Membranous Tonsilitis as a Clinical Presentation of Acute Monocytic Leukemia: A Rare Case Report

Stephani Linggawan[1], Eric Satrio Adi Wibowo[1], Catherine Keiko Gunawan[3], Budiono Raharjo[2], Anton Sumarpo[4], Yohanes Timothy Raharjo[5], Ni Made Intan Dwijayanti[6], Siprianus Ugroseno Yudho Bintoro[6]*

ARTICLE INFO

AUTHOR'S AFFILIATIONS
Department of Ear Nose and Throat, Faculty of Medicine, Wijaya Kusuma University Surabaya, Surabaya, East Java, Indonesia[1]
Department of Clinical Pathology, Faculty of Medicine, Wijaya Kusuma University Surabaya, Surabaya, East Java, Indonesia[2]
Medical profession study program, Faculty of Medicine, Maranatha Christian University, Bandung, West Java, Indonesia[3]
Department of Clinical Pathology, Maranatha Christian University, Bandung, West Java, Indonesia[4],
Faculty of Medicine Widya Mandala Surabaya Catholic University[5]
Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Hospital, Surabaya, East Java, Indonesia[6]

CORRESPONDING AUTHOR
Stephani Linggawan
Faculty of Medicine, Universitas Wijaya Kusuma Surabaya, Surabaya, East Java, Indonesia
E-mail:
dr.stephani.linggawan82@gmail.com

Article history

Received	27-02-2025
Revised	16-09-2025
Accepted	24-09-2025
Available online	30-09-2025

Please cite this article in APA 7th edition style as:
Linggawan, S., Gunawan, C. K., Raharjo, B., Sumarpo, A. (2025). Membranous Tonsilitis as a Clinical Manifestation of Acute Monocytic Leukemia: A Rare Case Report. *Jurnal Ilmiah Kedokteran Wijaya Kusuma, 14 (12), 172-178*

http://dx.doi.org/10.30742/jikw.v14i2.4290

Abstract

Background: Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy characterized by the clonal proliferation of immature myeloid precursor cells in the bone marrow and peripheral circulation. Hematologic manifestations such as anemia, thrombocytopenia, and leukocytosis are well-documented, its association with oral involvement, particularly tonsillitis, is a rare presenting feature. **Objective:** This case report emphasizes membranous tonsilitis as the primary presenting feature in acute monocytic leukemia (AML-M5). The aim of writing this case study is to provide an illustration that the causes of membranous tonsillitis, beside from the infection, can also be caused by infiltration of leukemia cells. **Case Presentation:** We report a case of a 27-year-old female presented with fever and was found to have a fluctuating mass on the right side of the neck along with gingival swelling and hyperemic, hypertrophic tonsils with a membranous exudate. The diagnosis from bone marrow aspiration and immunophenotyping revealed as acute monocytic leukemia (AML-M5). Bacterial and fungal infections were excluded through gram staining, potassium hydroxide (KOH) examination, and throat swab culture. The patient was initially stabilized with hydroxyurea, with subsequent clinical improvement, before being referred to a tertiary center for definitive management. **Result:** This diagnostic workup altogether from all the clinicians leads to the diagnosis of acute myeloid leukemia (AML-M5). **Conclusion:** This case highlights primary tonsilitis as the primary presenting feature of acute myeloid leukemia (AML-M5), emphasizing the need for continued monitoring and regular follow-up assessment to detect potential relapses and ensure optimal disease management

Keywords: Acute monocytic leukemia (AML-M5), Acute myeloid leukemia (AML) tonsilitis, Extramedullary manifestation

Case Report

INTRODUCTION

Acute myeloid leukemia (AML) encompasses a heterogenous group of hematologic malignancies characterized by the clonal proliferation of immature myeloid-derived blast cells within the bone marrow and peripheral blood (Vakiti et al. 2024). As the most common acute leukemia in adults, AML comprises approximately 15% to 20% of all leukemia cases, with an estimated annual incidence of 4.3 per 100,000 in the United States. Notably, AML exhibits a slightly higher incidence in males compared to females (Shallis et al. 2019; Sasaki et al. 2021).

To account for its biological heterogeneity, AML is classified into distinct subtypes based on its morphology, cytogenetic abnormalities, and molecular marker. Historically, the French-American-British (FAB) classification (M0-M7) was used; however, the World Health Organization (WHO) classification is now the standard, integrating genetic and immunophenotypic data to provide a more precise diagnostic framework (Masoumi-Dehshiri et al. 2014; Knottenbelt et al. 2015).

The uncontrolled proliferation of leukemic blasts severely disrupts normal hematopoiesis, ultimately leading to bone marrow failure, and subsequent cytopenias, including anemia, thrombocytopenia, and neutropenia (Masoumi-Dehshiri et al. 2014; Knottenbelt et al. 2015). Although AML typically manifests with symptoms related to cytopenia, oral manifestation—particularly tonsilitis remains uncommon. This case report emphasizes membranous tonsilitis as the primary presenting feature in acute monocytic leukemia (AML-M5) which is rare of the manifestation in AML . The aim of writing this case study is to provide an illustration that the causes of membranous tonsillitis, apart from infection, can also be caused by infiltration of leukemia cells. Here, we present a unique case of acute monocytic leukemia (AML-M5) presenting with membranous tonsilitis in a 27-year-old female, highlighting this atypical presentation and emphasizing its diagnostic implications.

CASE PRESENTATION

A 27-year-old female came to the hospital with chief complaint fever, headache, cough, rhinorrhoea, and odynophagia. Patient has no significant past medical history before. The patient complain of fever, headache, cough, rhinorrhoea, and odynophagia 3 days before admission. The patient also reported constitutional symptoms including malaise, profound fatigue, generalized myalgia and abdominal discomfort. The patient is from Flores and is of the Flores ethnic group. His eating habits include instant foods, including instant noodles and junk food while in Surabaya. The patient works as a programmer at a private company in Surabaya

Physical examination revealed a mobile, fluctuating mass on the right side of the neck, accompanied by gingival swelling persisting for the past 2 weeks. Further assessment identified conjunctival pallor, indicative of anemia. Otolaryngologic evaluation demonstrated hyperemia of the tympanic membrane, conchal edema, and hyperemic, hypertrophic tonsils with a distinct membranous exudate. Additionally, cervical lymph node palpation revealed multiple soft, mobile nodules, with the right-side lymph nodes being larger than those on the left, measuring approximately 0.5x1 cm.

Initial laboratory investigations revealed anemia (hemoglobin 9.9 g/dL [reference range: 12-16 g/dL]), leukocytosis (leukocyte count 95,900/µL [reference range: 4,000-11,000/µL]), and a normal platelet count. The C-reactive protein (CRP) level was markedly elevated at 62.2 mg/L (reference range: <5 mg/L), indicating a significant inflammatory response. Peripheral blood smear analysis demonstrated normochromic, normocytic erythrocytes, with 2 normoblasts per 100 leukocytes. Platelet morphology appeared unremarkable, with no evidence of clumping. Differential analysis revealed a marked increase in monocytes and their precursors, including 15% monoblast, 40% promonocytes, and 10% monocytes, consistent with monoblastic proliferation.

Gram staining, potassium hydroxide (KOH) examination, tonsillar membrane scraping, along with throat swab culture were performed to investigate a potential infectious etiology. Cytological analysis of the tonsillar scrapings revealed the presence of monoblasts, promonocytes, and

monocytes, raising suspicion for leukemic infiltration. Moreover, both staining yielded negative results, ruling out bacterial and fungal infection.

Bone marrow aspiration revealed hypercellular marrow with decreased erythropoietic activity with no evidence of dysplasia. Similarly, granulopoietic activity was diminished, while monoblast infiltration was accounted for 38.5% (45% of the monocytic lineage), with promonocytes comprising 41% (48% of the monocytic lineage) **(Figure 1)**. Additionally, megakaryopoiesis was reduced, with an observed myeloid-to-erythroid (M:E) ratio of 20:0.1. Taken together, the aspirate was consistent with acute monocytic leukemia (AML-M5).

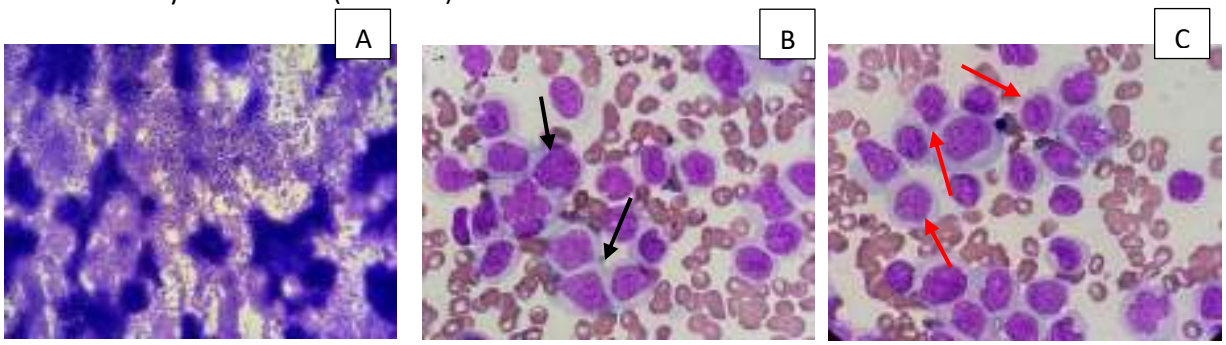

Figure 1. **A**. Bone marrow aspirate demonstrating (**A**) hypercellularity; (**B**) infiltration of monoblasts (black arrow); and (**C**) increased proportion of promonocytes (red arrow).

Immunophenotyping analysis by flow cytometry was performed to further confirm the diagnosis, revealing the expression of CD34(+), CD7(+/dim), HLA-DR (+), CD11c (+), CD14(+), CD64(+), CD117(+), CD13(+), and CD33(+). The expressions of CD34 and CD7 suggests immaturity or aberrant antigen expression. While the strong expression of CD14, CD64, and CD117 indicates monocytic differentiation. Furthermore, the absence of lymphoid markers supports a myeloid rather than lymphoid malignancy, thus confirming the diagnosis of acute monocytic lymphoid (AML-M5).

The patient was initiated on a 5-day cytoreductive treatment regimen consisting of oral route chemotherapy hydroxyurea (2 g/day) as a cytoreduction drug, along with supportive care including diclofenac potassium (50mg), pseudoephedrine-triprolidine (60mg/2.5mg), paracetamol (600mg), and codeine-phenyltoloxamine (30 mg) as needed for symptomatic relief. After 5 days post-treatment, ENT examination showed an intact tympanic membrane, resolved hyperemia, and a reduction in cervical lymph node size to 0.2 x 0.5 cm. The common side effect for hydroxyurea are gastrointestinal disturbance (nausea, vomiting, diarrhe/constipation, anorexia), liver and kidney disturbances, bone marrow suppression, (anemia, leukopenia and thrombocytopenia). In this patient, there were no side effects from the hydroxyurea drug. Upon completing the initial treatment, the patient was referred to a tertiary hospital for further management.

DISCUSSION

Acute myeloid leukemia (AML) represents a diverse group of aggressive myeloid malignancies characterized by the rapid clonal expansion of myeloid progenitor cells within the bone marrow and peripheral blood. The 2016 World Health Organization (WHO) classification refine the classification of AML based on recurrent genetic abnormalities, mutations, and cell lineage. AML-M5, also known as acute monocytic leukemia, is defined by ≥80% of all bone marrow cells being of monocytic lineage. Subtypes M0, M1, and M2 are predominantly granulocytic, differing in their degree of maturation, while M3 is characterized by abnormal promyelocytes. M4 exhibits both granulocytic and monocytic features. M6 is characterized by erythroid predominance, and M7 is distinguished by megakaryoblastic feature (Masoumi-Dehshiri et al. 2014; Hasserjian 2021). Given the biological and clinical heterogeneity of AML, individualized cytogenetic and molecular characterization is essential for accurate diagnosis, risk stratification, and treatment planning.

The pathogenesis of acute myeloid leukemia (AML) remains complex and unclear. However, clonal expansion and maturation blockade of hematopoietic stem cell (HSC) and progenitor cells are the hallmark of AML (Capelli et al. 2022; Wachter and Pikman 2024). Mutations in genes encoding epigenetic regulators include DNMT3A, ASXL1, TET2, IDH1, and IDH2, are commonly acquired during the early stages of leukemogenesis and play a pivotal role in establishing the founding clone. These genetic alterations have been found to disrupts the gene expression, promoting the expansion of abnormal immature leukemic cells known as blasts, leading to defective hematopoiesis (Blau and Blau 2015; Bullinger et al. 2017; Abelson et al. 2018).

The abnormal hematopoiesis in acute myeloid leukemia (AML) leads to profound disruption of normal erythropoiesis, and thrombopoiesis, resulting in significant hematologic deficits known as the classic triad of anemia, thrombocytopenia, and neutropenia. The impairment of erythropoiesis manifests as anemia, characterized by fatigue, malaise, pallor as observed in our patient. Meanwhile, thrombopoiesis impairment leads to thrombocytopenia, predisposing to an increased risk of bruising, petechiae, and prolonged bleeding. While neutropenia predisposes patients to serious infections (Döhner et al. 2016; El Jamal et al. 2022).

Extramedullary manifestations involving tissues outside the bone marrow can occur in AML, particularly in subtypes with monocytic differentiation. Leukemic infiltration has been reported in the skin, gingiva, spleen, liver and central nervous system. However, membranous tonsilitis as the primary presenting feature, as observed in our patient is exceedingly rare. This phenomenon is thought to be driven by the high expression of adhesion molecules — CD11c, CD14, CD64 — on leukemic cells, facilitating their migration and infiltration into extramedullary sites. These adhesion molecules mediate interactions between leukemic cells with endothelial cells, promoting their adhesion, transmigration across the endothelium and subsequent tissue infiltration, including the tonsils (Xing et al. 2019; Quispe et al. 2022; Singh et al. 2022; Bruserud et al. 2024).

As our patient exhibited with oral manifestations, particularly gingival swelling and tonsilitis, it is crucial to recognize these findings as potential indicators of an underlying systemic disease, as they can provide valuable diagnostic insights. While gingival swelling is a well-documented consequences of cytopenia due to impaired erythropoiesis, tonsilitis is a rare clinical manifestation in hematologic malignancies and warrants a thorough investigation (Khammissa et al. 2017). Tonsilitis is most frequently attributed to viral or bacterial infections, with standard diagnostic methods including gram staining, potassium hydroxide (KOH) examination, and throat swab culture (Anderson and Paterek 2023). However, despite the expectation of an infectious etiology, cytological analysis of the patient's tonsillar scraping revealed malignant hematopoietic cells, suggesting leukemic infiltration. Additionally, negative results from gram stain and KOH examination excluded bacterial and fungal infections.

The diagnosis of acute myeloid leukemia (AML) necessitates a comprehensive and multifaceted approach, incorporating various hematologic and pathological assessment (Ally and Chen 2024). A peripheral blood smear is an essential initial diagnostic tool, particularly in patients presenting with unexplained cytopenia, circulating blast cells, spontaneous bruising, or recurrent infections (Vakiti et al. 2024). In this case, the peripheral blood smear analysis demonstrated normochromic, normocytic erythrocytes alongside a prominent monoblastic proliferation, strongly indicative of an underlying myeloid malignancy. Further diagnostic confirmation requires bone marrow aspiration and biopsy, as these procedures provide critical insights into bone marrow cellularity, morphology, and blast percentage (Jain and Sharma 2024; Jawed et al. 2024). A definitive AML diagnosis is established when the bone marrow or peripheral blood blast reaches or exceeds 20%, a criterion met in our patient, consistent with acute monocytic leukemia (AML-M5) (Jain and Sharma 2024; Jawed et al. 2024). Moreover, immunophenotyping serves as a critical diagnostic modality, facilitating the precise classification of AML subtype by identifying distinct surface and cytoplasmic markers (Basharat et al. 2019; Stella et al. 2021; Döhner et al. 2022; Chennamadhavuni et al. 2023). In our patient, the findings

were consistent with myeloid lineage involvement, further substantiating the diagnosis of acute monocytic leukemia (AML-M5).

The strength in this case is that a fairly complete diagnosis was made from a complete blood test, blood smear evaluation, bone marrow aspiration test, immunophenotyping and a complete examination of tonsillitis membrane scrapings. The weakness of this study is that next-gene sequencing (NGS) was not performed, so it was not possible to identify the dominant genetic mutation in the patient. This resulted in a lack of information about prognosis and appropriate targeted therapy for the patient. Targeted therapy is needed for chemotherapy in AML.

Hydroxyurea, a ribonucleotide reductase inhibitor, was administered for initial cytoreduction in this case. By inhibiting DNA synthesis, hydroxyurea suppresses leukemic cell proliferation, aiding in the control of white blood cell counts and reducing the risk of complications such as leukostasis. However, hydroxyurea is not a curative therapy; definitive treatment for AML typically consists of induction therapy followed by consolidation therapy, which may include allogeneic hematopoietic stem cell transplantation (Musiałek and Rybaczek 2021). Therefore, ongoing treatment and monitoring is necessary to prevent adverse outcomes.

CONCLUSION

The diagnosis of acute monocytic leukemia (AML-M5) is complex and requires a comprehensive multimodal evaluation to ensure diagnostic accuracy. Leukemic infiltration of the tonsils is an uncommon manifestation of AML-M5, making a meticulous diagnostic approach essential for timely and effective management. The cause of membranous tonsillitis other than infection can also be caused by infiltration of leukemia cells, therefore it is necessary to carry out a microbiological examination such as gram staining and identification of leukemia cells from scrapings of the tonsillitis membrane. Although rare, AML can progress rapidly and lead to severe complications, underscoring the critical need for prompt recognition, accurate diagnosis, and immediate therapeutic intervention to improve patient outcomes.

CONFLICT OF INTEREST

The authors declare that they have no competing interests. This research received no specific grant from any funding drug pharmacies. The ethics of this case study have passed the ethics commission of the Faculty of Medicine, Wijaya Kusuma University, Surabaya, with the number 128/SLE/FK/UWKS/2024.

ACKNOWLEDGEMENTS

Not applicable

REFERENCES

Abelson, S. et al. 2018. Prediction of acute myeloid leukaemia risk in healthy individuals. *Nature* 559(7714), p. 400. https://doi.org/10.1038/s41586-018-0317-6.

Ally, F. and Chen, X. 2024. Acute Myeloid Leukemia: Diagnosis and Evaluation by Flow Cytometry. *Cancers* 16(22). https://doi.org/10.3390/cancers16223855

Anderson, J. and Paterek, E. 2023. Tonsillitis. *StatPearls*. Available at: https://www.ncbi.nlm.nih.gov/books/NBK544342/ [Accessed: 8 February 2025].

Basharat, M., Khan, S.A., Nasir Ud Din and Ahmed, D. 2019. Immunophenotypic characterisation of morphologically diagnosed cases of Acute Myeloid Leukaemia (AML). *Pakistan Journal of Medical Sciences* 35(2), p. 470. https://doi.org/10.12669/pjms.35.2.614

Blau, O. and Blau, O. 2015. Gene Mutations in Acute Myeloid Leukemia — Incidence, Prognostic Influence, and Association with Other Molecular Markers. *Leukemias - Updates and New Insights*. https://doi.org/10.5772/60928

Bruserud, Ø., Selheim, F., Hernandez-Valladares, M. and Reikvam, H. 2024. Monocytic Differentiation in Acute Myeloid Leukemia Cells: Diagnostic Criteria, Biological Heterogeneity, Mitochondrial Metabolism, Resistance to and Induction by Targeted Therapies. *International Journal of Molecular Sciences* 25(12), p. 6356. https://doi.org/10.3390/ijms25126356

Bullinger, L., Döhner, K. and Dohner, H. 2017. Genomics of Acute Myeloid Leukemia Diagnosis and Pathways. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 35(9), pp. 934–946. https://doi.org/10.1200/jco.2016.71.2208

Capelli, D., Menotti, D., Fiorentini, A., Saraceni, F. and Olivieri, A. 2022. Secondary Acute Myeloid Leukemia: Pathogenesis and Treatment. *Leukemia*, pp. 111–127. https://doi.org/10.36255/exon-publications-leukemia-secondary-acute-myeloid-leukemia

Chennamadhavuni, A., Lyengar, V., Mukkamalla, S.K.R. and Shimanovsky, A. 2023. Leukemia. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560490/ [Accessed: 7 February 2025].

Döhner, H. et al. 2016. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood* 129(4), p. 424. https://doi.org/10.1182/blood-2016-08-733196

Döhner, H. et al. 2022. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood* 140(12), pp. 1345–1377. https://dx.doi.org/10.1182/blood.2022016867

Hasserjian, R.P. 2021. Controversies in the recent (2016) World Health Organization classification of acute myeloid leukemia. *Best Practice and Research: Clinical Haematology* 34(1). doi: https://10.1016/j.beha.2021.101249

Jain, S. and Sharma, R. 2024. Laboratory Evaluation of Bone Marrow. *StatPearls*. Available at: https://www.ncbi.nlm.nih.gov/books/NBK603716/ [Accessed: 7 February 2025].

El Jamal, S.M., Najfeld, V., Coltoff, A. and Navada, S. 2022. Myelodysplastic Syndrome. *Atlas of Diagnostic Hematology*, pp. 98–109. Available at: https://www.ncbi.nlm.nih.gov/books/NBK534126/ [Accessed: 7 February 2025].

Jawed, Md.A. et al. 2024. An Extensive Analysis and Comparison of Bone Marrow Aspiration and Bone Marrow Trephine Biopsy at a Tertiary Care Hospital in Jharkhand for Various Hematological and Non-hematological Illnesses. *Cureus* 16(6), p. e62661. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC11258562/ [Accessed: 7 February 2025].

Khammissa, R.A.G., Fourie, J., Masilana, A., Lawrence, S., Lemmer, J. and Feller, L. 2017. Oral manifestations of thrombocytopaenia. *The Saudi Dental Journal* 30(1), p. 19. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC6112372/ [Accessed: 8 February 2025].

Knottenbelt, D.C., Patterson-Kane, J.C. and Snalune, K.L. 2015. Tumours of the cardiovascular system. *Clinical Equine Oncology*, pp. 512–543. doi: 10.1016/B978-0-7020-4266-9.00030-1.

Masoumi-Dehshiri, R., Hashemi, A., Neamatzadeh, H. and Zare-Zardeini, H. 2014. A Case Report: Acute Myeloid Leukemia (FAB M7). *Iranian Journal of Pediatric Hematology and Oncology* 4(4), p. 188. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC4293519/ [Accessed: 7 February 2025].

Musiałek, M.W. and Rybaczek, D. 2021. Hydroxyurea-The Good, the Bad and the Ugly. *Genes* 12(7). Available at: https://pubmed.ncbi.nlm.nih.gov/34356112/ [Accessed: 8 February 2025].

Quispe, R.A., Aguiar, E.M., de Oliveira, C.T., Neves, A.C.X. and Santos, P.S. da S. 2022. Oral manifestations of leukemia as part of early diagnosis. *Hematology, transfusion and cell therapy* 44(3), pp. 392–401. Available at: https://pubmed.ncbi.nlm.nih.gov/34862157/ [Accessed: 7 February 2025].

Sasaki, K. et al. 2021. De novo acute myeloid leukemia: A population-based study of outcome in the United States based on the Surveillance, Epidemiology, and End Results (SEER) database, 1980 to 2017. *Cancer* 127(12), pp. 2049–2061. Available at: https://onlinelibrary.wiley.com/doi/full/10.1002/cncr.33458 [Accessed: 6 February 2025].

Shallis, R.M., Wang, R., Davidoff, A., Ma, X. and Zeidan, A.M. 2019. Epidemiology of acute myeloid leukemia: Recent progress and enduring challenges. *Blood reviews* 36, pp. 70–87. Available at: https://pubmed.ncbi.nlm.nih.gov/31101526/ [Accessed: 6 February 2025].

Singh, P., Sharma, K., Maheshwari, A. and Sharma, S. 2022. Case Report Hemophagocytic lymphohistiocytosis secondary to T-cell Acute Lymphoblastic Leukemia with membranous tonsillitis. *Iran J Ped Hematol Oncol. 2022* 12(4), pp. 303–307. doi: http://10.18502/ijpho.v12i4.10919

Stella, S. et al. 2021. Molecular pathogenesis and treatment perspectives for hypereosinophilia and hypereosinophilic syndromes. *International Journal of Molecular Sciences* 22(2), pp. 1–22. doi: http://10.3390/ijms22020486

Vakiti, A., Reynolds, S.B. and Mewawalla, P. 2024. Acute Myeloid Leukemia. *StatPearls*. Available at: https://www.ncbi.nlm.nih.gov/books/NBK507875 / [Accessed: 6 February 2025].

Wachter, F. and Pikman, Y. 2024. Pathophysiology of Acute Myeloid Leukemia. *Acta Haematologica* 147(2), pp. 229–246. Available at: https://dx.doi.org/10.1159/000536152 [Accessed: 7 February 2025].

Xing, S. et al. 2019. Cytogenetics and associated mutation profile in patients with acute monocytic leukemia. *International Journal of Laboratory Hematology* 41(4), pp. 485–492. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/ijlh.13030 [Accessed: 7 February 2025].