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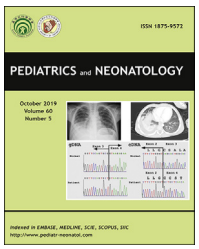

Short Communication

Vitamin B12 deficiency anemia in an exclusively breastfed infant born to an ileum-resected mother

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Vitamin B12 (cobalamin) is essential for folate metabolism and DNA synthesis. It acts as a cofactor for two key enzymatic reactions, methylation of homocysteine to methionine and conversion of methylmalonyl coenzyme A (CoA) to succinyl CoA.[1] Deficiency of vitamin B12 results in an accumulation of homocysteine and methylmalonic acid, resulting in hematologic and neurologic manifestations.[1] Although vitamin B12 deficiency is rare in developed countries, it is important to recognize this condition because early treatment can prevent potentially devastating neurologic sequelae.[1] In the majority of cases, vitamin B12 deficiency in infants is secondary to maternal deficiency that is caused due to either dietary deficiency or pernicious anemia.[2,3] Other rare causes include maternal gastric bypass surgery.[4,5] Impaired absorption of vitamin B12 after ileal resection has been well documented.[6] However, cases of vitamin B12-deficient infants secondary to maternal ileal resection have not been described in the literature. Here, we describe a case of vitamin B12 deficiency anemia in an exclusively breastfed infant born to a mother who underwent ileal resection.

The male patient was born after a normal pregnancy as the first child of non-consanguineous Japanese parents at 39 weeks of gestation. His mother was aged 32 years and primigravida. His birth weight and head circumference were 3260 g and 33.4 cm, respectively. The infant was exclusively breastfed, which resulted in good body weight gain. However, at a regular 4-month health check-up, the family physician noticed pallor in the conjunctivae and incomplete head control. Laboratory examination (Supplementary Table 1) revealed normocytic anemia, with the following data: hemoglobin level 6.6 g/dl, hematocrit 19.4%, red blood cell (RBC) count 2.21 $\times$ 10^{12}/l, reticulocyte count 24.3 $\times$ 10^{9}/l, mean corpuscular volume (MCV) 87.8 fL, white blood cell count 9.2 $\times$ 10^{9}/l with 29% of

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neutrophils, and platelet count 160 $\times$ 10^9/l. Peripheral blood smear examination demonstrated hypersegmented neutrophils, anisocytosis, poikilocytosis, and schistocytosis (Fig. 1a). A direct Coombs test showed a negative result with undetectable serum haptoglobin level (<10 mg/dl) and the following levels: lactate dehydrogenase 2665 U/l, total bilirubin 3.15 mg/dl, ferritin 311 ng/ml, iron 184 μg/dl, unsaturated iron binding capacity 82 μg/dl, and total iron binding capacity 266 μg/dl. The serum vitamin B12 level was 32 pg/ml (normal: 180–914 pg/ml), while that of folic acid was 33.7 ng/ml (normal: >4.0 ng/ml). Serum levels of methylmalonic acid and total homocysteine levels were highly increased to 12.0 nmol/ml (normal: <1.0 nmol/ml) and 122.0 nmol/ml (normal: <5.0 nmol/ml), respectively. Bone marrow examination revealed the presence of ring neutrophils (Fig. 1b), binucleated erythroblasts (Fig. 1c), and megakaryocytes with multiple separate nuclei (Fig. 1d), mimicking myelodysplastic syndrome. Based on the abovementioned findings, a diagnosis of megaloblastic anemia caused due to vitamin B12 deficiency was made.

Because our patient was exclusively breastfed, his mother was evaluated for vitamin B12 deficiency. Medical history showed that the mother had undergone resection of necrotic ileum (approximate length: 1.5 m) and sigmoid colon due to transmesenteric hernia at the age of 10 years. The blood cell count of the mother revealed macrocytic anemia with the following parameters: hemoglobin level 10.6 g/dl, hematocrit 31.7%, RBC count 3.04 $\times$ 10^{12}/l, reticulocyte count 60.8 $\times$ 10^9/l, and MCV 104.0 fL. Serum levels of vitamin B12, methylmalonic acid, and total homocysteine were 69 pg/ml, 2.2 nmol/ml, and 55.0 nmol/ml, respectively.

Based on these findings, the infant's vitamin B12 deficiency was attributed to inadequate intake of vitamin B12 due to maternal vitamin B12 deficiency after ileal resection. He was treated with intravenous thiamine disulfide phosphate, followed by oral mecobalamin and concurrent iron supplementation. Within a few days after the initiation of therapy, hematologic manifestations of the infant were rapidly improved. Furthermore, the mother was treated with oral mecobalamin supplementation. At 5 months of age, brain magnetic resonance imaging of the infant did not reveal significant abnormalities. At 8 months of age, the patient achieved normal developmental milestones.

We retrospectively evaluated the patient's levels of methylmalonic acid and total homocysteine at birth using a newborn-screening dried blood spot card. As anticipated, these levels were already elevated at birth (18.0 and 15.0 nmol/ml, respectively). These results suggested that the supply of vitamin B12 had been deficient during the fetal period. Moreover, the supply of vitamin B12 was inadequate even after birth, secondary to exclusive breastfeeding from the mother who had vitamin B12 deficiency. Although the mother was asymptomatic, she had subclinical vitamin B12 deficiency.

This case demonstrates that vitamin B12 deficiency may occur in exclusively breastfed infants born to mothers who have undergone ileal resection even in the absence of clinical and biological signs of maternal anemia. Therefore, a thorough evaluation of the maternal nutritional and operational history is essential to identify at-risk individuals. Adequate vitamin B12 should be supplemented to mothers during exclusive breastfeeding or to infants at risk, which include cases with subclinical vitamin B12 deficiency.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pedneo.2019.06.002.