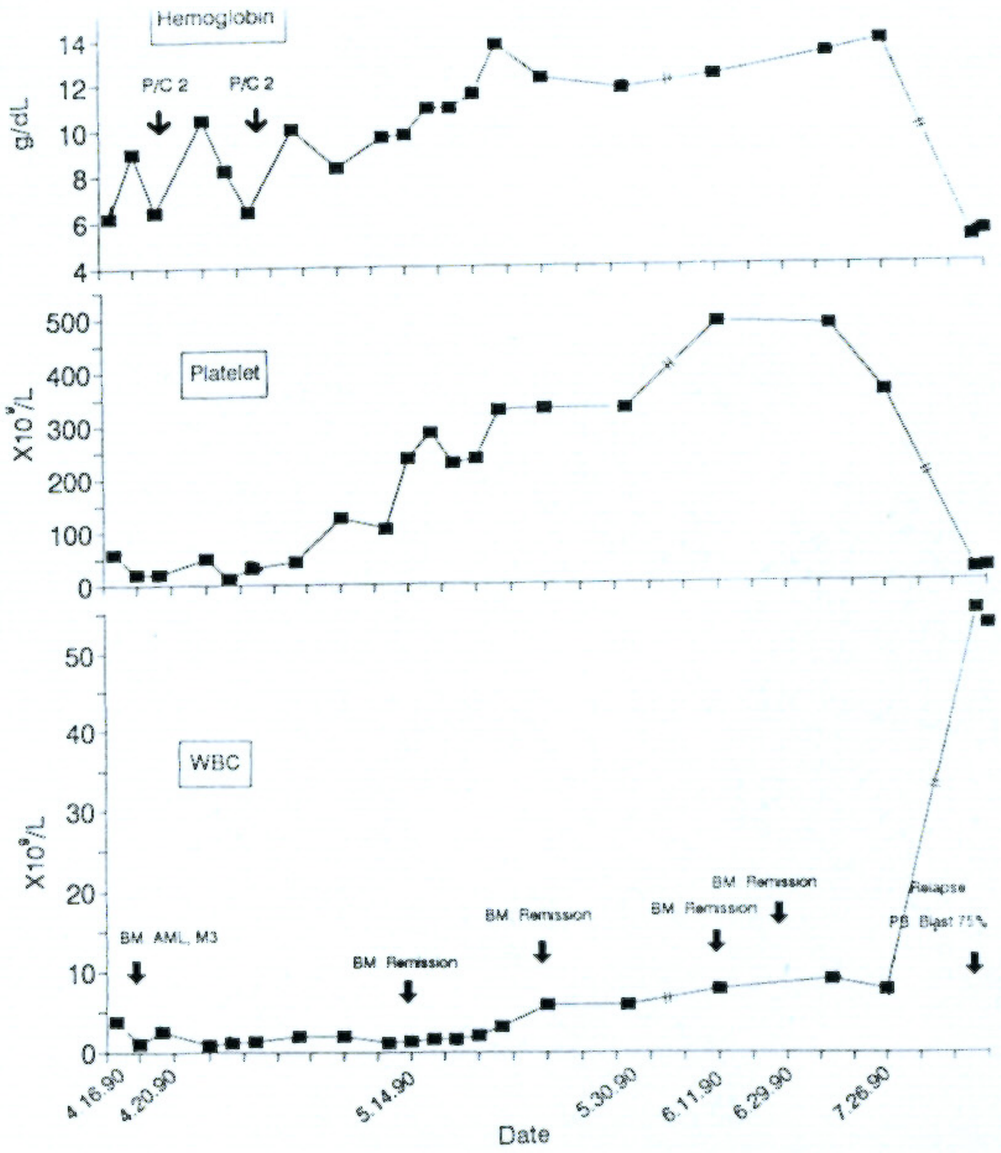

Fig. 2. (case 1). Sequential hematological changes from initial diagnosis until relapse

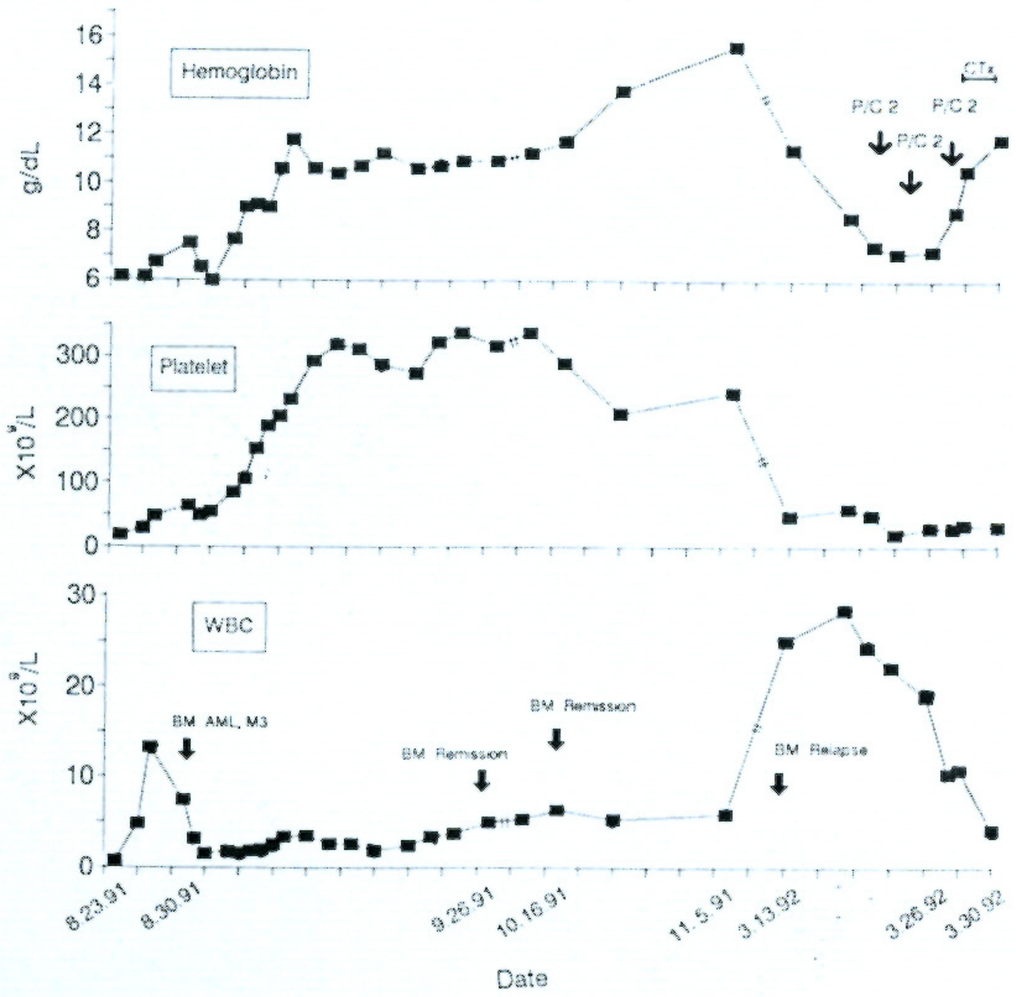

Fig. 4. (case 2). Sequential hematological changes from initial diagnosis until relapse

alized swelling of the left leg and scrotum. Hemoglobin was 6.1g/dL, leukocyte 0.6×10^9/L and platelet 18×10^9/L. A bone marrow study showed hypercellular marrow with 71% of myeloblasts and promyelocytes, which was diagnosed as an acute promyelocytic leukemia (Fig. 3). Incision and drainage of the abscess was performed and parenteral administration of antibiotics was started. The pus cultures were negative. His general condition deteriorated with increasing spread of cellulitis. Induction chemotherapy for the treatment of acute promyelocytic leukemia was withheld because of the poor physical condition of the patient. His platelet count and hemoglobin level began to improve (Fig. 4). From the 20th hospital day, the infection responded to the aggressive treatment with antibiotics and the leukocyte count began to rise. On October 26, a second bone marrow study was done. The bone marrow showed mild granulocytic hyperplasia with 1.4% of blasts and promyelocytes (Fig. 3). So, he was discharged in excellent physical condition and he continued well.

After five months, on May 16, 1991, his leukocyte count began to rise and bone marrow contained 86% of blasts and promyelocytes including many faggot cells. Induction chemotherapy for the treatment of acute promyelocytic leukemia was started but four days later, he died of intracranial hemorrhage.

DISCUSSION

Many cases of spontaneous remission in adults with acute myelogenous leukemia have been reported, but not all of these cases were well-documented. Since 1955, only a few cases have been reported. However such spontaneous complete remission still exists and the decrease in the frequency of spontaneous remission may be due to stricter criteria for complete remission and active chemotherapeutic treatment. Unfortunately, in the previous reports of spontaneous remissions, these remissions did not appear to carry with them an increase in overall patient's survival (Lachant et al., 1979, Van Eys et al., 1969).

In our cases, the diagnosis of acute promyelocytic leukemia was made in the presence of pancytopenia with myeloblasts and atypical promyelocytes over 30% including faggot cells in marrow aspirates. During the period of spontaneous remission, hemograms and bone marrow findings returned to normal. All clinical signs and symptoms of acute leukemia disappeared. At that time, we could not rule out the possibility of non-malignant disease including leukemoid reaction with maturation arrest (Levine et al., 1968, Innes et al., 1987). In tuberculosis patients such as case 1, their various bone marrow findings have been reported which mimic acute myelogenous leukemia (Twomey

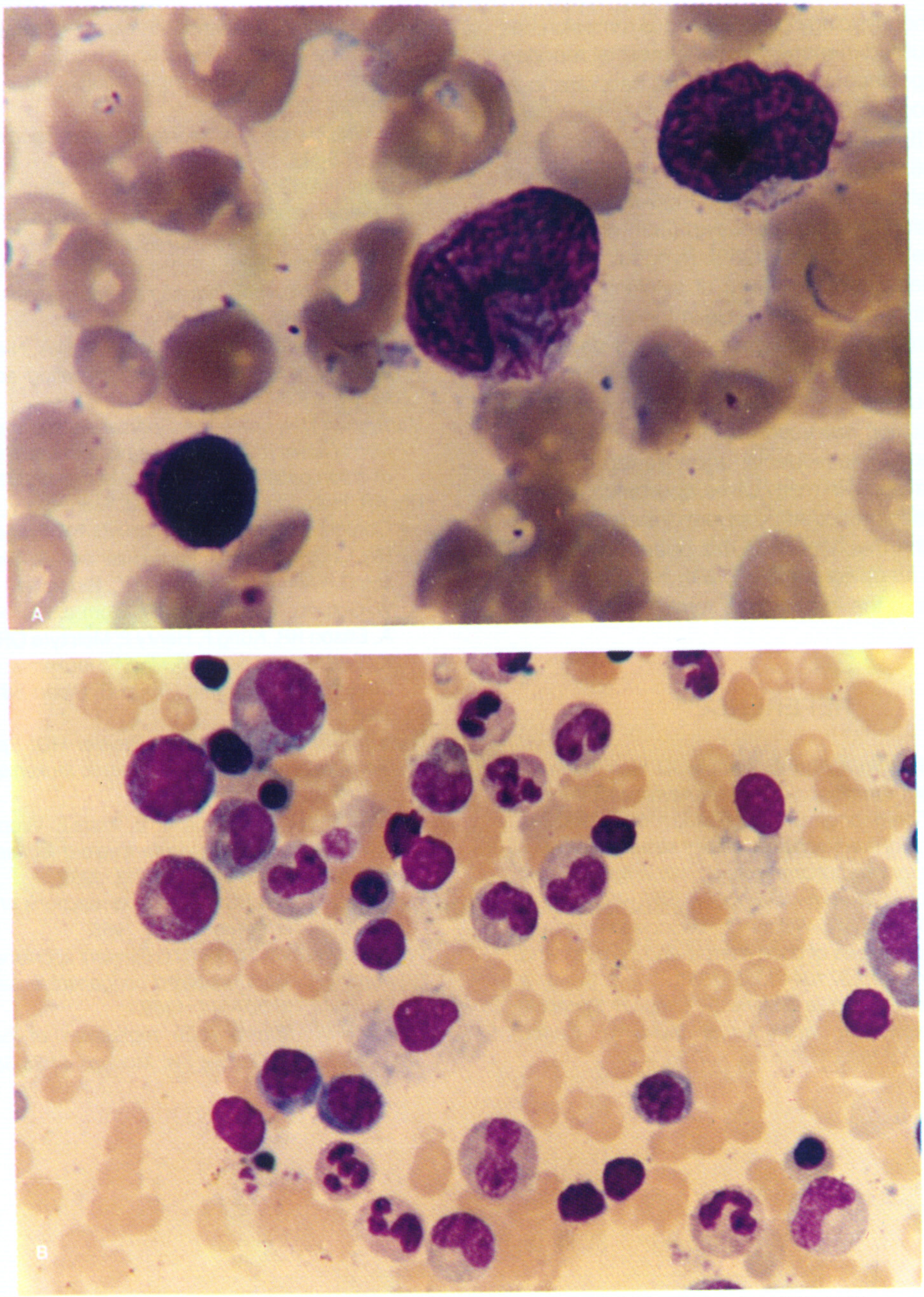

Fig. 3. (case 2). (A) Bone marrow aspirate obtained at the time of initial presentation. (Wright-Giemsa stain, ×1000). (B) Bone marrow during remission period showing normal distribution of hemopoietic cells. (Wright-Giemsa stain, ×400)

et al., 1965, Evans et al., 1952, Mildner, 1961). But the bone marrows of our cases were extremely infiltrated with a major cells containing multiple Auer rods as well as abnormal granularity. The blasts with the same morphologic abnormalities reappeared in peripheral blood later. Thus we ruled out the possibility of leukemoid reaction. Indeed, these cases are unpredictable and present diagnostic difficulties.

The pathophysiology of spontaneous remission has been discussed in many reports. Almost all reported cases of spontaneous remission have been associated with pyogenic infections (Lachant et al., 1979, Wiernik et al., 1976, Ruutu et al., 1982, Raza et al., 1985, Jehn, 1986, Narayanan, 1991). The associations of blood transfusion or hormonal change with spontaneous remission are also suggested (Ifrah et al., 1985, Antunez de Mayolo et al., 1989). Pyogenic infections are associated with activation of cytokine networks which are thought to have a role in the stimulation of normal hemopoiesis and suppression of neoplastic clones (DeLamater, 1988). But the mechanism of spontaneous remission is not yet clear. In case 2, initial manifestation was accompanied with leukocytosis and subsequent leukopenia, and followed by spontaneous remission. In many cases, spontaneous remission had been preceded by severe granulocytopenia. Whatever the mechanism of this phenomenon may be, there is an obvious analogy with the effect of cytotoxic drugs in the induction of remission.

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