

Dr. Lance D. Dworkin Department of Medicine Research Symposium

Pseudo-Thrombotic Microangiopathy by Vitamin B12 deficiency

Prajwal Hegde¹, Jennifer Kim¹, Caleb Spencer^{2*},

¹College of Medicine and Life Sciences, University of Toledo, Toledo, OH 43614

²Division of Internal Medicine, Department of Medicine, The University of Toledo,
Toledo, OH 43614

*Corresponding author: caleb.spencer@utoledo.edu

Keywords: Hemolytic Anemia, Vitamin B12, TTP
Published: 14 December 2023

Introduction: Vitamin B12 is a water-soluble vitamin primarily obtained from dairy and animal products. It is essential for several key enzymatic processes in the body, including DNA production. Vitamin B12 deficiency can manifest as pseudo-thrombotic microangiopathy (PTMA), which is an unusual clinical presentation of B12 deficiency. PTMA mimics primary thrombotic microangiopathies (TMAs) such as TTP, DIC, and HUS, with features like thrombocytopenia, schistocytes, and hemolytic anemia. In contrast to the aggressive treatment required for primary TMAs, PTMA can be effectively treated with B12 supplementation.

Case Presentation: A 73-year-old Caucasian male with a history of gout, hypertension, and hyperlipidemia presented with new-onset shortness of breath, bilateral leg pain, dizziness, tinnitus, and peripheral neuropathy. Physical examination revealed bilateral lower extremity edema, scleral icterus, and jaundice. Laboratory findings indicated normal folate levels, decreased vitamin B12 levels, elevated homocysteine, and elevated markers of hemolysis, including LDH (3137 U/L) and reticulocyte index (2.3). A peripheral blood smear exhibited macrocytic normochromic anemia with schistocytes and hypersegmented neutrophils. The patient began intramuscular and sublingual vitamin B-12 therapy, and substantial improvement in blood counts and reduced hemolytic markers were observed during a one-week follow-up.

Conclusion: PTMA is a crucial consideration in the differential diagnosis of TMA. A review by Fahmawi et al. in 2019 documented 41 cases of PTMA since 1971, suggesting that this remains a rare and potentially underdiagnosed condition. In contrast to true TMA, PTMA shows an excellent response to B12 supplementation alone, setting the standard for treatment. Physicians must remain vigilant about PTMA to prevent misdiagnosis and mistreatment. In fact, a review by Tran et al. demonstrated several adverse outcomes associated with unnecessary plasmapheresis, including anaphylaxis, hemothorax, and cardiac arrest. Recognizing PTMA could spare patients from unnecessary and risky treatments that are, at best, inefficacious and, at worst, life-threatening, when a significantly more feasible approach is available.

References

1. Ventura, P., Panini, R., Tremosini, S., Salvioli, G. *A role for homocysteine increase in haemolysis of megaloblastic anaemias due to vitamin B12 and folate deficiency: results from an in vitro experience.* Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 2004. **1739**: pp. 33–42. doi:10.1016/j.bbadis.2004.08.005
2. Durmaz, A., Dikmen, N. *Homocysteine effects on cellular glutathione peroxidase (GPx-1) activity under in vitro conditions.* Journal of Enzyme Inhibition and Medicinal Chemistry, 2007. **22**(6): pp. 733–738. doi:10.1080/14756360601164929
3. Tran, P. N., Tran, M.-H. *Cobalamin deficiency presenting with thrombotic microangiopathy (TMA) features: A systematic review.* Transfusion and Apheresis Science: Official Journal of the World Apheresis Association: Official Journal of the European Society for Haemapheresis, 2018. **57**(1): pp. 102–106. doi:10.1016/j.transci.2018.01.003
4. Walter, K., Vaughn, J., Martin, D. *Therapeutic dilemma in the management of a patient with the clinical picture of TTP and severe B12 deficiency.* BMC Hematology, 2015. **15**: p.16. doi:10.1186/s12878-015-0036-2
5. Hassouneh, R., Shen, S., Lee, O., Hart, R. A., Rhea, L. P., & Fadden, P. *Severe Vitamin B12 Deficiency Mimicking Microangiopathic Hemolytic Anemia.* Journal of Hematology, 2021. **10**(4); pp. 202–205. doi:10.14740/jh889
6. Chiasakul, T., Cuker, A. *Clinical and laboratory diagnosis of TTP: An integrated approach.* Hematology, 2018. **2018**(1): pp. 530–538. doi:10.1182/asheducation-2018.1.530
7. Favalaro, E. J., Pasalic, L., Henry, B., Lippi, G. *Laboratory testing for ADAMTS13: Utility for TTP diagnosis/exclusion and beyond.* American Journal of Hematology, 2021. **96**(8), 1049–1055. doi:10.1002/ajh.26241
8. Tun, A. M., Myint, Z. W., Rojas Hernandez, C., Guevara, E., Thein, K. Z., Oo, T. H. *Vitamin B12 Deficiency-Related Pseudo-Thrombotic Microangiopathy Might be Misdiagnosed and Treated with Plasma Product Therapy: Review of the Literature and Analysis of the Reported Cases.* Blood, 2017. **130**(Supplement 1): p.5576. doi:10.1182/blood.V130.Suppl_1.5576.5576
9. Fahmawi, Y., Campos, Y., Khushman, M., Alkharabsheh, O., Manne, A., Zubair, H., Haleema, S., Polski, J., Bessette, S. *Vitamin B12 deficiency presenting as pseudo-thrombotic microangiopathy: A case report and literature review.* Clinical Pharmacology: Advances and Applications, 2019. **11**: pp.127–131. doi:10.2147/CPAA.S207258
10. Ankar, A., & Kumar, A. (2023). *Vitamin B12 Deficiency.* StatPearls Publishing, 2023. <http://www.ncbi.nlm.nih.gov/books/NBK441923/>
11. Rao, V.R. *Vitamin B12 deficiency presenting with hyperpigmentation and pancytopenia.* Journal of Family Medicine and Primary Care, 2018. **7**(3): pp. 642–644. doi:10.4103/jfmjpc.jfmjpc_347_16
12. Abdalla, Elm., Al-Sadi, A., Fadul, A., Ahmed, A. H., & Musa, M. (n.d.). *Non-immune Intravascular Hemolytic Anemia, an Unusual Presentation of Severe Vitamin B-12 Deficiency.* Cureus, 2022. **14**(7): p.e26507. doi:10.7759/cureus.26507