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Acute mono-megakaryoblastic leukemia associated with extreme thrombocytosis and complex karyotype abnormalities

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Patient: Female, 55
Final Diagnosis: Acute leukemia
Symptoms: Thrombocytosis
Medication: Idarubicin HCl (Zavedos), Pfizer
Clinical Procedure: —
Specialty: Hematology

Objective: Adverse effect of drug therapy
Background: Thrombocytosis is usually seen in myeloproliferative disorders (MPD) and seldom in acute myeloid leukemias (AML). In acute megakaryoblastic leukemia, platelet counts might exceed $1000 \times 10^9/L$ in approximately 30% of patients, while others are frequently presented by cytopenias. To our best knowledge there is no report in the literature on acute mono-megakaryoblastic leukemia, especially with extreme thrombocytosis and complex karyotype abnormalities.

Case Report: We present the case of a 55-year-old woman with acute mono-megakaryoblastic leukemia with extreme thrombocytosis (greater than $2000 \times 10^9/L$) and complex karyotype abnormalities. The patient was first treated with anti-aggregate therapy and later the patient was put on a regimen consisting of idarubicin $10 \text{ mg}/\text{m}^2$ daily for 3 days and 200 mg Cytosar daily for 7 days. However, a severe pancytopenia occurred at the first day after chemotherapy and the patient died from intracranial hemorrhage.

Conclusions: Extreme thrombocytosis and complex karyotype abnormalities in acute mono-megakaryoblastic leukemia are associated with poor outcome.

Key words: acute leukemia • thrombocytosis • karyotype abnormalities

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Background

Thrombocytosis is usually seen in myeloproliferative disorders (MPD) and seldom in acute myeloid leukemias (AML). In

acute megakaryoblastic leukemia, platelet counts might exceed $1000 \times 10^9/L$ in approximately 30% of the patients, while others frequently presented by cytopenias [1]. Acute megakaryoblastic leukemia is a rare disease, accounting for only

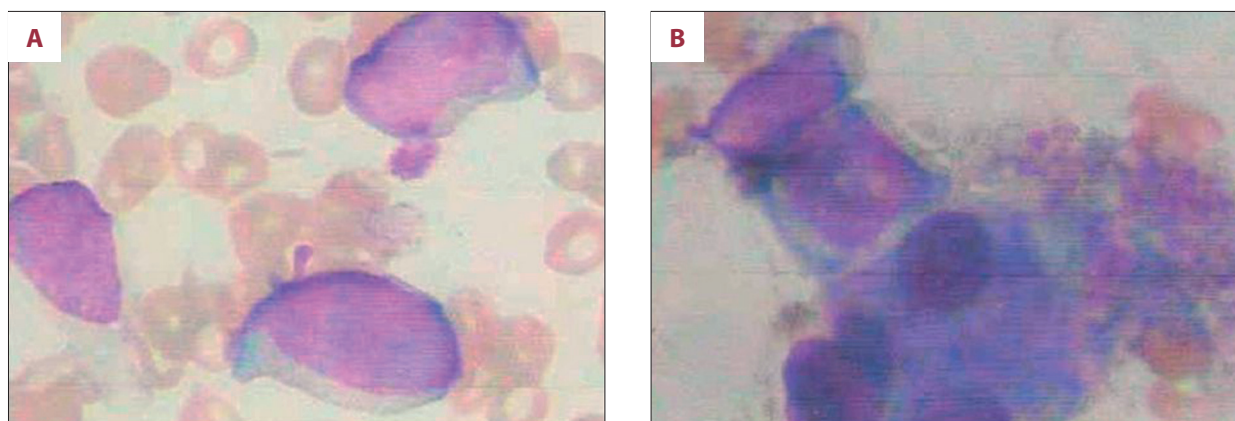


Figure 1. (A) Bone marrow smear: monoblastic cells. (B) Bone marrow smear: megakaryoblastic cells.

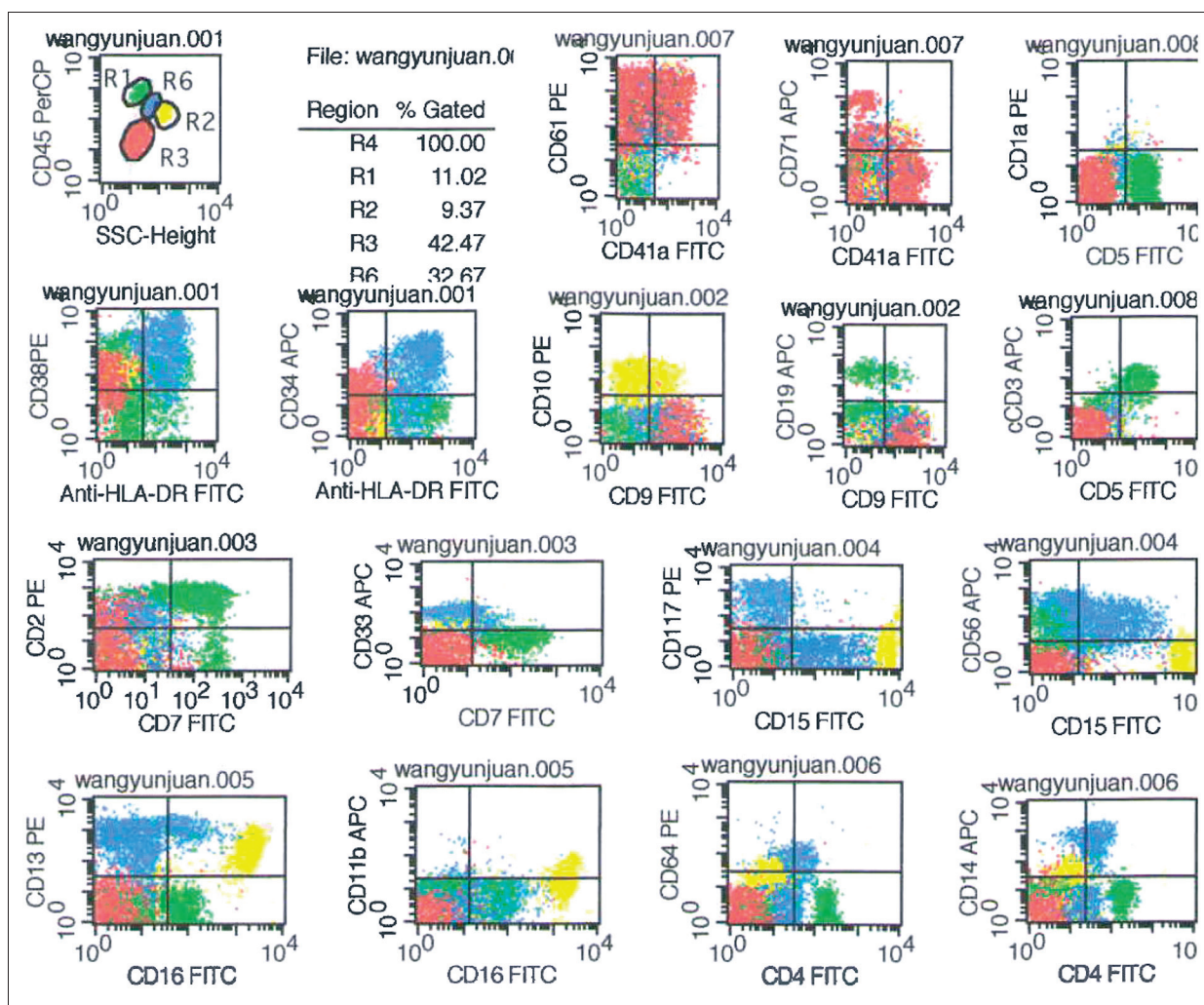


Figure 2. Flow cytometry profile of bone marrow blast cells.

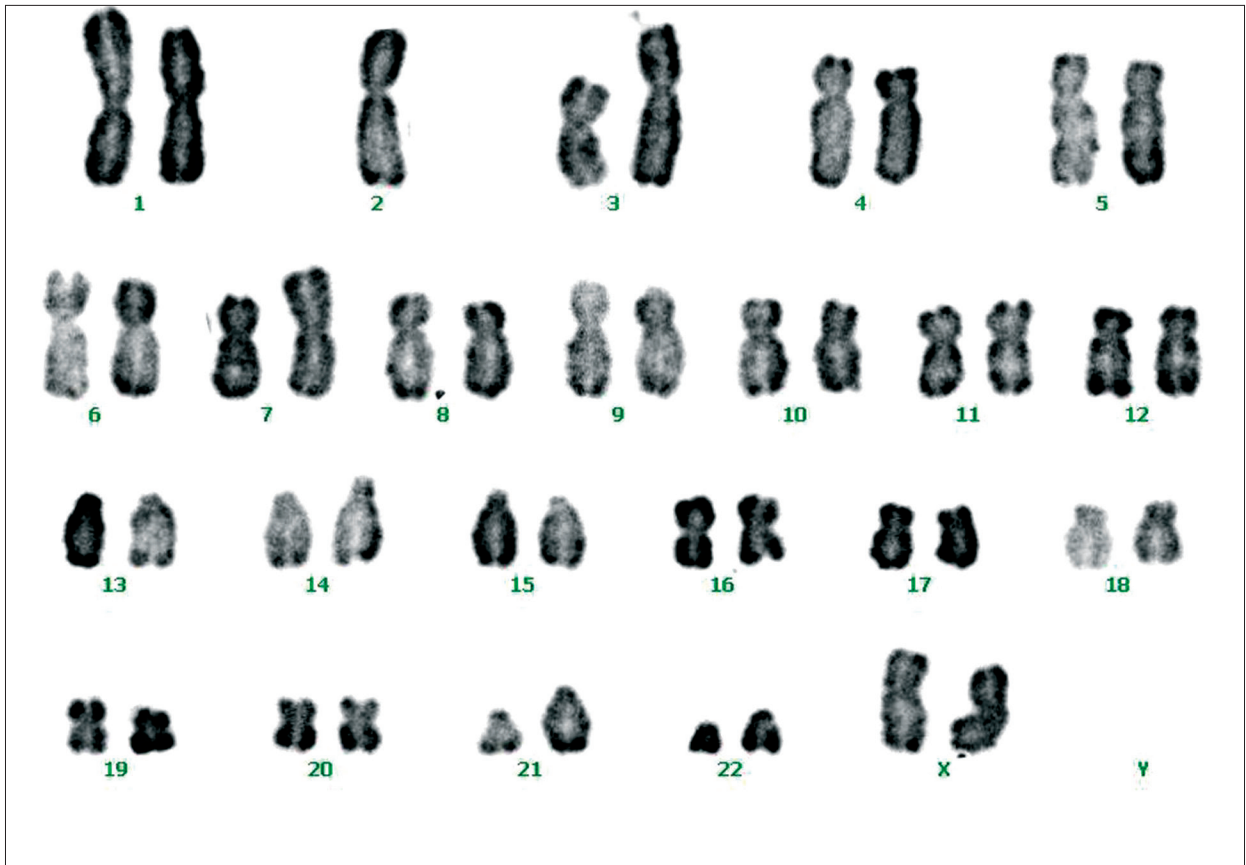


Figure 3. Karyotype analysis.

0.5–1.2% of newly diagnosed adult acute myeloid leukemias (AML) with poor outcomes [2,3]. To our best knowledge, this is the first report on acute mono-megakaryoblastic leukemia, especially with extreme thrombocytosis and complex karyotype abnormalities.

Case Report

We report a rare case of acute mono-megakaryoblastic leukemia with extreme thrombocytosis (more than $2000 \times 10^9/L$) and complex karyotype abnormalities. A 55-year-old woman was admitted to the Hematology Department with dyspepsia. There was no history of previous exposure to cytotoxic agents, long-time radiotherapy, or occupational toxins. There was multiple lymphadenopathy and no splenomegaly. A complete blood count showed extreme thrombocytosis (up to $2646 \times 10^9/L$), with normal hemoglobin (130 g/L), and normal white blood cells (WBC) ($9.7 \times 10^9/L$). Examination of peripheral blood film revealed blasts were about 60%.

The bone marrow aspirate was hypercellular. There was immature monoblast cells (Figure 1A) (up to 61.5%), as well immature megakaryoblast cells (Figure 1B) (up to 21.7%).

Regarding all cytochemical reactions: myeloperoxidase was slightly positive, a-Naphthyl acetate esterase was partly slightly positive (the further inhibition test by NaF was positive), and the PAS reaction was partly positive in the blast cells.

The immunophenotype was determined on lysed bone marrow sample by flow cytometry (Figure 2). The results were: R6 abnormal myeloblast cells accounting for 32.67%, expressing HLA-DR, CD45, CD33, CD56, and CD13; partial cells expressing CD117, CD34, CD9, CD2, CD16, CD64, CD14, and CD61; R3 may be megakaryocytes accounting for 42.47% expressing CD45, CD9, and CD61; and partial cells expressing CD34, CD41a and few cells expressing CD2.

Cytogenetics was performed using bone marrow specimens, which were cultured according to standard methods. Twenty-four metaphases were analyzed to detect clonal abnormalities following ISCN guidelines (1995). The bone marrow karyotype revealed (Figure 3): 41~45, xx, -2, add(3)(p24), del(3)(q24), -5, -6, i(7)(q10), -8, -12, -14, -17, -21, add(21)(q22), del(22)(q12) [CP12]/46, xx[3]. The presence of BCR-ABL (p210BCR-ABL and p190BCR-ABL), JAK2-V617F and FIP1-PDGFR α mRNAs were studied by reverse transcription polymerase chain reaction (RT-PCR) bone marrow cells. The results were negative.

The patient was first treated with anti-aggregate therapy because of the extreme thrombocytosis. Later on the patient was put on a regimen consisting of idarubicin 10 mg/m² daily for 3 days and 200 mg Cytosar daily for 7 days. However, a severe pancytopenia (platelet: 34×10⁹/L; hemoglobin; 83 g/L; white blood cell: 0.1×10⁹/L) occurred at the first day after chemotherapy and the patient died from intracranial hemorrhage.

Discussion

In the WHO classification, acute megakaryoblastic leukemia is defined by more than 20% of blasts of megakaryocyte lineage in the bone marrow aspirate as determined by morphology and immuno flow cytometry. In this case, the bone marrow aspirate showed more than 20% of monoblast cells and megakaryoblast cells, respectively. Further immunophenotyping confirmed the diagnosis. The short duration of symptoms, the normal blood counts 1 month before admission, and the absence of BCR-ABL and JAK2-V617F rearrangement suggest that this patient had *de novo* AML.

References:

1. Peterson BA, Levine EG: Uncommon subtypes of acute nonlymphocytic leukemia: clinical features and management of FAB M5, M6 and M7. *Semin Oncol*, 1987; 14: 425–34
2. Pagano L, Pulsoni A, Vignetti M et al: GIMEMA. Acute megakaryoblastic leukemia: experience of GIMEMA trials. *Leukemia*, 2002; 16: 1622–26
3. Tallman MS, Neuberger D, Bennett JM et al: Acute megakaryocytic leukemia: the Eastern Cooperative Oncology Group experience. *Blood*, 2000; 96: 2405–11

The chromosome abnormalities so far described in adult acute megakaryoblastic leukemia appear to be associated with trisomy 8, -7/del(7q), -5/del(5q), aberrations of 3q21q26, i(12)(p10), and other structural changes [4]. The reports of AML with thrombosis and karyotype abnormalities are rare. Balatzenko et al. reported a patient with acute megakaryoblastic leukemia with extreme thrombocytosis and p190(bcr/abl) rearrangement [5].

Chang et al. reported a patient with acute myelogenous leukemia associated with extreme symptomatic thrombocytosis and chromosome 3q translocation [6]. Lim et al. reported a patient with t(1;3)(p36;q21) and extreme thrombocytosis [7]. In this case, the patient showed complex karyotype abnormalities, which was consistent with this patient's poor outcome.

Conclusions

Acute mono-megakaryoblastic leukemia associated with extreme thrombocytosis and complex karyotype abnormalities is rare. Extreme thrombocytosis and complex karyotype abnormalities in acute mono-megakaryoblastic leukemia are associated with poor outcome.

4. Dastugue N, Lafage-Pochitaloff M, Pagès MP et al, Groupe Français d'Hématologie Cellulaire: Cytogenetic profile of childhood and adult megakaryoblastic leukemia (M7): a study of the Groupe Français de Cytogénétique Hématologique (GFCH). *Blood*, 2002; 100: 618–26
5. Balatzenko G, Guenova M, Zechev J, Toshkov S: Acute megakaryoblastic leukaemia with extreme thrombocytosis and p190(bcr/abl)rearrangement. *Ann Hematol*, 2004; 83: 381–85
6. Chang VT, Aviv H, Howard LM, Padberg F: Acute myelogenous leukemia associated with extreme symptomatic thrombocytosis and chromosome 3q translocation: case report and review of literature. *Am J Hematol*, 2003; 72: 20–26
7. Lim G, Kim MJ, Oh SH et al: Acute myeloid leukemia associated with t(1;3)(p36;q21) and extreme thrombocytosis: a clinical study with literature review. *Cancer Genet Cytogenet*, 2010; 203: 187–92