International Journal of Research in Medical Sciences
Thomas A et al. Int J Res Med Sci. 2025 Sep;13(9):3879-3882
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20252813

Case Report

Atypical megaloblastic anemia: mimicking myelodysplastic syndrome and presenting as heart failure

Arppana Thomas[1]*, Akhil Rajeev[1], Jinu Chandran[1], Praseeda[2], Merin Thomas[2]

[1]Department of General Medicine, Travancore Medical College, Kollam, Kerala, India
[2]Department of Pathology, Travancore Medical College, Kollam, Kerala, India

Received: 20 July 2025
Accepted: 19 August 2025

***Correspondence:**
Dr. Arppana Thomas,
E-mail: Arppana97@gmail.com

ABSTRACT

Megaloblastic anemia is a reversible hematological disorder caused by impaired DNA synthesis, most commonly due to vitamin B12 or folate deficiency. Mostly it presents with anemia, neuropathy but severe cases can mimic bone marrow failure syndrome or even heart failure-like symptoms. We report a case of a 57-year-old male who presented with progressive fatigue, tingling sensations, and exertional breathlessness. Examination revealed pallor, glossitis, knuckle hyperpigmentation, and peripheral neuropathy. Laboratory investigations showed pancytopenia with a dimorphic blood picture and hypersegmented neutrophils. A positive direct coombs test (DCT) and persistent anemia even after packed red blood cell transfusion initially raised possibility of myelodysplastic syndrome (MDS). However, a markedly low serum vitamin B12 level and megaloblastic changes in peripheral smear and normal bone marrow finding confirmed the diagnosis of vitamin B12 deficiency. Our patient responded dramatically to parenteral vitamin B12 therapy, with rapid improvement. This case highlights the importance of considering nutritional deficiencies in patients with pancytopenia and atypical systemic features. Early recognition and treatment can prevent misdiagnosis, avoid unnecessary interventions, and prevent irreversible neurological complications.

Keywords: Megaloblastic anemia, Vitamin B12 deficiency, Pancytopenia, Dimorphic blood picture, Peripheral neuropathy, Bone marrow biopsy

INTRODUCTION

Megaloblastic anemia is a macrocytic anemia characterized by impaired DNA synthesis, most commonly resulting from deficiencies in vitamin B12 or folate.[1] These deficiencies are often associated with dietary insufficiency, malabsorption syndromes, gastrointestinal surgeries, or chronic gastrointestinal disorders.[2,3] The hematological hallmark of megaloblastic anemia is macrocytosis, accompanied by varying degrees of cytopenias and the presence of hypersegmented neutrophils on peripheral smear.[3,4] While isolated anemia is the typical presentation, a more severe and less common manifestation involves pancytopenia a reduction in red blood cells, white blood cells, and platelets.[2-4] This can pose a significant diagnostic challenge, frequently mimicking bone marrow failure syndromes such as MDS or aplastic anemia.[5] The pathogenesis of pancytopenia in megaloblastic anemia lies in ineffective hematopoiesis and increased apoptosis of hematopoietic precursors within the bone marrow. In addition to hematologic abnormalities, vitamin B12 deficiency has well-recognized neurological sequelae, including peripheral neuropathy, ataxia, cognitive impairment, and neuropsychiatric disturbances.[6,7] These complications can become irreversible if treatment is delayed. Hence, early recognition and intervention of vitamin B12 supplementation are essential to prevent long-term morbidity. Although rare, patients with profound anemia may present with symptoms suggestive of cardiac dysfunction due to high-output heart failure, further complicating the clinical picture.[8] In such cases, nutritional

deficiencies may be overlooked during initial evaluation, leading to misdiagnosis and unnecessary investigations or interventions. We present a case of a 57-year-old male who initially presented with exertional breathlessness and pancytopenia. The clinical picture raised suspicion for cardiac pathology and possible bone marrow failure, including MDS. However, further investigations revealed profound vitamin B12 deficiency with classic megaloblastic changes on peripheral smear and bone marrow. The patient responded dramatically to parenteral vitamin B12 therapy. This case highlights the importance of including nutritional deficiencies in the differential diagnosis of pancytopenia and underscores the need of systematic clinical evaluation to avoid diagnostic delays and inappropriate management.

CASE REPORT

A 57-year-old male, a chronic smoker and strict vegetarian residing in Andaman, presented to with complaints of progressive fatigue, tingling sensations in both lower limbs, and breathlessness on exertion for the past two months. He also reported intermittent dizziness and difficulty in walking, particularly on uneven surfaces. There was no history of fever, palpitations, chest pain, bleeding tendencies, jaundice, recurrent infections, or significant weight loss. His dietary history revealed strict vegetarianism for over two decades, with minimal intake of dairy products and no vitamin supplementation.

Physical examination

On examination he was pale looking, had glossitis with a smooth tongue (Figure 1) hyperpigmentation was present over the dorsal aspects of the knuckles (Figure 2). Neurological examination showed signs of peripheral neuropathy, diminished vibration and position sense in the lower limbs. Romberg's sign was positive. Others systemic examinations were within normal limits.

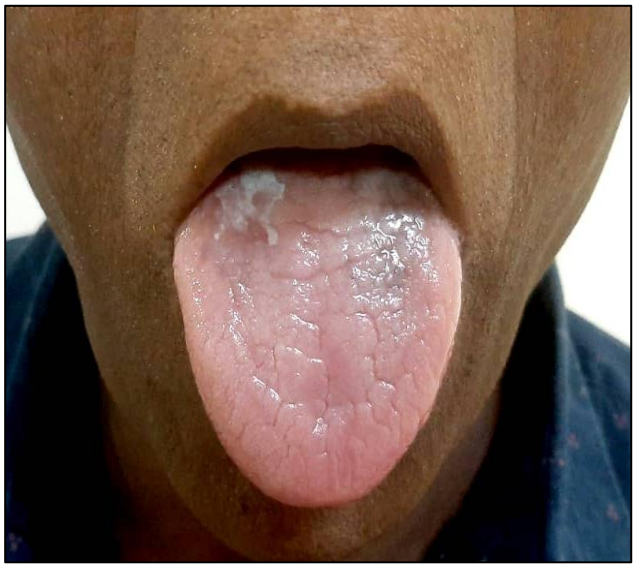

Figure 1: Glossitis.

Figure 2: Hyperpigmented knuckles.

Investigations

Blood investigations revealed pancytopenia with haemoglobin: 6.2 mg/dl, total leukocyte count: 2100 cells/mm^3, platelet count :110×10^9/L. Liver and renal function tests were within normal limits. Patient had persistent fall in haemoglobin level and fever spikes despite transfusion of packed red blood cell. DCT done was positive A possibility considered was MDS due to pancytopenia or an autoimmune hemolytic anemia in view of positive DCT. ANA profile, Ultrasound of the abdomen done was within normal limits. Peripheral smear showed dimorphic blood picture comprising both macrocytic and microcytic cells, pancytopenia, hypersegmented neutrophils (Figure 3). Chest X ray was taken to rule out any malignancy and it revealed reticulonodular pattern (Figure 4). Further workup showed reduced serum vitamin B12: 30 pg/mL (Normal: 187-833 pg/mL), normal serum ferritin. Bone marrow aspiration showed anisocytosis, hyper segmented neutrophils, and thrombocytopenia, with evidence of erythroid hyperplasia. Bone marrow biopsy revealed normocellular marrow with a prominent erythroid lineage. No abnormal or blast cell infiltrates were identified, ruling out primary marrow neoplasms or infiltrative pathology.

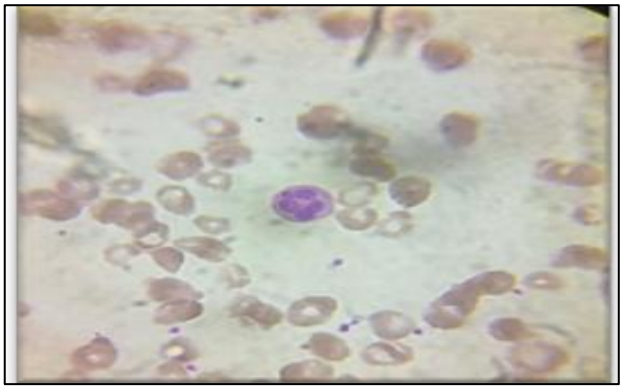

Figure 3: Peripheral smear showing hyper segmented neutrophils.

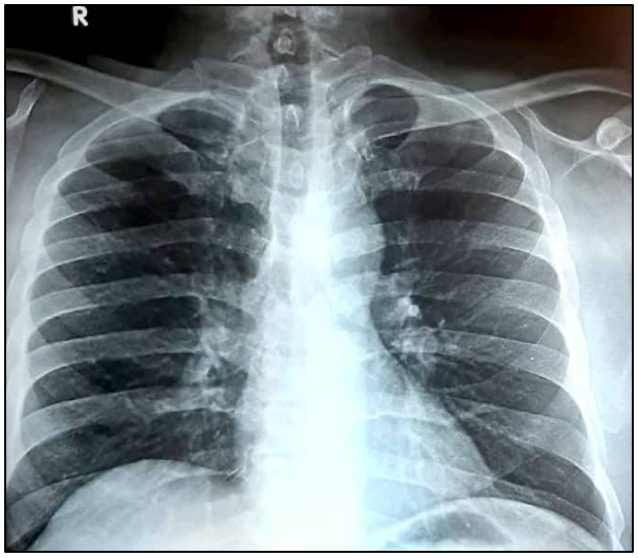

Figure 4: Reticulonodular pattern.

Diagnosis

Megaloblastic anemia secondary to vitamin B12 deficiency.

Treatment

The patient was initiated on parenteral vitamin B12 therapy with intramuscular cyanocobalamin administered at a dose of 1000 mcg daily for one week, followed by weekly injections for four weeks, and then monthly maintenance therapy. Supportive care included dietary care, counselling to promote long-term dietary adequacy, oral antifungal treatment for candidiasis, regular monitoring of hematological parameters, and neurological assessments.

Follow up

Within two weeks of initiating therapy, the patient reported significant improvement in fatigue and breathlessness Hematologic recovery, showed improvement in hemoglobin and cell counts, within 2 weeks of treatment initiation. Neurological symptoms, including paresthesia and imbalance, began to subside gradually. Repeat peripheral smear showed resolution of macrocytosis and reduction in erythroid precursors. The patient is on B12 supplementation and monthly follow up with ongoing neurological recovery.

DISCUSSION

Megaloblastic anemia due to vitamin B12 deficiency is typically characterized by macrocytic anemia, but in severe cases, it may present with pancytopenia and clinical features that mimic more serious hematologic or systemic conditions.[10,11] Rarely, severe anemia can lead to high-output cardiac failure, presenting as exertional breathlessness and prompting a misdiagnosis.[11,12] In the present case, the presence of pancytopenia, dimorphic blood picture, and marrow hypercellularity initially raised concerns for MDS. A positive DCT further confused the clinical picture, suggesting autoimmune hemolytic anemia. However, transient or false-positive DCT has been occasionally reported in megaloblastic anemia due to erythroid hyperplasia and increased apoptosis, which may expose intracellular antigens.[13,14] The diagnosis was made by a combination of peripheral smear findings macrocytosis, hypersegmented neutrophils and neurological features such as peripheral neuropathy, all of which was suggestive of vitamin B12 deficiency. Additional clinical features included glossitis, knuckle hyperpigmentation, and oral candidiasis, pointing toward a nutritional etiology, particularly in the context of the patient's strict vegetarian diet. Bone marrow aspiration and biopsy revealed classical megaloblastic changes, including erythroid hyperplasia and absence of dysplasia or blasts, ruling out MDS and other marrow-infiltrative disorders. In this patient, the markedly reduced serum vitamin B12 level and the hematologic response to parenteral B12 therapy confirmed the diagnosis. Timely recognition and intervention were helpful to prevent serious complications, as neurological manifestations may become irreversible if treatment is delayed. This case underscores the importance of considering nutritional deficiencies in the evaluation of pancytopenia and highlights the need for a systematic approach to avoid misdiagnosis.

CONCLUSION

Megaloblastic anemia, though a reversible condition, can present with atypical and misleading features such as pancytopenia, cardiac-like symptoms, and a myelodysplastic picture. This case highlights the importance of suspicion for vitamin B12 deficiency, particularly in high-risk individuals such as vegetarians and those with neurological symptoms. Prompt recognition and timely initiation of vitamin B12 therapy can prevent irreversible neurological damage and to avoid unnecessary diagnostic interventions.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Fielder JF. A 28-year-old woman presented to Kijabe Mission Hospital with severe dyspnea. MedGenMed. 2005;7(2):67.
2. Guevara NA, Perez E, Sanchez J, Rosado F, Sequeira Gross HG, Fulger I. A Case Report of Cold Agglutinin Disease, Severe B12 Deficiency, and Pernicious Anemia: A Deadly Coincidence. Cureus. 2023;15(4):45
3. Osman H, Alwasaidi TA, Al-Hebshi A, Almutairi N, Eltabbakh H. Vitamin B12 deficiency presenting with microangiopathic hemolytic anemia. Cureus. 2021;13:0.

4. Vucelić V, Stancić V, Ledinsky M, Getaldić B, Sović D, Dodig J, et al. Combined megaloblastic and immunohemolytic anemia associated--a case report. Acta Clin Croat. 2008;47(4):239-43.
5. Hill QA, Hill A, Berentsen S. Defining autoimmune hemolytic anemia: a systematic review of the terminology used for diagnosis and treatment. Blood Adv. 2019;3(12):1897-906.
6. Hassouneh R, Shen S, Lee O, Hart RA, Rhea LP, Fadden P. Severe vitamin B12 deficiency mimicking microangiopathic hemolytic anemia. J Hematol. 2021;10(4):202-5.
7. Yousaf Z, Ata F, Iqbal P, Muthanna B, Khan AA, Akram J, et al. Autoimmune hemolytic anemia associated with vitamin B12 deficiency and viral illness in DiGeorge syndrome. Case report and literature review. Clin Case Rep. 2021;9(6):e04308.
8. Acharya U, Gau JT, Horvath W, Ventura P, Hsueh CT, Carlsen W. Hemolysis and hyperhomocysteinemia caused by cobalamin deficiency: three case reports and review of the literature. J Hematol Oncol. 2008;1:26.
9. Sadagopan N. Severe hemolytic anemia due to vitamin B12 deficiency in six months. Hematol Rep. 2022;14(3):210-12.
10. Mohanty B, Ansari MZ, Kumari P, Sunder A. Cold agglutinin-induced hemolytic anemia as the primary presentation in SLE-a case report. J Family Med Prim Care. 2019;8(5):1807-8.
11. Swiecicki PL, Hegerova LT, Gertz MA. Cold agglutinin disease. Blood. 2013;122(7):1114-21.
12. Imashuku S, Kudo N, Takagishi K, Saigo K. Two cases of primary cold agglutinin disease associated with megaloblastic anemia. Case Rep Hematol. 2015;2015:913795.
13. De La Puerta R, Carpio N, Sanz G, Solves P. A case of megaloblastic anemia simulating a cold autoimmune hemolytic anemia. Immunohematology. 2020;36(3):89-92.
14. Cikrikcioglu MA, Benli AR, Erkal H, Korkmaz F, Tukek T. Masked vitamin B12 deficiency anemia as if it was haemolytic anemia. Eur J Intern Med. 2008;19(8):0-4.
15. Koubaissi SA, Degheili JA. Severe cobalamin deficiency disguised as schistocytes: a case report. Am J Case Rep. 2019;20:1691-4.

Cite this article as: Thomas A, Rajeev A, Chandran J, Praseeda, Thomas M. Atypical megaloblastic anemia: mimicking myelodysplastic syndrome and presenting as heart failure. Int J Res Med Sci 2025;13:3879-82.