



A case of non-immune haemolytic anaemia in the context of severe haematinic deficiency in pregnancy

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- Although iron deficiency is the most common cause of anaemia in pregnancy, B12 and folate deficiencies may occur.
- Folate deficiency is more common than B12 deficiency due to increased folate requirements in pregnancy and extensive normal body stores of B12.¹
- The cause of anaemia should be formally investigated prior to commencement of treatment.
- Non-immune haemolytic anaemia can occur secondary to B12 and folate deficiencies.
- Correction of the underlying vitamin deficiencies will result in resolution of the haemolysis.

Case Report

Presentation:

- A 25-year old G4P2 presented at 31+1 weeks gestation the day after receiving a Monofer infusion, with nausea, vomiting and a jaundiced appearance.
- The Monofer infusion had been organised due to haemoglobin 81g/dL on bloods at 28/40. Haematinics had not been analysed.
- Initial investigations at presentation:** haemoglobin 71g/dL, platelet count 99x10⁹/L and bilirubin 44µmol/L. Liver function tests were otherwise normal.
- Over the following hours, haemoglobin fell to 54g/dL and platelet count to 78x10⁹/L. Two units of packed red cells were administered.

Key haematological investigations:

- Folate <0.38µg/L, B12 116ng/L
- LDH 3197U/L, Haptoglobin <0.1g/L, ADAMTS13 activity 62.9%
- Direct antiglobulin test (DAT) was negative.

Blood film:

Mixed picture with pencil cells, hypochromic microcytic red blood cells (RBCs) and prominent teardrop RBCs. Toxic granulated neutrophils with left shift of the entire myeloid spectrum. Occasional hypersegmented neutrophils. Minor platelet clumping.

Diagnosis:

Non-immune haemolysis likely secondary to severe B12 and folate deficiencies, with features of iron deficiency evident on the blood film.

Management:

- IM Cyanocobalamin 1mg was commenced immediately, and administered on alternate days for two weeks. This was followed by a maintenance regime.
- Folic acid supplementation (5mg OD) was commenced the following day, to reduce the risk of subacute combined degeneration of the cord. This was continued for 90 days.

	Day 1	Day 3	Day 5	Day 6	Day 13
Haemoglobin (g/dL)	54	67	68	73	102
Platelet count (x10 ⁹ /L)	78	61	67	71	370
LDH (U/L)	3197	2404	2481	1966	491
Folate (µg/L)	<0.38				3.39
B12 (ng/L)	116				831

Table 1: summary of haematological investigations from the time of commencement of medical therapy on the day of admission (Day 1). Note two units of packed red cells were given on Day 1 following the results of the full blood count.

Delivery and ongoing care:

- The patient had a spontaneous vaginal delivery at 36+3 weeks gestation, with an estimated blood loss of 150ml.
- There were no fetal abnormalities.
- She was referred to dietetics and gastroenterology in light of combined nutrient deficiency.

Discussion

- Non-immune haemolytic anaemia can occur secondary to B12 and folate deficiencies, with a presumed mechanism of intramedullary haemolysis.²
- Appropriate correction of vitamin deficiencies results in resolution of the haemolysis, and normalisation of haemoglobin and platelet counts.
- Where both B12 and folate supplementation are required, B12 supplementation should be commenced first to reduce the risk of subacute combined degeneration of the cord.

- The cause of anaemia should be formally investigated prior to commencement of treatment. A confirmed diagnosis of iron-deficiency anaemia is a prerequisite for Monofer administration.
- In this case, Monofer administration may have contributed to the patient's presentation by triggering haematopoietic collapse in the context of depleted B12 and folate.
- Formal evaluation of the cause of this patient's anaemia at 28/40 could have resulted in early correction of vitamin deficiencies, and thus the patient may have avoided a hospital admission with multiple investigations, and administration of blood products.

References

- Khan A, Robinson S. Vitamin B12 and Folate in Pregnancy. In: Pavord S, Hunt B, eds. The Obstetric Haematology Manual. 2nd ed. Cambridge: Cambridge University Press; 2018: 29-39.
- Zhang Q, Shan KS, Ogunnaike BA, Amewuame-Kpehor A, Nace T. An Exceedingly Rare Presentation of Severe Folate Deficiency-Induced Non-Immune Hemolytic Anemia. Cureus. 2020 Jun 11;12(6):e8570.