CASE REPORT

Vitamin B12 Deficiency Presenting as Pancytopenia in Pregnancy: A Case Report

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Abstract

Vitamin B12 deficiency is a well-known cause of megaloblastic anaemia and pancytopenia. However, the incidence in pregnancy is rarely reported. We present a case of a 32-year old multigravid woman who was diagnosed with megaloblastic anaemia since 22 weeks gestation and progressed to develop severe pancytopenia at 30 weeks gestation. She was also diagnosed with vitamin B12 deficiency related to dietary and sociocultural habits. Folate and iron levels were normal throughout pregnancy. Treatment with parenteral cyano-cobalamin resulted in sustained improvement of haematological parameters. The pregnancy was carried to term and the baby was born weighing 2,050gm but otherwise well at birth and had normal developmental milestones thereafter. This case illustrates the clinical presentation of maternal vitamin B12 deficiency and demonstrates the importance of detecting and treating maternal vitamin B12 deficiency during pregnancy in at-risk patients. Failure to diagnose and institute treatment carries significant risks to both mother and child. Oral vitamin B12 supplementation should be considered for patients who are strict vegetarians or consume very little animal products.

Introduction

Pregnancy is associated with a steady and physiologic fall in serum vitamin B12 as well as red cell vitamin B12 with reports of mean serum vitamin B12 to be 300pg/ml in the first trimester, 250pg/ml in the second and 190pg/ml in the third trimester.[1] This physiologic fall is attributed to transfer of vitamin B12 to the foetus, hemodilution and changes in vitamin B12 binders (transcobalamin I). However, pregnancy alone is not the predisposing factor of vitamin B12 deficiency; other conditions such as pernicious anaemia, B12 malabsorption and nutritional deficiency attributed to a vegetarian diet need to be considered.

Vitamin B12 deficiency commonly presents with megaloblastic anaemia, and rarely, pancytopenia. The correlation between maternal and neonatal vitamin levels and corresponding neonatal homocysteine levels has been established. Vitamin B12 deficiency can potentially affect the pregnancy [2] depending on the severity of the deficiency; in severe cases, it can result in intrauterine death. Most effective treatment method is through administring parenteral vitamin B12. We report a case of a multigravida who presents with pancytopenia as a result of vitamin B12 deficiency.

Case Summary

A 32-year old gravida 8 para 7 was admitted at 31 weeks gestation with severe anaemia and

reduced effort tolerance. Her haemoglobin level was 6.4 g/dL. Patient was a small built lady who weighed 53 kg at 31 weeks gestation and is 152cm tall. She was pale requiring no other abnormalities were found after a thorough examination. The uterus size corresponded to her gestation period but the foetus was slightly below the 10th centile on the growth chart. There was no other evidence of foetal growth restriction at this stage and subsequent follow-ups showed normal foetal growth velocity.

She was diagnosed with mild anaemia (haemoglobin level of 10.0 g/dL) at 5 weeks gestation. Total white cell count was 5.6 x 10^9/L and the platelet level was 168 x 10^9/L. No further investigation was conducted and she was given supplements in the form of oral ferrous fumarate 200mg daily, folate 5mg daily and vitamin B complex (1 mg vitamin B1, 1.5mg vitamin B2, 10mg vitamin B3). Despite being compliant to the above treatment, her haemoglobin level continued to decline. The MCV was high (>100 fl) at 22 weeks gestation indicating macrocytic anaemia. Her serum vitamin B12 was slightly low 160 pmol/L (normal 179-660 pmol/L) while serum folate, iron and ferritin were normal (serum ferritin 62.3 ng/mL, serum iron 49.1µg/dL, serum plasma folate 18.7 nmol/L). Full blood picture showed macrocytic red cells, moderate anisopoikilocytosis and reduced number of platelet (120 x 10^9/L) without any clumping. The oral supplement was continued. At 30 weeks of pregnancy, she developed pancytopenia (haemoglobin 7.2 g/dl, total white cell count 2.9 x 10^9/L and platelet 55 x10^9/L) and the level of vitamin B12 dropped to 110 pmol/L. Her serum iron, ferritin and folate levels were normal. Plasma lactate dehydrogenase level was high at 2,476U/l (normal value of 313–618 U/l) but other laboratory results indicated normal liver and renal function. No auto-antibodies were present. Schilling test was not done in view of the pregnancy. The results of serial haematological parameters are shown in Figure 1.

She was given two units of packed red cell in view of severe anaemia at 31 week of pregnancy. In view of worsening vitamin B12 deficiency despite oral supplements, 100µg of intramuscular cyano-cobalamin was given daily for one week followed by a weekly injection from 34 weeks onwards. Subsequently normalisation of white cell count, platelet count and MCV was seen and there was sustained improvement in the haemoglobin level.

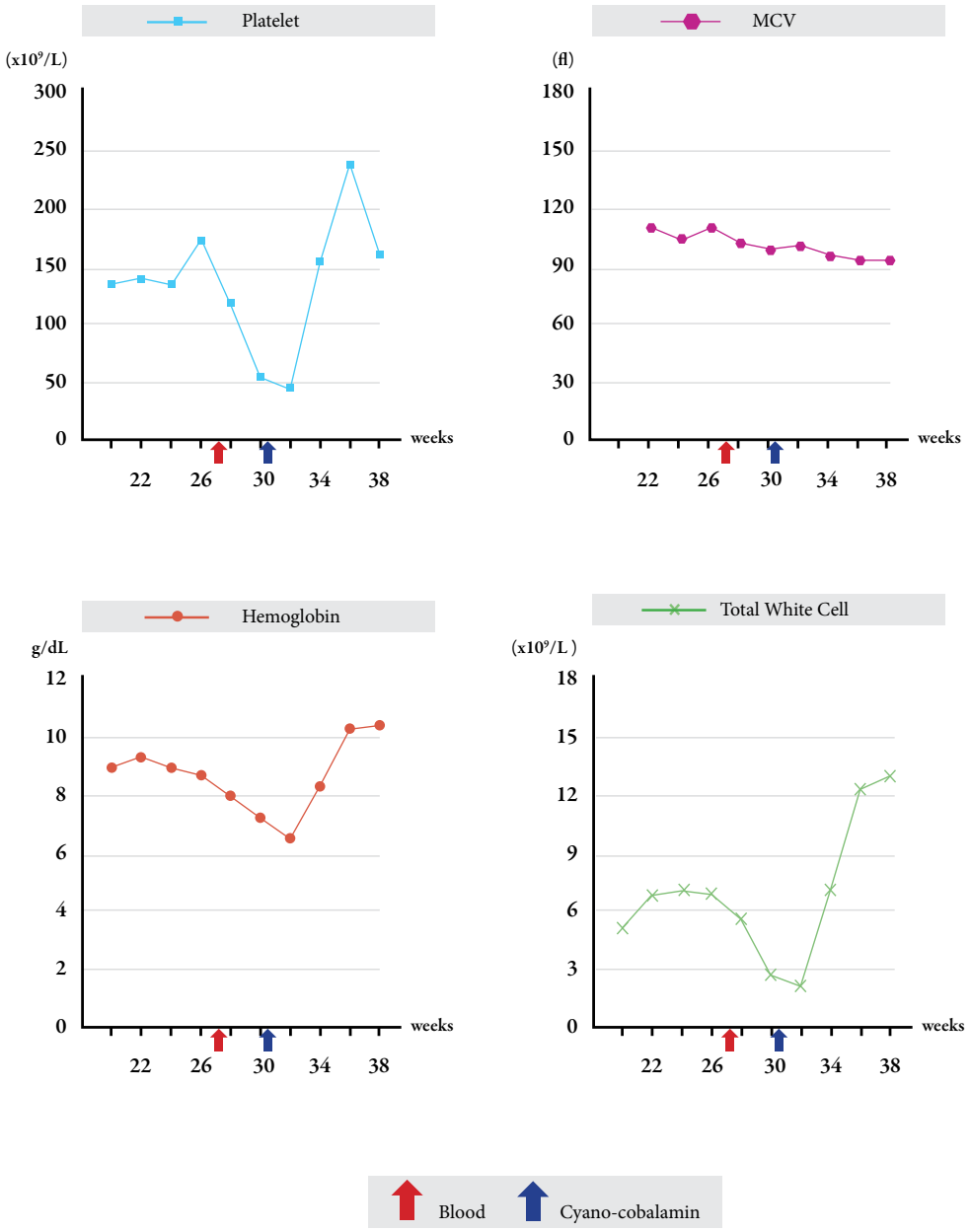
The patient was not a vegetarian but had limited financial resources. She could only afford meat or chicken once weekly with small portions per serving. Her main diet consisted of bread, rice and green vegetables. She did not smoke, use recreational drug usage or consume alcohol. Her past medical history was unremarkable and she had never undergone any surgery. In her past pregnancies, she had been diagnosed with anaemia attributed to iron deficiency but there was no record of pancytopenia prior to this pregnancy. Between 1998 to 2006, she had seven pregnancies, six of which were delivered at term and the birth weights of the babies ranged between 1.55kg and 3.5kg. She delivered a 800g baby during her 5th pregnancy and the baby died on day 5 of life due to severe prematurity.

She went into spontaneous labour at 38 weeks gestation requiring an emergency caesarean section due to evidence of foetal distress. The baby weighed 2050g and was vigorous at birth with normal Apgar score. There was no clinical evidence of anaemia or other neonatal problems. At 6 months follow-up, the baby was well with no evidence of neurological sequelae and had normal developmental milestones.

Discussion

We presented a case of a multigravida who was diagnosed with pancytopenia secondary to vitamin B12 deficiency. She responded to parenteral vitamin B12 treatment and had a good pregnancy outcome. The diagnosis was made based on the demonstration of

Figure 1: Hematological parameters before and after treatment



megaloblastic changes in the peripheral blood, the presence of low serum vitamin B12 level and normal serum folate.

The cause of vitamin B12 deficiency in this patient is likely to be nutritional deficiency based on her dietary history and her haematological parameters. Although she was not a vegetarian, there was minimal intake of animal products due to limited financial resources. Although pregnancy causes a reduction in serum vitamin B12 level, it alone does not cause vitamin B12 deficiency. Low levels of serum vitamin B12 have been documented among pregnant mothers in India who habitually took small portions of non-vegetarian foods

due to religious and socio-economic reasons.[3] Another possible cause is mal-absorption of vitamin B12, which could be due to deficiency of intrinsic factor. Schilling test to investigate for mal-absorption is not performed in this patient due to pregnancy. Pernicious anaemia is rare in women of reproductive age group.

The effects of vitamin B12 deficiency in pregnancy depends largely on the severity of the deficiency. Most pregnancies proceed uneventfully but spontaneous abortion, intra-uterine death and low birth weight have been reported. There are reported cases of increased insulin resistance in the off-springs and infants who have low vitamin B12 levels at birth. The infants are also at risk of developmental defects and neurological damage.[4-7] A list of potential complications related to B12 deficiency is shown in Box 1. Low birth weight and intra-partum foetal distress in this patient's newborn could be attributed to utero-placental insufficiency related to vitamin B12 deficiency; however, so far, the evidence supporting this is not consistent. In mothers who are deficient in vitamin B12 breast feeding may worsen the deficiency in the offspring. However, breastfeeding may still be encouraged among mothers of low socio-economic group as the benefits outweigh the risks. In this patient, since the vitamin B12 deficiency was diagnosed and treated prenatally, the infant is unlikely to suffer from the sequelae of vitamin B12 deficiency.

Box 1: Potential complications of vitamin B12 deficiency in pregnancy

- Spontaneous abortion
- Intra-uterine death
- Low birth weight infant
- Increased insulin resistance
- Developmental defects
- Neurological sequelae
- Intellectual impairment

Treatment of vitamin vitamin B12 deficiency in pregnancy is similar to that of non-pregnant patients. Generally, if there is no evidence of mal-absorption, oral B12 supplementation can be used. However, in this patient, parenteral vitamin B12 was used instead because the status of absorption could not be determined and it ensured better compliance to treatment compared with oral supplementation. An initial dosage of 100 to 1000ug initial dosage of 100 to 1000ug intramuscular injections can be given daily, on alternate days or weekly for 10 to 14 injections, followed by maintenance dose if needed. This patient showed improvement with the dose of 100ug daily for 7 days and weekly for subsequent weeks until delivery.

There is limited data on the prevalence of vitamin B12 deficiency in pregnancy. Most of the reported cases of vitamin B12 deficiency are among the Indian population and attributed to strict vegetarian diet or minimal non-vegetarian products in the diet. A comparative study done to determine the profile of vitamin B12 and folate status in Malaysians during 1987/88 and 1992/93 found an increasing prevalence of vitamin B12 deficiency compared with folate deficiency.[8] Therefore, we recommend that pregnant and lactating women who are at risk of vitamin B12 deficiency to be given vitamin B12 oral supplementation in the dose of 2.6ug daily, as recommended by the World Health Organization.[9]

Conclusion

This case illustrates the clinical presentation of maternal vitamin B12 deficiency and demonstrates the importance of detecting and treating maternal vitamin B12 deficiency during pregnancy in at-risk patients. Failure to diagnose and institute treatment may carry significant risks to both mother and child. Oral vitamin B12 supplementation should be considered for patients who are strict vegetarians or consume little animal products in their diet.

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