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Vitamin B_{12} deficiency in a breast fed infant

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SUMMARY We report the case of a 5 month old breast fed infant who presented with a history of vomiting, pallor, and failure to thrive. Investigations showed severe nutritional vitamin B_{12} deficiency with a megaloblastic pancytopenia. This deficiency was due to low vitamin B_{12} concentrations in the maternal breast milk, and subsequent investigations showed maternal pernicious anaemia. Treatment of the infant with vitamin B_{12} resulted in a rapid clinical and haematological improvement. This case represents an unusual presentation of pernicious anaemia.

Dietary vitamin B_{12} deficiency in infancy is rare, and most reported cases are breast fed infants of mothers who themselves are deficient in vitamin B_{12}, usually on the basis of deficient (particularly vegetarian) diets.[1–4] The development of haematologic, neurologic, and metabolic abnormalities in the breast fed offspring of these mothers is usually the presenting feature of the maternal deficiency, which itself may be mild. The case reported here is that of a breast fed infant whose vitamin B_{12} deficiency presented as vomiting, failure to thrive, and megaloblastic pancytopenia at 5–6 months of age. Although maternal serum vitamin B_{12} concentrations and blood film were normal, concentrations of vitamin B_{12} in the breast milk were very low. Subsequent studies showed maternal vitamin B_{12} deficiency due to subclinical pernicious anaemia. Three similar cases, two of whom had prominent neurologic abnormalities, have been reported.[5–7]

Case report

A girl, the first born infant of healthy unrelated parents (birth weight 3080 g), was exclusively breast fed and maintained the 25–50th weight percentile until 3–4 months of age when vomiting became a problem. This did not respond to the introduction of solids and in the three months before admission she gained only 250 g. Pallor was first noted by her local physician at 5 months of age, and anaemia was diagnosed (haemoglobin concentration 74 g/l). Treatment with oral iron was without effect, and at the time of her referral to the Adelaide Children's Hospital a complete blood count showed pancytopenia with a haemoglobin of 70 g/l, white cell count $7{\cdot}5\times10^9$/l, absolute neutrophil count 530×10^6/l, and platelets 55×10^9/l.

On admission, she was found to be a pale placid infant, with a weight of 5640 g (<3rd percentile), length 66 cm (10th–25th percentile), and head circumference 43 cm (10th percentile). There was no lymphadenopathy and no organomegaly. Neurodevelopmental assessment was consistent with postnatal age, and maternal dietary history was normal. Subsequent investigations of mother and infant are shown in the table.

Table *Results of investigations on infant and mother*

Investigation	*Infant*	*Mother*
Haemoglobin (g/l)	52	136
White cell count ($\times10^9$/l)	3·1	6·6
Absolute neutrophil count ($\times10^6$/l)	400	4550
Platelet count ($\times10^9$/l)	46	>200
Serum vitamin B_{12} (pmol/l)*	<37	273
Serum folate (nmol/l)†	49	9–8
Breast milk vitamin B_{12} (pmol/l)‡	—	44·3
Schilling test	Normal	Abnormal
Barium meal and follow through	Normal	Not tested
Gastric parietal cell antibody	Negative	Positive +
Thyroid cytoplasmic antibody	Not tested	Positive ++
Intrinsic factor antibody	Negative	Positive +++
Free thyroxine index§	Not tested	55
Thyroid stimulating hormone (IU/l)‖	Not tested	126

*Serum vitamin B_{12} normal range=221–885 pmol/l.
†Serum folate normal range=6·8–47·7 nmol/l.
‡Breast milk vitamin B_{12} normal range=207–1549.
§Free thyroxine index normal range 75–150.
‖Thyroid stimulating hormone normal result <10 IU/l.

The infant's blood film showed appreciable poikilocytosis and anisocytosis with macrocytic changes. The reticulocyte count was 1·4% and there were two nucleated red cells per 100 white cells. Occasional myelocytes and metamyelocytes were seen. A bone marrow biopsy specimen showed appreciable megaloblastic changes with considerable disparity between nuclear and cytoplasmic development in all cell lines, and there was a myeloid: erythroid ratio of 2:1. The low serum vitamin B_{12} concentrations prompted further studies in the infant, including a Schilling test and gastric acid secretion studies all of which gave normal results.

Breast milk vitamin B_{12} concentrations were determined using the same competitive protein binding assay used to determine serum vitamin B_{12} concentrations. Although the validity of this assay system for breast milk B_{12} was not determined, the concentration of 44·3 pmol/l was considerably lower than concentrations determined in our laboratories, using the same assay system, on breast milk samples from healthy lactating women (206·6–1549·4 pmol/l).[4] Also, the concentration of 44·3 pmol/l is low compared with other published normal ranges of breast milk vitamin B_{12} determined by other methods.[8 9] Overall, the low breast milk vitamin B_{12} concentrations suggested subclinical maternal vitamin B_{12} deficiency, and subsequent investigations showed classical (Addisonian) pernicious anaemia and hypothyroidism.

The infant was transfused and vitamin B_{12} (250 μg) was administered as part of her Schilling test. Serial blood counts showed a rapid improvement in neutrophil and platelet counts (see figure). Vomiting stopped coincident with the administration of vitamin B_{12}, and a considerable 'character' change, manifested by increased activity and responsiveness, was noted in the child by both parents and hospital staff. The mother was treated with thyroxine and parenteral vitamin B_{12}. Follow up of the infant at 12 and 18 months showed a clinically normal child with normal haematology and serum vitamin B_{12} concentrations. Now, at 8 years of age she is functioning normally in an age appropriate school setting.

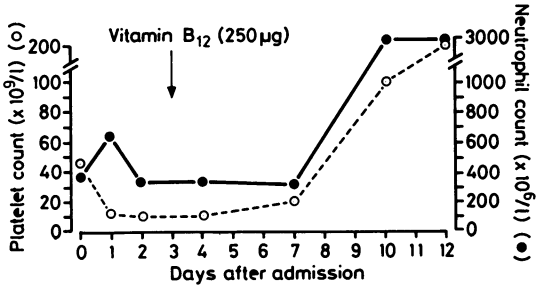

Figure *Neutrophil and platelet counts before and after treatment with 250 μg vitamin B_{12}.*

Discussion

The estimated vitamin B_{12} requirements of the growing infant are 0·06–0·10 μg/day and the normal neonatal vitamin B_{12} stores are of the order of 20–25 μg.[10] Therefore the normal newborn infant has sufficient vitamin B_{12} stores to last for six to eight months, even in the presence of inadequate dietary intake or defective vitamin B_{12} absorption.[10] On the other hand, the vitamin B_{12} stores of the infant of a deficient mother may be as low as 2–5 μg[10] and although normal breast milk has considerable vitamin B_{12},[8 9] the vitamin B_{12} content of the breast milk of deficient mothers is low, as shown by this and other cases.[1–7] Overall, the vitamin B_{12} state of the breast fed infant of a vitamin B_{12} deficient mother is precarious, with marginal stores being aggravated by inadequate dietary intake.

In the present case the maternal complete blood picture and serum vitamin B_{12} concentration were normal. The low breast milk vitamin B_{12} concentration was the only clue to the mother's aberrant vitamin B_{12} state. A similar situation has been described in one other case.[2]

Based on the estimated daily requirements presented above, adequate vitamin B_{12} intake with a breast milk B_{12} concentration of 44·3 pmol/l would require an intake of 1–1½ litres of milk per day. While this would appear achievable, we speculate that the onset of vomiting at 3 months of age in the present case was critical in limiting vitamin B_{12} deficiency. Also, as discussed below, the vomiting itself may have been caused by vitamin B_{12} deficiency. Alternatively, because our normal range for breast milk vitamin B_{12} is considerably higher than other published normal ranges,[8 9] it is possible that our assay method may have overestimated breast milk vitamin B_{12} and that inadequate intake was present from an early age.

The clinical features of vitamin B_{12} deficiency in infancy are predominantly neurologic and haematologic. Neurologic features include an acquired movement disorder, developmental regression, torpor, and even coma.[1–4 6 7] The appreciable character change noted in our patient after the administration of vitamin B_{12} suggests that her placidity on presentation was an early neurologic feature. Other case reports,[6 7] including one from this institution,[4] have reported long term developmental and neurologic sequelae of vitamin B_{12} deficiency in infancy. In general, such sequelae seem to be associated with profound neurologic abnormalities at the time of

presentation and presumably the absence of such abnormalities in the present case may explain the good long term outcome.

The haematologic features of vitamin B_{12} deficiency—namely, a megaloblastic pancytopenia—were well illustrated in our case. Other reported features such as mild hepatosplenomegaly, diarrhoea, and a curious palmar pigmentation appear variable, and were not seen in our patient. Vomiting has not been reported previously in association with vitamin B_{12} deficiency in infancy, but was the presenting complaint in our case. The absence of any structural cause, and the prompt resolution of vomiting coincident with the administration of vitamin B_{12} suggest that the vomiting was a symptom of the vitamin B_{12} deficiency.

Three other cases of occult maternal pernicious anaemia presenting as symptomatic vitamin B_{12} deficiency in a breast fed child have been reported.[5–7] Haematologic features were prominent in the case described by Lampkin *et al*,[5] while developmental regression was the presenting complaint in the case of Sadowitz *et al*,[6] and obtundation with hypothermia was seen in the case of Johnson and Roloff.[7]

In summary, a case of vitamin B_{12} deficiency in the breast fed infant of a mother with occult pernicious anaemia is presented. Vomiting and a megaloblastic pancytopenia were features of the infant's presentation. A low breast milk vitamin B_{12} concentration was the only clue to the maternal deficiency. This case serves to emphasise that vitamin B_{12} deficiency presenting at less than 6 months of age is almost exclusively seen in breast fed infants of vitamin B_{12} deficient mothers. In the absence of a deficient maternal diet (particularly a strict vegetarian diet), occult pernicious anaemia should be considered as the reason for the maternal deficiency.

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