REACTIVE THROMBOCYTOSIS IN A PATIENT UNDERGOING TREATMENT FOR VITAMIN B12 DEFICIENCY

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ABSTRACT

This case reports describes the presentation and management of a middle-aged patient with significant and chronic nutritional deficiencies (Vitamin B12) contributed to by a history of schizoaffective disorder. The patient presents acutely with altered mental state secondary to sepsis and severe anaemia. Upon acute stabilisation and completion of replacement therapy, subsequent laboratory monitoring demonstrated significant levels of thrombocytosis requiring an urgent transfer back to the acute hospital for further evaluation and management. This case demonstrates the phenomena of reactive thrombocytosis post-Vitamin B12 replacement in the context of severe malnutrition and B12 deficiency.

Key words: Reactive thrombocytosis; Vitamin B12 deficiency; hypokalaemia; anaemia; Schizoaffective disorder

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CASE PRESENTATION AND MANAGEMENT OF CASE

Mr G, a 40-year-old Chinese male, was initially admitted to an acute hospital after being found unconscious with a GCS of 5 (E1V2M2), requiring intubation and admission to the intensive care unit (ICU). History taken by the paramedics from the family revealed that the patient had been anorexic and had not been eating for the two days prior. On examination, the patient was jaundiced, cachectic with a BMI of 12, and in a poor general condition. Pressure sores were noted over his left hip, while hematomas were also noted over his left temporal region, and left thigh. Preliminary investigations showed severe pancytopenia—with haemoglobin (Hb) levels at 1.7g/dL (Reference range 13.6–16.6 g/dL), and a platelet count of 36 x 10^9/L (Reference range 150–360 x 10^9/L). This was associated with low haptoglobin levels and raised unconjugated bilirubin suggestive of haemolytic anaemia. Peripheral blood film showed hypersegmented neutrophils while the Direct Coomb's test was negative. He was noted to have a severe vitamin B12 deficiency of 90 µmol/L (Reference range 145–569 µmol/L). A CT brain was done showing no signs of intracranial haemorrhage. The renal panel showed elevated creatinine levels suggestive of an acute kidney injury while the inflammatory markers, i.e., C-reactive protein (CRP) and ketone levels, were also noted to be raised. A chest X-ray concurrently showed signs suggestive of a right lower zone pneumonia. Mr G was given intravenous fluids and antibiotics for elevated creatinine levels and pneumonia respectively. For his malnutrition, he was started on a 1,800 kcal diet with 60 g of protein per day supplemented by oral Fresubin 2 cal/ml feeds.

Mr G had a past medical history of schizoaffective disorder with manic symptoms but had defaulted follow-ups and was not on treatment. He had also previously been worked-up for anaemia and thrombocytopenia six years ago attributed to poor oral intake with significantly low levels of vitamin B12 at 44 µmol/L (Reference range 145–569 µmol/L) and folate at 9.3 nmol/L (Reference range 8–40 nmol/L) resulting in ineffective erythropoiesis. Previous work-up for autoimmune, malignant, or congenital causes of bicytopenia were unremarkable (including G6PD enzyme levels, hepatitis serology, ANA, ENA, ANCA/anti-MPO/anti-PR3, anti-dsDNA, anti-intrinsic factor, and anti-parietal cell antibodies).

With regards to the patient's current presentation, his GCS drop was attributed to his severe anaemia as well as sepsis. The clinical impression for the underlying reason behind the patient's bicytopenia was a severe Vitamin B12 deficiency on a background of severe malnutrition. His malnourishment was in turn related to disorganised and anorexic behaviour from a relapse of his schizoaffective disorder. During resuscitation, he was given three pints of blood transfusion, and upon stabilisation of his condition, Mr G was started on a customised nutritional supplementation and feeding regime. He was also treated with subcutaneous mecobalamin and IV folate replacement, which brought about significant reticulocyte response. He received a regimen of regular intramuscular doses of cyanobalamin 1 mg weekly for three weeks followed by monthly injections and intravenous folinic acid 10 mg once daily for three days followed by a daily 5 mg dose of folic acid.

His Hb levels increased to 8.9 g/dL while his platelet levels increased to 323 x 10^3 u/L. On stabilisation, the patient was transferred to a tertiary psychiatric hospital for further management of his schizoaffective disorder.

Blood tests repeated subsequently, however, demonstrated further increases in the patient's platelet levels, from 686 u/L and eventually up to 865 u/L over a course of three

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days. The patient was then placed on regular full blood count monitoring, with an early haematological referral arranged for his thrombocytosis. He was also reviewed regularly for thromboembolic complications such as any neurological deficits or cardiorespiratory symptoms. Later in the admission, the patient reported chest pain associated with up-trending troponin levels as well as ECG changes of tall T waves over the lateral leads.

The decision was made for the patient to be transferred back to the acute restructured hospital for further evaluation in view of concerns of thromboembolic risks and possible acute coronary syndrome. He was later referred for an urgent haematology consultation. As he was sent to another institution, the subsequent management of his clinical condition was not known due to restrictions in accessing patient data.

DIAGNOSES/PROBLEMS IDENTIFIED

Vitamin B12 deficiency is a common condition associated with megaloblastic anaemia.[1] The effects of Vitamin B12 deficiency can be multiple and systemic. Haematological manifestations are related to bone marrow suppression and while reduced erythropoiesis commonly results in megaloblastic anaemia, pancytopenia may also occur affecting all cell lines. Neuropsychiatric manifestations may also occur, including symptoms of peripheral neuropathy, areflexia, diminished sense of proprioception, and spinal cord subacute combined degeneration (SACD).[2] While routine screening for Vitamin B12 levels are not recommended, screening may be appropriate for patients with significant risk factors.[2] Screening may be warranted in patients with one or more risk factors such as gastric or small intestine resections, inflammatory bowel disease, use of metformin for more than four months, use of proton pump inhibitors or histamine H2 blockers for more than 12 months, vegans or strict vegetarians, and adults older than 75 years.[2] Besides addressing reversible causes of its deficiency, replacement of Vitamin B12 can be achieved via oral supplementation or intramuscular injections in cases of severe deficiency or neurological symptoms.[3] Monitoring of response rate to therapy may include monitoring of reticulocyte response, haemoglobin concentration, improvement of hyper segmented neutrophils, and decrease in serum methylmalonic acid.[4]

Vitamin B12 replacement in the context of thrombocytopenia may result in reactive thrombocytosis or secondary thrombocytosis, which is also otherwise commonly caused by infection, inflammatory conditions, haemolysis, iron deficiency, malignancies, and even exercise. Vitamin B12, being essential in DNA synthesis, is involved in hematopoietic processes. Replacement of Vitamin B12 in the context of severe deficiency might result in a rebound effect following marrow recovery and megakaryocyte production. Inflammation and the release of cytokines may also stimulate and potentiate this process.[5] The management of reactive thrombocytosis involves addressing its underlying cause. While usually benign, patients at high-risk of thromboembolic complications or with platelet counts exceeding 1,000,000/μL may require anti-thrombotic therapy. In cases of thrombosis, plateletpheresis may also be considered.[5]

CLINICAL PRACTICE POINTERS

This case demonstrates the phenomena of reactive thrombocytosis post-Vitamin B12 replacement in the context of severe malnutrition and B12 deficiency. This emphasises the need for routine follow-up and full blood count monitoring even after blood counts show an improving trend following replacement therapy. It is also important to evaluate patients for thromboembolic complications and to be mindful of clinical circumstances in which an urgent haematological consult may be necessary. While Vitamin B12 deficiency may contribute to bicytopenia, it is prudent to consider differentials of malignancies or myeloproliferative disorders should there be any relevant clinical red flags that might be unmasked following replacement therapy. As haematopoiesis accelerates post-replacement therapy, iron supplementation may also be necessary especially for patients with relevant risk factors for iron deficiency. As potassium is also utilised in this process, subsequent regular monitoring of the patient's renal panel in the initial phase of potassium replacement may be warranted to treat the hypokalaemia.[6]

In this patient's presentation, there is also a significant overlay of how manifestation of the patient's psychiatric condition has influenced his medical condition, which emphasises the importance of comanaging psychiatric conditions with the community care physicians. The chronicity and severity of the patient's malnutrition bring to attention a probable significant duration of untreated disorganised behaviour. It bears emphasis for community medical and mental health practitioners to be vigilant with regards to early signs of relapses and unusual behaviour that might influence medical outcomes.

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