A Middle-aged Man with High-grade Fever, Non-productive Cough, Weight Loss for 2 Weeks.

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Abstract:

A 55-year-old man, a carpenter in northeastern Thailand with no underlying disease presented with acute onset of fever with chills, non-productive cough, weight loss of 3 kilograms in 2 weeks. He also experienced easily fatigue and tiredness for 1 month. He went to local hospital and was diagnosed pancytopenia. He received 3 units of packed red cells and 1 unit of platelet concentrate without significant improvement. Then he was referred to another hospital for investigation. After blood smear review, there were many abnormal white blood cells with numerous small cytoplasmic granules. The bone marrow examination and cytogenetics revealed diagnosis of acute promyelocytic leukemia. So, in case of pancytopenia without apparent causes, blood smear and bone marrow examination can be helpful in definite diagnosis.

Keywords: Pancytopenia, promyelocytic leukemia, high-grade fever

Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) with distinctive biologic and clinical features that is now highly curable. Most patients are young, present with leukopenia or pancytopenia and exhibit a life-threatening coagulopathy because of procoagulant released from cytoplasmic granules. The leukemic promyelocytes cells from almost all patients have a balanced reciprocal translocation[1] between chromosomes 15 and 17 which generates a fusion transcript joining the PML (promyelocyte) and RAR-α (retinoic acid receptor-α) genes[2]. They have the unique ability to undergo differentiation with exposure to retinoic acid and both differentiation and apoptosis with exposure to arsenic trioxide (ATO)[3]. Because APL patients can be cured up to 80-90% according to risk classification with ATRA (all trans retinoic acid), ATO (arsenic trioxide) and chemotherapy, so definite diagnosis is required and, in the patients suspected APL, treatment with ATRA should be started without delay because bleeding from coagulopathy is serious and major cause of death. There are 2 variants of APL, hypergranular and microgranular. Multiple Auer rods were common in hypergranular promyelocytes but in microgranular variant,

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the leukemic promyelocytes were characterized by striking nuclear folding, and the nuclei frequently appeared bilobed or reniform. However, the granularity of the leukemic cells may show considerable variation, even within the same patient[4]. The definite diagnosis of APL requires demonstration of balanced reciprocal translocation between chromosome 15 and 17 by cytogenetic study or FISH (Fluorescence in situ hybridization).

Case Presentation

A 55-year-old man, a carpenter in north-eastern Thailand, presented with high-grade fever with chills for 2 weeks. He also experienced non-productive cough, easily tiredness and weight loss of 3 kilograms in the past 2 weeks. He had anorexia, normal bowel movement and urination. At the local hospital, the complete blood count showed pancytopenia with promyelocytes and myelocytes. Then antibiotics, along with packed red cell and platelet transfusion was administered without significant improvement. He was subsequently referred to another medical center hospital for investigation and further management. On admission at this hospital, vital signs showed body temperature of 39.4^{o}C, heart rate 100/minute, blood pressure 141/83 mmHg, respiration 26/min and oxygen saturation of 97%. He had no palpable lymphadenopathy, liver and spleen was also impalpable. No skin bleeding was detected. Investigation revealed Hct 26%, WBC 2.32 x 10^9/L, PMN 15%, L 44%, M 30%, promyelocyte 10%, platelet 22.0 x 10^9/L, MCV 87.6 fL, MCH 30.9 pg, LDH 467 U/L (120-246), PT 13.4 second, INR 1.18, APTT 28.9 second, C 25.3, TT 8.6 second, C 7.1, fibrinogen 217.4 mg/dL, uric 1.9 mg/dL, anti-HIV negative, chest x-ray: borderline cardiomegaly, no pulmonary infiltration, bilateral paratracheal shadowing (Figure 1), ultrasound abdomen showed multiple gall stones with evidence of chronic cholecystitis. Review of blood smear found many abnormal white blood cells having bilobed nuclei with numerous cytoplasmic granules. (Figure 2A and 2B) Then bone marrow aspiration and biopsy with cytogenetic study was performed. The finding revealed hypercellular bone marrow 3+ with decreased erythroid cells, many abnormal cells with numerous fine granules similar seen in blood smear and rarely seen Auer's rod (Figure 3A, 3B and 4) These abnormal cells were consistent with abnormal promyelocytes and so the diagnosis of acute promyelocytic leukemia, microgranular variant was made. Because of low initial white blood cells and platelet count, the patient was classified intermediate risk group. ATRA was started on the following day without delay.

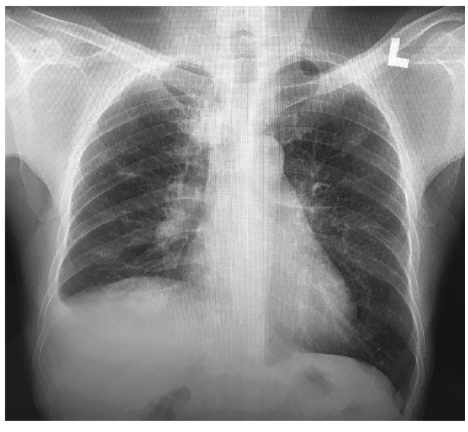

Figure 1 Chest x-ray shows bilateral paratracheal shadowing

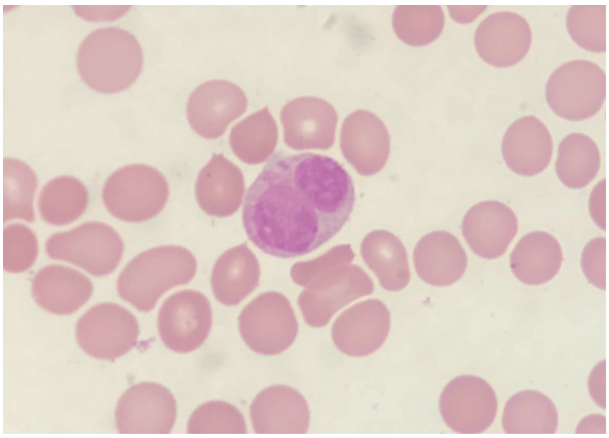

Figure 2A Blood smear shows immature myeloid cell with binucleated nucleus and cytoplasmic granules consistent with abnormal promyelocyte (x100)

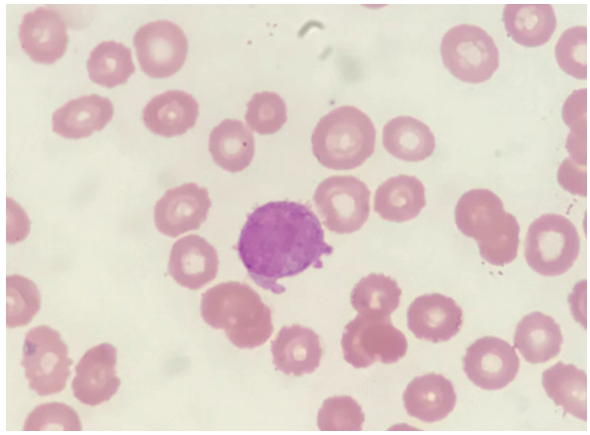

Figure 2B Blood smear shows abnormal promyelocyte with numerous cytoplasmic granules (x100)

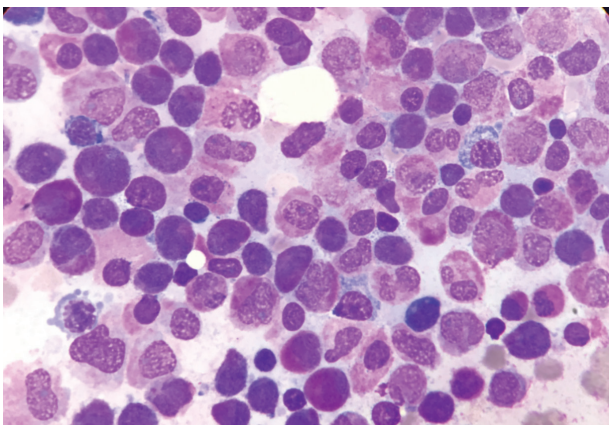

Figure 3A Bone marrow smear shows hypercellular marrow with increased promyelocytes (x100)

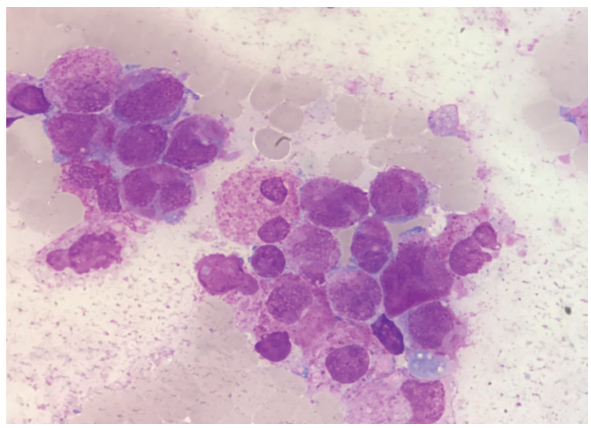

Figure 3B Bone marrow smear shows abnormal promyelocytes with binucleated and numerous granules (x100)

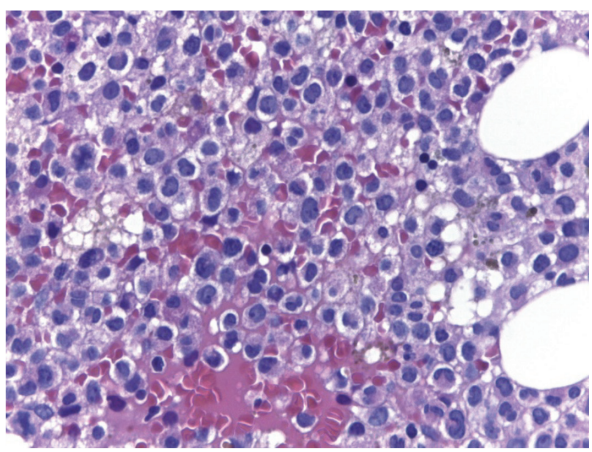

Figure 4 The bone marrow core biopsy shows markedly hypercellular marrow with numerous blastoid cells with moderate amount of eosinophilic cytoplasm (x40)

Discussion

This patient was a 55-year-old man with acute illness. He had intermittent high-grade fever, cough, easily tiredness, anorexia and weight loss. He had no organomegaly or significant bleeding lesion. CBC showed pancytopenia, so differential diagnosis should be bone marrow failure by myelophthisis from abnormal cells, infection, marrow necrosis, drug-related effect or destruction of hematopoietic precursors in the bone marrow such as hemophagocytosis. Because his clinical, blood and bone marrow aspirate cytology were suspicious of acute promyelocytic leukemia, so ATRA should be initiated without delay for cytogenetic or FISH study. Finally, on day 5 after admission, bone marrow cytogenetics revealed t (15;17) (q24; q21) which is characteristic of acute promyelocytic leukemia. This patient had no clinical bleeding, which is common in typical APL, because of early transfusion from the local hospital.

Conclusion

The authors reported case of APL which was able to make early diagnosis from blood and bone marrow smear. In case suspected APL, early initiation of ATRA should be done before definite diagnosis by cytogenetic or FISH study.

Conflict of interest

The author has declared no conflict of interest.

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