Clin. Lab. 2025;71:XXX-XXX

CASE REPORT

Acute Myelomonocytic Leukemia Misdiagnosed as Histiocytic Necrotizing Lymphadenitis

Si R. Xu, Zhao Chen, Zhi P. Deng

Zigong First People's Hospital, Zigong, Sichuan, China

SUMMARY

Background: **Acute Myelomonocytic Leukemia (AMML) is a rare malignant neoplasm that is classified as a subtype of Acute Myeloid Leukemia (AML). In the case described herein, the initial pathology results from a lymph node biopsy leaned towards Histiocytic Necrotizing Lymphadenitis, but ultimately, immunohistochemistry of the lymph node confirmed the diagnosis of Acute Myelomonocytic Leukemia.**
Methods: **Cervical lymph node biopsy.**
Results: **In this case, the initial pathological diagnosis after cervical lymph node biopsy favored histiocytic necrotizing lymphadenitis. However, immunohistochemical analysis revealed the presence of immature cell proliferation in the lightly stained areas, characterized by irregular nuclear shapes and visible mitotic figures. Further investigation showed that these immature cells were positive for CD68 and Lys, weakly positive for myeloperoxidase (MPO), and partially positive for CD4, CD8, granzyme B (GrB), and TIA1. The Ki67 proliferation index was approximately 70%, indicating a high rate of cell proliferation. Based on these immunohistochemical findings, the patient was ultimately diagnosed with Acute Myelomonocytic Leukemia (AMML).**
Conclusions: **For patients presenting with cervical lymphadenopathy and fever, it is crucial to stabilize the condition while concurrently seeking the underlying cause. Timely completion of relevant examinations, including cervical lymph node biopsy, is essential for definitive diagnosis.**
(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.241145)

Correspondence:
Zhi P. Deng
Zigong First People's Hospital
Zigong, Sichuan
China
Phone: +86 13608158051
Email: dengzp1016@163.com

Case Report accepted December 10, 2024

KEYWORDS

acute myelomonocytic leukemia, lymph node puncture biopsy, histiocytic necrotizing lymphadenitis

CASE REPORT

A 39-year-old female presented to the hospital primarily due to intermittent fever for two weeks accompanied by swelling of the right cervical mass. She reported that approximately two weeks ago, she began experiencing intermittent fever without apparent cause, with the highest recorded temperature reaching 38.8℃, primarily at night, accompanied by chills without shivering or skin rash. Additionally, she noted progressive enlargement of the right cervical mass, which was tender to palpation. She denied cough, sputum production, or discomfort in her limbs and joints. Upon initial presentation, routine blood tests including complete blood count, C-

reactive protein (CRP), and serum amyloid A protein (SAA) were unremarkable. Cervical lymph node ultrasound revealed bilateral lymphadenopathy, with more significant enlargement on the right side. She was treated with "Clindamycin Phosphate Dispersible Tablets 150 mg orally three times a day" without satisfactory response. There was no significant change in her weight since the onset of symptoms. The patient had a history of "bronchitis" for over 30 years, presently asymptomatic regarding cough and sputum, and a history of "gastrointestinal urticaria" for over 10 years, recurring approximately every 2 - 3 years, currently not treated specifically. At the time of admission, she exhibited an acute sick appearance with painful expression. Multiple enlarged lymph nodes were palpable in the neck, the largest measuring approximately 2 x 2 cm, with mild tenderness. No other significant abnormalities were noted upon the rest of the physical examination.

Upon admission, the patient's initial blood results were as follows: RBC: 4.85 x 10^{12}/L (reference value 4 x 10^{12}/L - 5.5 x 10^{12}/L), HGB 143 g/L (reference value 115 g/L - 150 g/L), WBC 3.27 x 10^{9}/L (reference value 4 x 10^{9}/L - 10 x 10^{9}/L), NEU 1.59 x 10^{9}/L (reference value 1.8 x 10^{9}/L - 6.3 x 10^{9}/L), LYM 0.86 x 10^{9}/L (reference value 1.1 x 10^{9}/L - 3.2 x 10^{9}/L), MON 0.77 x 10^{9}/L (reference value 0.1 x 10^{9}/L - 0.6 x $10^{9/}$L), and improve the infection index tips: CRP < 5 mg/L (reference value 0 mg/L - 8 mg/L), SAA 21.75 mg/L (reference value 0 mg/L - 10 mg/L), IL-6 11.75 pg/mL (reference value 0 ng/mL - 0.05 ng/mL), ESR 20 mm/hour (reference value 0 mm/hour - 15 mm/hour), fibrinogen 4.20 g/L (reference value 2 g/L - 4 g/L), no obvious abnormalities were found in biochemical detection. Biochemical tests were within normal limits, and serologic tests for tuberculosis, herpes simplex virus, rubella virus, cytomegalovirus, Toxoplasma, and Epstein-Barr virus antibodies were negative.

Cervical lymph node ultrasound revealed multiple strong internal and weak external echoes in the I - V regions of the right neck, with thickened cortices. The largest node, located in region I, measured approximately 39.8 x 9.6 mm. Similar findings were observed in the left neck regions I - IV, with the largest node in region I measuring about 23.8 x 7.0 mm. Color Doppler flow imaging (CDFI) demonstrated vascular flow signals in all nodes (Figures 1 - 2). Initial consideration was given to acute cervical lymphadenitis, and treatment with thymus extract to modulate immunity was initiated. However, this approach proved ineffective. A cervical lymph node biopsy was subsequently performed, and the initial pathological report suggested histiocytic necrotizing lymphadenitis. Despite maintaining the original treatment plan, the patient continued to experience intermittent fever. The subsequent pathological immunohistochemical analysis of the lymph node revealed proliferation of immature cells in lightly stained areas with irregular nuclei and visible mitotic figures. These immature cells were positive for CD68 and Lys, weakly positive for MPO, and partially positive for CD4, CD8, GrB, and TIA1, with a Ki67 proliferation index of approximately 70% (Figures 3 - 4). Based on these findings, the final diagnosis was acute myelomonocytic leukemia. The patient was discharged and will undergo subsequent chemotherapy.

DISCUSSION

Cervical lymphadenopathy can be caused by a wide range of conditions, ranging from infectious diseases to autoimmune and allergic disorders, and includes both benign and malignant tumors. In most cases, cervical lymphadenitis is related to reactive changes in response to bacteria, viruses, chlamydia, or mycoplasma pathogens, or it may be associated with the presence of primary hematological malignancies such as Hodgkin's disease and non-Hodgkin's lymphoma. The patient in this case is a middle-aged female presenting with enlarged cervical lymph nodes accompanied by fever. Her complete blood count (CBC) revealed a decrease in white blood cells with an increase in monocytes, and elevated CRP and SAA. Combined with the cervical lymph node biopsy pathology, the initial consideration was the presence of histiocytic necrotizing lymphadenitis. Histiocytic necrotizing lymphadenitis, also known as Kikuchi-Fujimoto disease (KFD), is a benign and self-limiting condition characterized by tender localized (predominantly cervical) lymphadenopathy along with mild fever, night sweats, and flu-like symptoms [1,2]. This condition primarily affects young adult females in Asia and is rare in European countries, where it may pose diagnostic challenges. Consequently, our initial diagnosis for this patient was erroneous; however, subsequent immunohistochemical analysis confirmed the presence of acute myelomonocytic leukemia (AMML). Leukemia is a collective term for malignant hematologic disorders originating from hematopoietic stem cells, characterized by uncontrolled proliferation of tumor cells [3]. Acute myeloid leukemia (AML) is heterogeneous due to the uncontrolled proliferation of clonal hematopoietic cells [4,5]. These aberrantly proliferating cells are blocked in their maturation and differentiation processes, leading to functional impairment and accumulation of immature myeloid precursors, also known as blasts [6,7]. Although AML is rare with fewer than 20,000 new cases annually in the United States, it is the most common form of acute leukemia in adults [8]. The median age at diagnosis is 68 years [7]. The incidence of AML increases significantly with age; it is 1.3 cases per 100,000 people among those under 65 years, but rises to 12.2 cases per 100,000 among those aged 65 and older [9]. AMML, as a subtype of AML, is a rare malignancy. According to the 2017 update of the World Health Organization (WHO) classification of tumors, unless associated with therapy-related, myelodysplastic-related changes, or well-known recurrent genetic abnormalities such as Inv (16), it should be classified as “AML not otherwise specified” [10,11]. The cytological

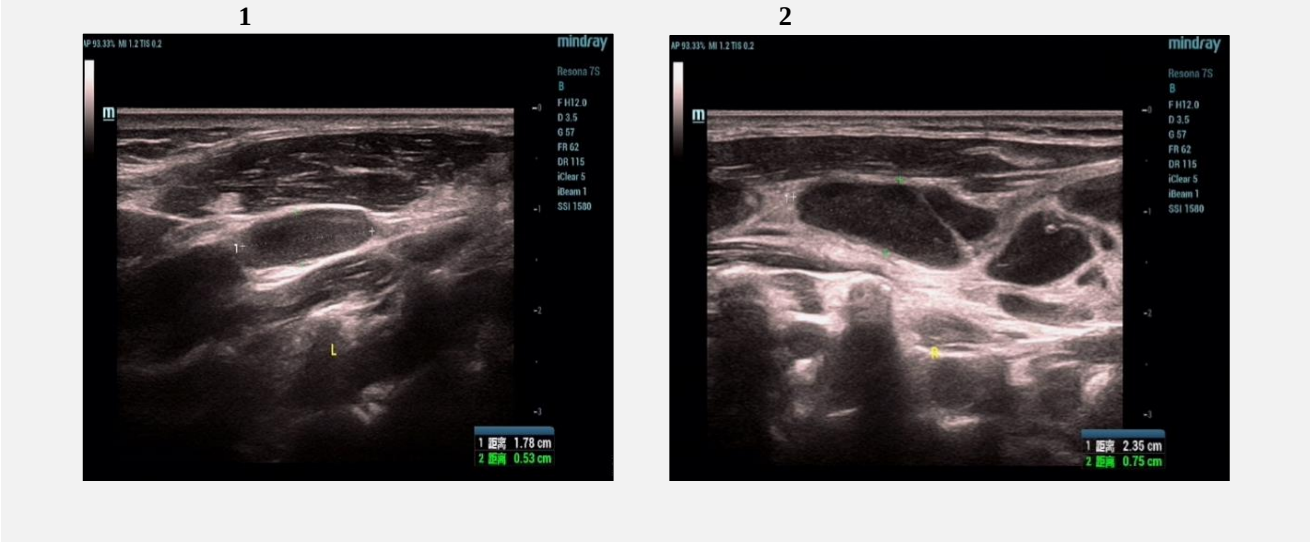

Figure 1 - 2. Cervical Lymph Node Ultrasound: Multiple hypoechoic areas with thickened cortex are observed in regions I - IV on the left side of the neck, the largest located in region I, measuring approximately 23.8 x 7.0 mm. CDFI: Hilar blood flow signals are visible within all of them. Multiple hypoechoic areas with thickened cortex are observed in regions I - V on the right side of the neck, the largest located in region I, measuring approximately 39.8 x 9.6 mm.

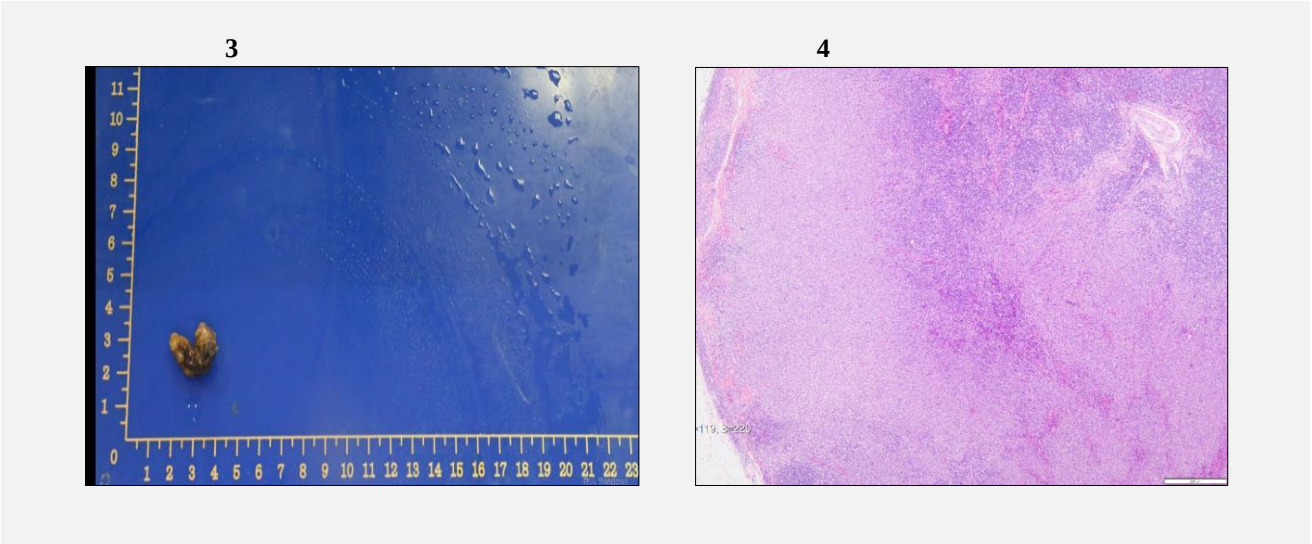

Figure 3 - 4. Lymph Node Pathological Immunohistochemical Report: Proliferation of immature cells is observed in the lightly stained area with irregular nuclei and visible mitotic figures. The immature cells in the lightly stained area are positive for CD68, Lys, weakly positive for MPO, partially positive for CD4, CD8, GrB, TIA1, and with a Ki67 positive rate of approximately 70%.

features of myelomonocytes in AMML are typically distinct, facilitating direct diagnosis by experienced cytologists [12]. However, in some cases, the morphology of these cells can be misleading, increasing diagnostic challenges [13]. Early or pre-diagnostic symptoms may include fever, fatigue, recurrent infections, hematomas, pallor, petechiae, and bleeding from the skin and mucous membranes [11]. Previous studies have shown that oral manifestations and cervical lymphadenopathy occur in approximately 20 - 69% of patients with acute leukemia, but are more commonly observed in acute lymphocytic leukemia [3]. In this case, we ultimately

diagnosed the patient with AMML based on the immunohistochemical results of the lymph node pathology. For AMML, early diagnosis and prompt treatment are crucial. Although a significant number of patients can be cured with chemotherapy alone, many require allogeneic hematopoietic stem cell transplantation (HSCT) for a definitive cure. Referral for HSCT evaluation should begin shortly after initial diagnosis [14]. The treatment strategies for AMML are similar to other subtypes of AML, primarily employing cytotoxic chemotherapy (such as combination regimens with anthracyclines and cytarabine) and high-dose chemotherapy [15]. However, given the advanced age and high comorbidity burden among AMML patients, which often results in poorer tolerance, individualized treatment plans are crucial. In recent years, targeted therapies (e.g., FLT3 inhibitors, IDH inhibitors) and immunotherapies (e.g., CAR-T cell therapy) have shown promising potential in AML, although their efficacy in AMML remains unvalidated.

CONCLUSION

This case highlights the significance of maintaining a high index of suspicion for hematologic malignancies, particularly in young individuals presenting with cervical lymphadenopathy and fever, even when initial blood tests and lymph node biopsy pathology suggest histiocytic necrotizing lymphadenitis. The diagnostic process should include appropriate additional examinations, such as lymph node immunohistochemistry, to ensure accurate diagnosis.

Acknowledgment:
We would like to thank other members of the Department of Respiratory Medicine, Zigong First People's Hospital of Technology for the constructive criticism.

Ethical Approval:
This study was approved by the ethics committee of Zigong First People's Hospital. All procedures performed in the studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

References:

1. Lin HC, Su CY, Huang CC, Hwang CF, Chien CY. Kikuchi's disease: a review and analysis of 61 cases. Otolaryngol Head Neck Surg 2003 May;128(5):650-3. (PMID: 12748557)

2. Lin HC, Su CY, Huang SC. Kikuchi's disease in Asian children. Pediatrics 2005 Jan;115(1):e92-6. (PMID: 15629971)

3. Watson E, Wood RE, Maxymiw WG, Schimmer AD. Prevalence of oral lesions in and dental needs of patients with newly diagnosed acute leukemia. J Am Dent Assoc 2018 Jun;149(6):470-80. (PMID: 29606275)

4. Pelcovits A, Niroula R. Acute Myeloid Leukemia: A Review. R I Med J (2013) 2020 Apr 1;103(3):38-40. (PMID: 32236160)

5. Papaemmanuil E, Gerstung M, Bullinger L, et al. Genomic Classification and Prognosis in Acute Myeloid Leukemia. N Engl J Med 2016 Jun 9;374(23):2209-21. (PMID: 27276561)

6. Prada-Arismendy J, Arroyave JC, Rothlisberger S. Molecular biomarkers in acute myeloid leukemia. Blood Rev 2017 Jan;31 (1):63-76. (PMID: 27639498)

7. Pollyea DA, Bixby D, Perl A, et al. NCCN Guidelines Insights: Acute Myeloid Leukemia, Version 2.2021. J Natl Compr Canc Netw 2021 Jan 6;19(1):16-27. (PMID: 33406488)

8. Shallis RM, Wang R, Davidoff A, Ma X, Zeidan AM. Epidemiology of acute myeloid leukemia: Recent progress and enduring challenges. Blood Rev 2019 Jul;36:70-87. (PMID: 31101526)

9. De Kouchkovsky I, Abdul-Hay M. 'Acute myeloid leukemia: a comprehensive review and 2016 update'. Blood Cancer J 2016 Jul 1;6(7):e441. (PMID: 27367478)

10. Le Beau MM, Larson RA, Bitter MA, Vardiman JW, Golomb HM, Rowley JD. Association of an inversion of chromosome 16 with abnormal marrow eosinophils in acute myelomonocytic leukemia. A unique cytogenetic-clinicopathological association. N Engl J Med 1983 Sep 15;309(11):630-6. (PMID: 6577285)

11. Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016 May 19;127(20):2391-405. (PMID: 27069254)

12. Bain BJ, Bene MC. Morphological and Immunophenotypic Clues to the WHO Categories of Acute Myeloid Leukaemia. Acta Haematol 2019;141(4):232-44. (PMID: 30965338)

13. Liu K, Yu Y, Chai X, et al. Atypical Acute Monocytic Leukemia: a Lymphoma Presentation and Association with Complex Karyotype. Ann Clin Lab Sci 2018 Nov;48(6):805-7. (PMID: 30610055)

14. Becker M, Farina KA, Mascarenhas J. Acute myeloid leukemia: Current understanding and management. JAAPA 2024 Jan 1;37 (1):34-9. (PMID: 38128137)

15. Thol F, Ganser A. Treatment of Relapsed Acute Myeloid Leukemia. Curr Treat Options Oncol 2020 Jun 29;21(8):66. (PMID: 32601974)