Pseudo thrombotic microangiopathy- differentiating between TMA and TTP

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Introduction

- Pseudo thrombotic microangiopathy (pseudo- TMA) is a relatively uncommon pathology in severely Vitamin B12 deficient patients and can present with microangiopathic hemolytic anemia (MAHA), thrombocytopenia and schistocytosis
- The prevalence of Vitamin B12 deficiency is 5-15%, and approximately 2.5% of cases present with pseudo – TMA.
- These cases can often masquerade as more serious conditions such as thrombotic thrombocytopenic purpura (TTP) leading to the use of plasma product therapy when not truly indicated.

Case Presentation

	Case 1	Case 2
Age/Gender	52/Female	33/Female
Pertinent history	Alcoholic cirrhosis	Iron deficiency anemia on iron supplementation
Presenting symptoms	Lower extremity and abdominal pain, cough, shortness of breath, lightheadedness	One week history of palpitations
CBC	Hb 6.3 g/dL MCV 94.3 fL WBC 2.97 k/mcL Platelets 83 k/mcL	Hb 3.1 g/dL MCV 125.7 fL WBC 3.22 k/mcL Platelets 70 k/mcL.
Hemolysis parameters and Coombs test	Haptoglobin <10 mg/dL LDH 1958 U/L Coombs test negative	Haptoglobin <10 mg/dL LDH 1902 U/L Coombs test negative
RCI index	0.55, indicating hypo-proliferation	0.36, indicating hypo-proliferation
B12 levels	<150 pg/mL	<150 pg/mL
Peripheral smear	Rare schistocytes	Slight schistocytosis and hyper-segmented neutrophils
Methylmalonic acid	---	26,683 nmol/L
Workup	-Parietal cell antibody positive -Intrinsic factor antibody positive	-Intrinsic factor antibody positive
Treatment	-Daily 1000 mcg IM Vit B12 injections for a total of 7 days -4 doses of weekly IM Vit B12 injections -Subsequent monthly IM Vit B12 injections	-Daily 1000 Vit B12 IM injections while admitted -4 doses of weekly Vit B12 IM injections –Subsequent monthly IM Vit B12 injections

- Both cases above had extensive workup for additional causes of pancytopenia that was negative: no nutritional deficiencies noted, no infectious causes.
- No evidence of DIC or TTP (normal ADAMTS13 activity),
- Both patients had antibodies indicative of pernicious anemia as the cause of their severe Vitamin B12 deficiency.

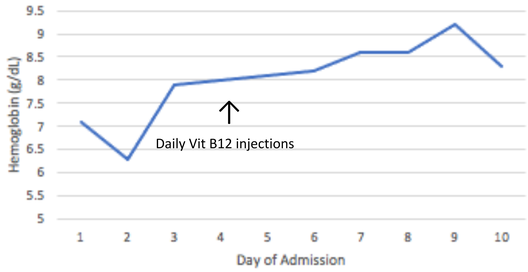

Figure 1: Case 1- hemoglobin trend with B12 repletion

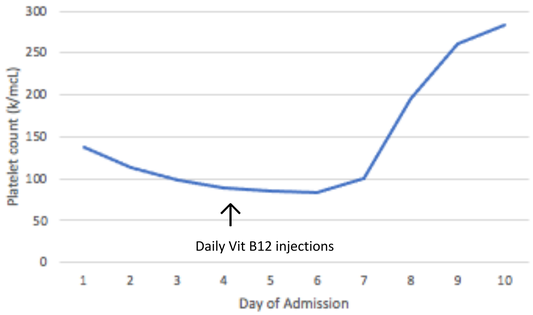

Figure 2: Case 1- platelet trend after with B12 repletion

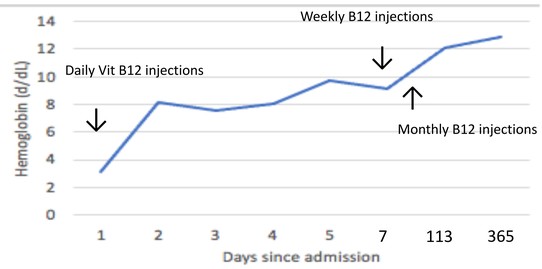

Figure 3: Case 2- hemoglobin trend with B12 repletion

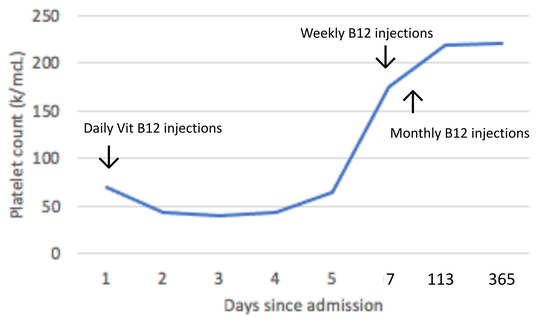

Figure 4: Case 2- platelet trend after with B12 repletion

Discussion

- Pseudo-TMA can be difficult to recognize thus it is important to keep this disease process on the differential for patients with thrombocytopenia and hemolytic anemia.
- It can be even increasingly difficult to distinguish from thrombotic thrombocytopenic purpura (TTP) as both cases present with severe thrombocytopenia and anemia, severely elevated LDH, decreased haptoglobin, and severely low Vitamin B12.
- In prior reviews, approximately 40% of patients with pseudo-TMA were treated with plasmapheresis[1]. If diagnosed appropriately, one can avoid unnecessary treatment with plasmapheresis and increasing costs of healthcare.
- TTP can ruled out with a normal ADAMTS13 activity. A further difference to note is that reticulocyte index is low due to B12 deficiency in pseudo-TMA, which would be elevated in TMA.
- Disproportionately high LDH is a notable finding in with pseudo TMA secondary to vit B12 deficiency as well.

Conclusion

- These cases emphasize the importance of early recognition of a condition that can be treated very easily and to avoid unnecessary and expensive plasma product therapy.

References

1. Aung M Tun, Zin W Myint, Cristhiam Rojas Hernandez, Elizabeth Guevara, Kyaw Zin Thein, Thein Hlaing Oo; 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): 5576
2. 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. Clin Pharmacol. 2019 Aug 27;11:127-131.