



## Case Report

# A rare combination of acute myeloid leukemia with Vit B12 deficiency: Case report



Mohammad Nour Kitaz<sup>a,\*</sup>, Rama Zazo<sup>b</sup>, Muhammad Alsabbagh<sup>c</sup>, Muhammad Diabi<sup>d</sup>,  
Salam Alnahr<sup>e</sup>, Anwar Chammout<sup>f</sup>

<sup>a</sup> Department of Neurosurgery, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

<sup>b</sup> Department of Laboratory, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

<sup>c</sup> Department of Pathology, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

<sup>d</sup> Department of Gastroenterology, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

<sup>e</sup> Department of Hematology, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

<sup>f</sup> Head of Oncology Department, Aleppo University Hospital, University of Aleppo, Aleppo, Syria

## ARTICLE INFO

## Keywords:

Acute myeloid leukemia  
Vitamin B12 deficiency  
Case report

## ABSTRACT

**Introduction and importance:** Acute myeloid leukemia (AML) is a malignant disease with several risk factors from hematologic disorders, which almost presents as anemia. AML is characterized by the presence of myeloblast in the blood picture. On the other hand, macrocytic anemia characterized by the presence of megaloblastic marrow morphology. We are presenting a rare case of combined Acute myeloid leukemia with macrocytic anemia.

**Case presentation:** A 45 years old married woman was admitted for hyperthermia, dysuria, and chills. She had suffered from general malaise, weakness, and myalgia for two months. In her laboratories, the peripheral blood sample showed: HGB 26.1% (5.6 g/dL), RBCs 1.4 M/ $\mu$ L, WBC 13.3 K/ $\mu$ L. The blood smear showed megaloblastic features, so she was diagnosed with macrocytic anemia, and the treatment was blood transfusion, antibiotics, and muscular Vit B12. After one month, the peripheral blood sample showed an elevation of WBC, the bone marrow aspiration showed myeloblast infiltration represents 60% of the total events, and the flow cytometry for the bone marrow aspiration agrees with Acute Myeloblastic leukemia with Maturation M2 (AML-M2).

**Clinical discussion:** The incidence of macrocytic anemia and leukemia in one patient is infrequent, case reports give scarce information concerning a potential increased occurrence of leukemia in patients putting up with macrocytic anemia. Several theories discussed the reasons for the association of the two conditions.

**Conclusion:** we need more research on similar cases to identify the pathological mechanism.

## 1. Background

Acute myeloid leukemia (AML) is a malignant disease characterized by the presence of more than 20% blasts in the bone marrow as a result of the maturation stop of its cells in the early stages of maturity. Previous hematologic diseases are the most common risk factor for AML, including myelodysplastic syndrome, aplastic anemia, and myeloproliferative disorders [1].

Most of AML signs and symptoms refer to anemia development, which almost present as a constant feature. These signs include pallor, fatigue, weakness, palpitations, and dyspnea on exertion [2,3].

Also, the myeloblast is almost present in the blood picture [4].

Vitamin B12 is necessary for normal cell division, and its deficiency causes macrocytic anemia. megaloblastic changes in bone marrow aspirate usually diagnose macrocytic anemia [5].

The most common features of macrocytic anemia include:

Anemia, cytopenia, jaundice, megaloblastic marrow morphology, and neurologic symptoms [6].

Despite the similarity between acute myeloid leukemia and Vitamin B12 deficiency presentations, they are rarely combined. In our case, we are presenting a rare combination of the two diseases.

**Abbreviations:** AML, Acute myeloid leukemia.

\* Corresponding author. Aleppo University Hospital, University of Aleppo, Aleppo, Syria.

E-mail address: [mohnour97ki@gmail.com](mailto:mohnour97ki@gmail.com) (M.N. Kitaz).

<https://doi.org/10.1016/j.amsu.2022.104500>

Received 15 May 2022; Received in revised form 19 August 2022; Accepted 21 August 2022

Available online 25 August 2022

2049-0801/© 2022 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

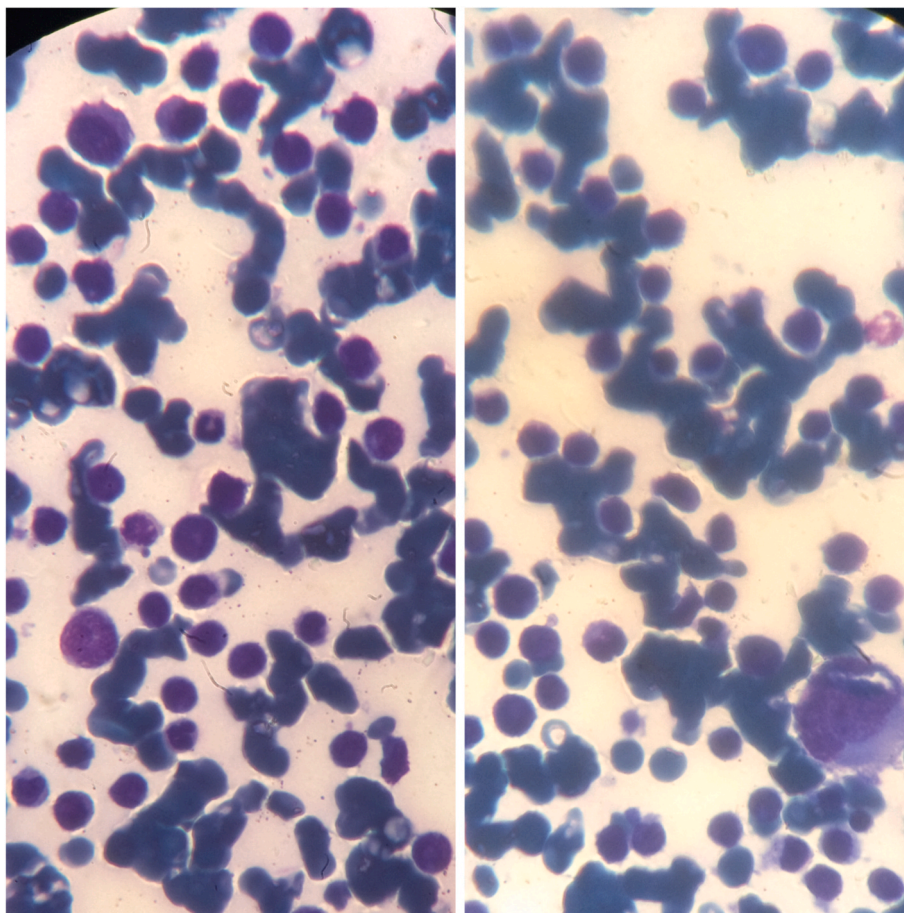


Fig. 1. Bone marrow aspiration - myeloblast infiltration (60% of the total).

## 2. Case presentation

A 45 years old woman was admitted to Aleppo university hospital clinic for hyperthermia, dysuria, and chills. She had suffered from malaise, weakness, and myalgia for two months. In her medical history, she underwent a tonsillectomy. The patient was a negative smoker for 20 years, and showed no familial diseases.

On physical examination she was pale, the temperature was 38.4 °C, the pulse was 90, and the blood pressure was 90/60. there were cervical lymphadenopathies, and there was no hepato-splenomegaly or neurological symptoms.

Peripheral blood sample showed: HGB 26.1% (5.6 g/dL), RBCs 1.4 M/ $\mu$ L, WBC 13.3 K/ $\mu$ L (GRA 64.5%, LYM 29%, MID 6.4%), PLT 61 K/ $\mu$ L, LDH 1624 U/L, CRP 55 mg/L, and Vitamin B12 170 ng/mL, the rest of the values were normal.

Blood smear showed megaloblastic features (anisocytosis, poikilocytosis, marked macrocytic, ovalocyte) which suggested macrocytic anemia.

In urinalysis; the abnormal findings were blood: +, protein: +, WBC: 20–30, RBCs: 5–7, granular casts: ++, Bacteria: +, mucus threads: ++. The urine culture was not available.

Chest X-ray was normal, ultrasonography showed enlarged round-shaped lymph nodes with hyperechoic hilum located on both sides of the neck and were prominent on the left side. liver, spleen, and urinary system were normal.

Treatment was started with blood transfusion, antibiotics, and muscular Vit B12 (1mg daily).

After one month, the overall condition did not improve, but the urinary symptoms disappeared.

The peripheral blood sample showed: WBC 19.8 K/ $\mu$ L, PLT 135 K/ $\mu$ L,

HGB 7.8 g/dL. Due to unexplained elevation of WBC, bone marrow aspiration was performed, and the results did not support for the previous diagnosis due to the presence of myeloblasts that indicates leukemia.

A peripheral blood sample flow cytometry showed that the blast population (CD117+, HLA-DR+, and CD34+) comprised 60% of the total events. Therefore, acute leukemia was an unlikely possibility. The myeloid population comprised 29% of the total events and expressed a maturation pattern within the normal limits. The monocytic population (CD45++, CD14+, CD13++, CD33++ and HLA-DR+) was increased comprising 18% of the total events. No aberrant expression was detected in this population. The lymphoid population was 34% of the total events. T cells comprised the majority of the lymphocytes. No phenotypic abnormality was detected.

The patient remained under follow-up, but due to constant malaise and paleness, she returned to the hospital.

A second bone marrow aspiration was performed, the results showed myeloblast infiltration represents 60% of the total events [Fig. 1]. A bone marrow aspiration sample sent for flow cytometry, the results showed an abnormal gated population which represents (78.5%) expresses: CD11b, CD13, CD14, CD33, CD34, CD117, CD163 positive and negative for CD5, CD10, C619 these flow cytometric results agree with Acute Myeloblastic leukemia with Maturation M2 (AML-M2).

Chemical treatment was started with Cytarabine 200 mg for 5 days with Doxorubicin 60 mg for 2 days. After 14 days a bone marrow aspiration showed a decrease in myeloblasts (hypoplasia and myeloblasts <5%) [Fig. 2], the second phase of treatment was Cytarabine 1.5 g for 5 days.

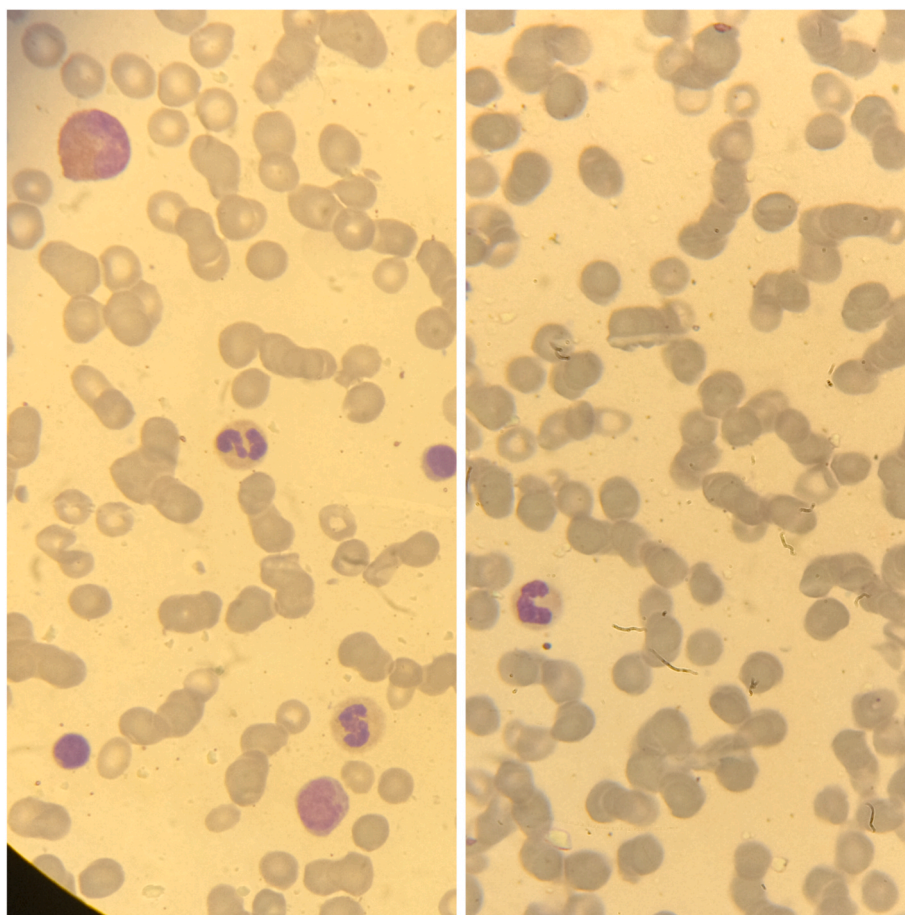


Fig. 2. Bone marrow aspiration (after the treatment) – myeloblasts <5% and hypoplasia.

### 3. Discussion

The incidence of macrocytic anemia and leukemia in one patient is infrequent, and normally enhances the anticipation of whether this finding is incidental or whether there are any relations between the two comparatively uncommon disorders [7].

Case reports give scarce information concerning a potential increased occurrence of leukemia in patients putting up with macrocytic anemia, as current case reports cannot provide risk estimates [7].

To clarify this issue, studies of major series of patients with macrocytic anemia are required. Yet, there is a paucity of literature on this issue [7].

For example, Wilkinson (1949) announced two cases of myeloid leukemia over 1,480 patients with macrocytic anemia observed through a twenty-year duration [8].

Nevertheless, the importance of the observation is uncertain as it was not possible to determine how many patients were lost to follow-up. In some minor series, the leukemia cases were absent [9–12].

Consequently, there has not been established or excluded the possibility of an increased occurrence of leukemia in patients with macrocytic anemia [7].

The theory of somatic mutation could explain the development of leukemia in patients with macrocytic anemia since the chromosome abnormalities disappear upon application of B12 treatment, these abnormalities might form leukemia [7].

Pure chance is the most acceptable theory in the light of the low incidence of the Combination. But another opinion said that an essential genetic defect in the blood-forming organs rises the possibility of occurrence of both leukemia and macrocytic anemia [13].

In macrocytic anemia, vitamin B12 and folic acid could correct the

abnormal response of granulocytic, and it was used in many cases to treat the combination of leukemia and macrocytic anemia, so, it might be the leucocytes respond exaggerate to these agents [13].

Vitamin B12 therapy could accelerate neoplasm growth, which was common when acute leukemia was treated with folic acid, and it seems the same mechanism [14,15].

Vitamin B12 is necessary for the growth and function of plasma cells, as gamma-globulins was returned to normal levels after it was low in vitamin B12 deficiency cases [16].

And it was suggested that the cause of serum vitamin B12 reduction was the plasma cells' consumption of it [16].

Vitamin B12's low levels might inhibit Cell maturation generally, and it seems that it is influencing neoplastic lymphocytes also, and since the fast growth of the tumor was restrained by the low level of vitamin B12, so the vitamin B12 treatment Support leukemia [14].

AML diagnosis needs either recognizing  $\geq 20\%$  myeloid blasts in the BM (or PB) or revealing some particular cytogenetic irregularities [17, 18].

Bone marrow aspirate is one of the most essential diagnostic materials in the diagnostic examination of AML [19,20].

The next procedure after investigating AML is to categorize AML into a subtype, for stratifying patients according to risk, anticipating the prognosis, and planning for therapeutic procedures. AML is categorized into subtypes by The WHO<sup>1</sup> classification, depending on cytogenetic irregularities, gene mutations, non-blast cells' dysplasia, and therapeutics history [17,18].

The ASH/CAP guidelines have summarized the main information

<sup>1</sup> WHO: world health organization.



that the clinical team and the pathologist require to investigate about AML subtypes: medical record, therapeutics history, cytogenetic studies (karyotyping and FISH), molecular outcomes (next-generation sequencing [NGS] and gene panels), myeloid blasts count (by manual evaluation of BM perfusion, FC investigation, or CD34 IHC staining of BM biopsy), cytogenetic investigation, and checking the extramedullary tissue [17,20,21].

Molecular genetic analysis and cytogenetic investigation, comprising FISH examination have given novel insights into the diagnostic workup of AML [20,21].

In case of uncertainty of a subtype, Real-time reverse transcriptase (RT) polymerase chain reaction (PCR) is growingly being performed to recognize transcripts of fusion proteins [20,21].

#### 4. Conclusion

Several theories discussed the reasons for the association of acute myeloid leukemia and Vitamin B12 deficiency, but we need more research on similar cases to identify the pathological mechanism.

#### Ethical approval

Not required for case reports at our hospital. Single case reports are exempt from ethical approval in our institution.

#### Sources of funding

There are no sources of funding.

#### Author contributions

AC, SA: supervisor, Physician.  
MNK, RZ, MA, MD: analyzed and interpreted the patient data, Wrote the manuscript.  
MNK, RZ: revision.  
MNK was the corresponding author.

#### Registration of research studies

1. Name of the registry: N/A
2. Unique Identifying number or registration ID: N/A
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): N/A

#### Guarantor

Mohammad Nour Kitaz

#### Consent

Written informed consent was obtained from the parent for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this

journal.

#### Declaration of competing interest

The authors declare that they have no competing interests.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104500>.

#### References

- [1] K. Seiter, E. Besa, Acute Myelogenous Leukemia, Erişim, 2006. <http://www.emedicine.com/med/topic34.htm>.
- [2] Dane R. Boggs, Maxwell M. Wintrobe, G.E. Cartwright, The acute leukemias: analysis of 322 cases and review of the literature, *Medicine* 41 (3) (1962) 163–225.
- [3] C. Patrick Burns, et al., Analysis of the presenting features of adult acute leukemia: the French-American-British classification, *Cancer* 47 (10) (1981) 2460–2469.
- [4] Michael Stanley, et al., Classification of 358 cases of acute myeloid leukemia by FAB criteria: analysis of clinical and morphologic features, in: *Chronic and Acute Leukemias in Adults*, Springer, Boston, MA, 1985, pp. 147–174.
- [5] D.L. Mollin, A.V. Hoffbrand, The diagnosis of folate deficiency, *Haematologica* 3 (1965) 1.
- [6] Ralph Green, Ananya Datta Mitra, Megaloblastic anemias: nutritional and other causes, *Med. Clin.* 101 (2) (2017) 297–317.
- [7] Vagn Gerhard Nielsen, Mogens Krogh Jensen, Pernicious anaemia and acute leukaemia: a case report with cytogenetic studies, *Scand. J. Haematol.* 7 (1) (1970) 26–31.
- [8] JohnF. Wilkinson, Megalocytic anaemias, *Lancet* 253 (6548) (1949) 336–340.
- [9] J. Waldenström, Perniciös anämi och cancer ventrikuli, *Nord. Med.* 25 (1945) 729–735.
- [10] N.R. Christoffersen, M. Clausager-Madsen, Hvorledes gir det med patienter med anæmia perniciosa? *Ugeskr. Lq.* 108 (1946) 1123–1127.
- [11] Johannes Mosbech, Aage Videbaek, Mortality from and risk of gastric carcinoma among patients with pernicious anaemia, *Br. Med. J.* 2 (1950) 4675, 390.
- [12] JØRGENSEN, JØRGEN, The mortality among patients with pernicious anemia in Denmark and the incidence of gastric carcinoma among the same, *Acta Med. Scand.* 139 (6) (1951) 472–481.
- [13] E.K. Blackburn, Pernicious anaemia complicated by granulocytic leukaemia, *J. Clin. Pathol.* 10 (3) (1957) 258.
- [14] A.C. Parker, M. Bennett, Pernicious anaemia and lymphoproliferative disease, *Scand. J. Haematol.* 17 (5) (1976) 395–397.
- [15] Sidney Farber, Some observations on the effect of folic acid antagonists on acute leukemia and other forms of incurable cancer, *Blood* 4 (2) (1949) 160–167.
- [16] C.K.V. van Dommelen, R.J. Olie, G. Slagboom, B12 lack (“Pernicious anaemia”), possibly caused by “parasitization”(consumption by a neoplasm), in a case of Waldenström’s Macroglobulinaemia, *Acta Med. Scand.* 176 (5) (1964) 611–618.
- [17] Martin S. Tallman, et al., Acute myeloid leukemia, version 3.2019, NCCN clinical practice guidelines in oncology, *J. Natl. Compr. Cancer Netw.* 17 (6) (2019) 721–749.
- [18] Mario Cazzola, Introduction to a review series: the 2016 revision of the WHO classification of tumors of hematopoietic and lymphoid tissues, *Blood* 127 (20) (2016) 2361–2364.
- [19] de Haas, Valérie, Nofisat Ismaila, Ling Zhang, Initial diagnostic workup of acute leukemia: ASCO clinical practice guideline endorsement summary of the CAP and ASH guideline, *J. Oncol. Pract.* 15 (2) (2019) 101–105.
- [20] Tracy I. George, et al., Evaluation of testing of acute leukemia samples: survey result from the College of American Pathologists, *Arch. Pathol. Lab Med.* 141 (8) (2017) 1101–1106.
- [21] Daniel A. Arber, et al., Initial diagnostic workup of acute leukemia: guideline from the College of American Pathologists and the American Society of Hematology, *Arch. Pathol. Lab Med.* 141 (10) (2017) 1342–1393.