Clin. Lab. 2025;71:XXX-XXX

CASE REPORT

Central Nervous System Relapse in a Patient with Acute Myeloid Leukemia Following Chemotherapy

Shanmei Lv, Qing Wang

Medical Clinical Laboratory of Shaoxing People's Hospital, (The First Hospital of Shaoxing University), Shaoxing, P.R. China

SUMMARY

Background: **Acute myeloid leukemia (AML) is a hematologic malignancy. It is the most common form of acute leukemia among adults. Recent treatment advances have drastically improved outcomes for these diseases, but the overall survival (OS) is still exceptionally low due to the infiltration of leukemic cells in the central nervous system (CNS).**
Methods: **Standard microscopic examination of cells in the cerebrospinal fluid (CSF), analysis of the chemical composition of the cerebrospinal fluid, and to integrate flow cytometry (FCM) to analyze the phenotypic characteristics of cells to find leukemia cells.**
Results: **Pandy's test was positive in CSF, protein content was measured at 102.60 mg/dL, and leukemia cells were observed under microscopes. It was the gold standard for diagnosis. FCM also found 99.6% leukemia cells (CD33bri/CD13-/HLA-DR+/CD11c+/CD64dim/CD56+/CD117-/CD34-/CD38+/CD45dim/CD19-/CD15+/CD14-). The chromosomal karyotype also showed abnormalities.**
Conclusions: **Early detection of leukemia cells invading the central nervous system by routine examination in cytogenetic abnormalities, monocytic subtypes of AML patients, such as routine smear examination of CSF, has great clinical value for early detection, diagnosis, and intervention of patients with CNSL.**
(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.240813)

Correspondence:
Shanmei Lv
Medical Clinical Laboratory
Shaoxing People's Hospital
No. 568, North Zhongxing Road
Shaoxing City 312000 Zhejiang Province
China
Phone: +86 17858521850
Email: lvsm0713@163.com

KEYWORDS

acute myeloid leukemia (AML), central nervous system involvement (CNS involvement), cerebrospinal fluid (CSF)

INTRODUCTION

Acute myeloid leukemia (AML) is a heterogenous disease that affects the production of clonal hematopoietic blood cells in the bone marrow and refers to a diverse group of aggressive hematologic malignancies involving the proliferation of leukemic blasts committed to the granulocytic, monocytic, erythroid, or megakaryocytic lineages [1]. Central nervous system (CNS) involvement remains a significant challenge and can lead to serious complications and mortality. We present a patient with AML suffering from CNS by infiltration of leukemic blasts and exhibiting facial paralysis.

Case Report accepted August 14, 2024

CASE PRESENTATION

The patient, a 50-year-old male, was diagnosed with KMT2A-mutated acute myeloid leukemia (AML) a month ago. He underwent the IA (Idarubicin and Cytarabine) chemotherapy regimen for the treatment of his AML on May 15, 2024. The patient exhibited facial paralysis a month later. Physical examination: Body temperature is 36.5℃; Pulse rate is 111 beats/minute; Blood pressure is 140/102 mmHg. No pallor, no palpable enlargement of superficial lymph nodes, no adventitious sounds in both lungs, no abnormality in the neurological examination, no edema in the lower extremities. Clinical laboratory analysis showed a white blood cell count of 16.43 x 10^9/L, with a neutrophil percentage of 91.7%, lymphocyte percentage of 7.4%, and monocyte percentage of 0.9%, hemoglobin level is at 89.0 g/L, platelet count at 787.0 x 10^9/L, reticulocyte percentage is elevated at 9.02%. Chromosome Karyotype Analysis: 47, XY+8[4]/46, XY,t(11;14)(q23;q32)[3]/47, XY,+8, t(11;14)(q23;q32) [4]/46, XY[9]. Pandy's test was positive (+) in cerebrospinal fluid (CSF), white blood cell count of 40 x 10^6/L, leukemia cells were observed under high power microscopes (Figure 1), the flow cytometry analysis of the CSF sample revealed 99.6% CD33bri/CD13-/HLA-DR+/CD11c+/CD64dim/CD56+/CD117-/CD34-/CD38+/CD45dim/CD19-/CD15+/CD14- abnormal myeloid progenitor (monocytic) cells (31,130/31,251, Figure 2A). Based on clinical symptoms, laboratory tests and other results, the patient was diagnosed with central nervous system (CNS) involvement of AML. The intrathecal (IT) injection included a combination of Methotrexate (MTX), Cytarabine (Ara-C), and Dexamethasone (DMX) and was used for the treatment of this patient. It is administered via lumbar puncture, where the drugs are first diluted with cerebrospinal fluid (CSF) and then slowly injected into the spinal canal. The dosage and frequency are determined based on the individual patient's condition, usually weekly or every other week. After the treatment, the patient's symptoms improved significantly. Only 25.2% abnormal myeloblast CD33bri/CD13-/HLA-DR+/CD11c+/CD64dim/CD56+/CD117-/CD34-/CD38+/CD45dim/CD19-/CD15+/CD14- cells were detected in CSF by flow cytometry (93/369, Figure 2B).

DISCUSSION

AML is the most common form of acute leukemia in adults, although it accounts for just 1% of adult cancer deaths in the US. The median age at diagnosis is 68 years. The 5-year OS is approximately 30%, with wide variations between age groups, ranging from 50% in younger patients, but less than 10% in patients older than 60 years [2,3]. KMT2A (lysine methyltransferase 2a) gene is located at chromosomal position 11q23 and is involved in the regulation of gene expression. During development and differentiation, mutations or rearrangements in the KMT2A gene have been associated with various types of leukemia, particularly AML and acute lymphoblastic leukemia (ALL) [4,5]. Rearrangement of the KMT2A leukemias is frequently associated with central nervous system (CNS) involvement, which is associated with adverse outcomes in adults with AML [6,7]. Despite current improvements in the treatment of acute leukemia, CNS involvement remains a significant clinical challenge. The CNS involvement is more common in acute lymphocytic leukemia (ALL) than in adult acute myeloid leukemia (AML). CNS involvement in AML is rare, occurring is less than 5% of cases [8]. Involvement of the nervous system in AML is a relatively rare presentation of extramedullary disease of this myeloid leukemia. Involvement of the central nervous system (CNS) by infiltration of leukemic blasts may be identified during the disease process, may be detected either at the time of initial AML diagnosis or later during therapy progress, or at the time of relapse. The incidence is even higher after allogeneic hematopoietic stem cell transplantation (allo-HSCT) [9]. The study found that among newly diagnosed AML patients, those with CNS involvement had significantly shorter 5-year disease-free survival and overall survival than those without CNS involvement (18% vs. 50% and 19% vs. 46%, respectively) [10,11]. Most treatment regimens combine multiple doses of intrathecal chemotherapy, high-dose systemic methotrexate and/or cytarabine and cranial irradiation [12]. Historically, treatment of a CNS relapse involves intensive systemic therapy and cranial or craniospinal radiotherapy (RT) along with intrathecal (IT) therapy and consideration of allogeneic hematopoietic cell transplant [13]. Abnormal myeloid progenitor cells were found in the CSF of the patient with KMT2A AML, and facial paralysis appeared during chemotherapy at the same time. It was consistent with the paper that it was likely to be associated with the central nervous system. After intrathecal injection of a high dose of the chemotherapy drug cytarabine, the number of blast cells in CSF decreased and the clinical symptoms were relieved. The results of the chromosomal karyotype analysis (47, XY+8[4]/46,XY,t(11;14)(q23;q32)[3]/47, XY, +8, t(11;14)(q23;q32) [4]/46, XY[9]) also suggested that the abnormal cell population was predominant (11/20). Trisomy 8 was commonly observed in certain hematological malignancies, such as AML and myelodysplastic syndrome (MDS) [14]. These were risk factors for CNS involvement.

We emphasize the importance of vigilant monitoring and a high index of suspicion for CNS involvement in AML patients, especially those with high-risk features. Based on this case, we propose the following recommendations: 1) We pay more attention to the routine cell smear examination of CSF in cytogenetic abnormalities, monocytic subtypes of AML patients; 2) We should enhance communication with the clinical physicians positively and provide support for timely treatment of patients.

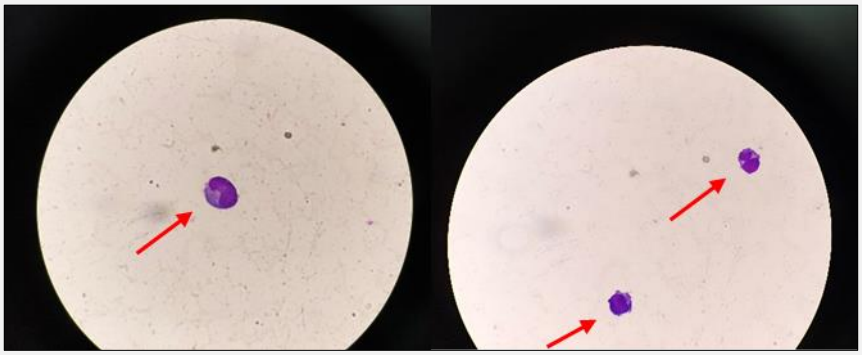

Figure 1. Abnormal immature cells in CSF.

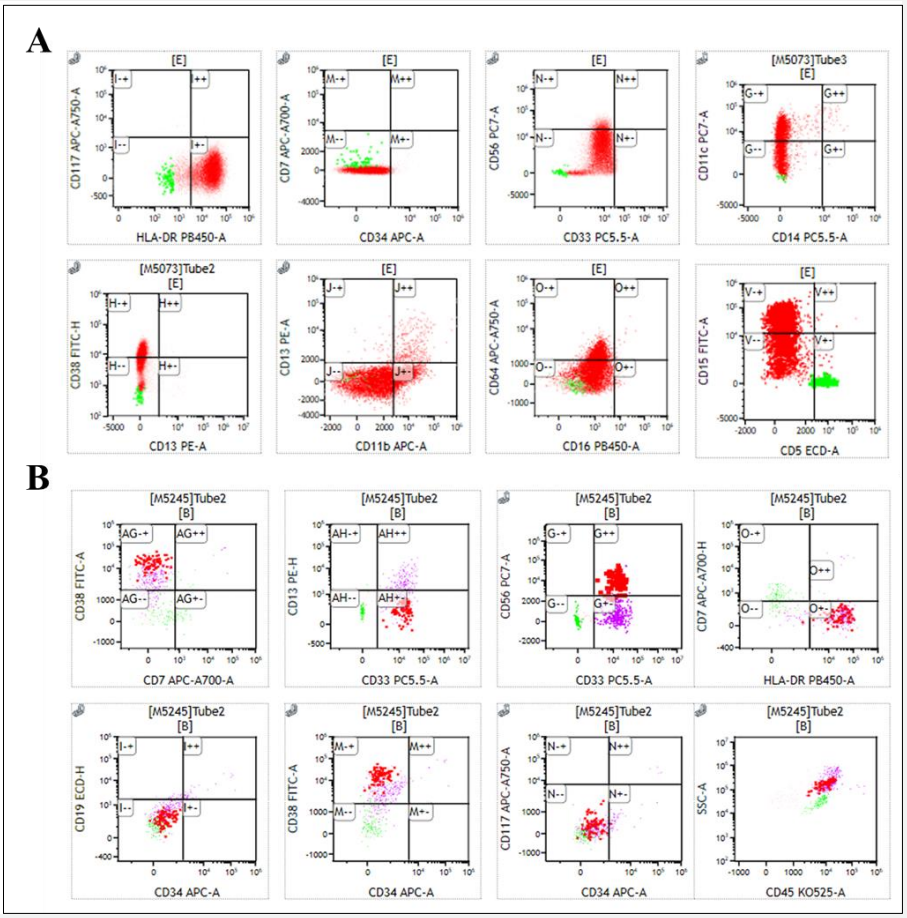

Figure 2. A. Abnormal myeloid progenitor (monocytic) cells (31,130/31,251), B. Abnormal myeloid progenitor (mono-cytic) cells (93/369).

Sources of Support:
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Interest:
All authors declare that they have no competing interests.

References:

1. DiNardo CD, Erba HP, Freeman SD, Wei AH. Acute myeloid leukaemia. Lancet 2023 Jun 17;401(10393):2073-86. (PMID: 37068505)

2. Shimony S, Stahl M, Stone RM. Acute myeloid leukemia: 2023 update on diagnosis, risk-stratification, and management. Am J Hematol 2023 Mar;98(3):502-26. (PMID: 36594187)

3. Pollyea D A, Bixby D, Perl, A, et al. NCCN Guidelines Insights: Acute Myeloid Leukemia, Version 2.2021. J Natl Compr Canc Netw 2021;19:16-27. (PMID: 33406488)

4. Meyer C, Larghero P, Lopes BA, Marschalek R. The KMT2A/MLL consensus gene structure: a comprehensive update for research and diagnostic implications. Leukemia 2024;38:1403-6. (PMID: 38678092)

5. Castiglioni S, Di Fede E, Bernardelli C, et al. KMT2A: Umbrella Gene for Multiple Diseases. Genes (Basel) 2022;13:514. (PMID: 35328068)

6. Issa GC, Zarka J, Sasaki K, et al. Predictors of outcomes in adults with acute myeloid leukemia and KMT2A rearrangements. Blood Cancer J 2021;11:162. (PMID: 34588432)

7. Hernandez-Sanchez A, Gonzalez T, Sobas M, et al. Rearrangements involving 11q23.3/KMT2A in adult AML: mutational landscape and prognostic implications - a HARMONY study. Leukemia. Epub 2024 Jul 4. (PMID: 38965370)

8. Paul S, Short NJ. Central Nervous System Involvement in Adults with Acute Leukemia: Diagnosis, Prevention, and Management. Curr Oncol Rep 2022;24:427-36. (PMID: 35141858)

9. Siegal T, Benouaich-Amiel A, Bairey O. Neurologic complications of acute myeloid leukemia. Diagnostic approach and therapeutic modalities. Blood Rev 2022 May;53:100910. (PMID: 34836656)

10. Del Principe MI, Buccisano F, Soddu S, et al. Involvement of central nervous system in adult patients with acute myeloid leukemia: Incidence and impact on outcome. Semin Hematol 2018; 55:209-14. (PMID: 30502849)

11. Alakel N, Stolzel F, Mohr B, et al. Symptomatic central nervous system involvement in adult patients with acute myeloid leukemia. Cancer Manag Res 2017;9:97-102. (PMID: 28435324)

12. Larson RA. Managing CNS disease in adults with acute lymphoblastic leukemia. Leuk Lymphoma 2018;59:3-13. (PMID: 28535095)

13. Cortes J, O'Brien SM, Pierce S, Keating MJ, Freireich EJ, Kantarjian HM. The value of high-dose systemic chemotherapy and intrathecal therapy for central nervous system prophylaxis in different risk groups of adult acute lymphoblastic leukemia. Blood 1995;86:2091-7. (PMID: 7662956)

14. Backhaus D, Jentzsch M, Bischof L, et al. Risk Stratification, Measurable Residual Disease, and Outcomes of AML Patients with a Trisomy 8 Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. Cancers (Basel) 2021;13:5679. (PMID: 34830834)