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SEVERE VITAMIN B12 DEFICIENCY IN INFANT WITH PANCYTOPENIA

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ABSTRACT
Vitamin B12 deficiency and associated megaloblastic anemia is generally a problem involving children, pregnant women and the elderly in developing countries. Vitamin B12 deficiency in early childhood is frequently seen in babies born to mothers with vegetarian diets and vitamin B12 deficiency. In addition to neurological symptoms such as hypotonia, tremor and convulsion, findings such as abnormal pigmentation, sparse and dull hair, lack of appetite, vomiting, diarrhea, glossitis, oral moniliasis, hepatomegaly, splenomegaly, rejection of solid foods and growth retardation may be observed. If infantile B12 deficiency is diagnosed and treated early, neurological symptoms resolve in as little as 3-6 months, while in cases diagnosed late neurological findings take at least 6 months to improve, and the process may sometimes take years. We describe a patient referred to our hospital due to pancytopenia and neuromotor retardation and diagnosed with vitamin B12 deficiency.

INTRODUCTION

Vitamin B12 deficiency is one of the most common causes of childhood megaloblastic anemia. It frequently develops in association with dietary intake deficit. In the first 2 years of life it manifests with anemia, neutropenia, thrombocytopenia, growth and development retardation and progressive neurological findings associated with deficiency in mother's milk, particularly in developing countries. Early diagnosis of vitamin B12 deficiency in childhood, and particularly infancy, when growth and development are very rapid, is important in terms of preventing neurological and psychomotor injury and achieving recovery [1, 2].

CASE REPORT

A 1-year-old male patient was referred to our hospital with a preliminary diagnosis of sepsis from the health center to which he presented with fever and diarrhea persisting for the previous week. He was born on term by non spontaneous vaginal delivery, weighing 3600 g and with no complications during birth. There was no consanguinity between the parents, and he had a healthy sibling. The patient was still receiving mother's milk with no additional foods. He was able to hold his head erect and had been able to sit unsupported for the previous 1 month. Six or seven times in the previous week he had produced watery, yellowish-green, odorless diarrhea. Reddening and scabbing persisted around the mouth and neck region. For the previous 2 days he had been febrile, lethargic and uninterested in his surroundings. Physical examination findings were body weight: 7.6 kg(< 3 p), height:81 cm (75-90 p), temperature:36.1°C, heart rate: 156/min, respiration rate:24/min, BP: 92/61 mmHg and SatO2: 98. He was conscious, apathetic and uninterested in his surroundings. Hyperemic, occasionally crusty cutaneous lesions were observed in the perioral, cervical and pelvic region, with diffuse petechial eruptions in the umbilical region and extremities(Figures 1,2). The skin and conjunctiva were pallid, and the liver was palpable 2 cm beneath the ribs. The spleen was not palpable. Hb was 6.2 g/dl, Htc: 17.8%, WBC:3800/mm³, PLT: 40,000/mm³, MCV:100fL, RDW:24fL, ANS: 300 and Rtc: 1.6%. No atypical cells were observed in peripheral smear,

erythrocytes were hyperchromic and normocytic, no findings of hemolysis were encountered, there was no hypersegmentation in neutrophils, and platelets were single and unclumped. Complete urine test was normal. Sedimentation rate was 48 mm/h, Na:132 Meq/lt and albumin: 2.3 gr/dl. Other electrolyte and biochemistry values were normal.CRP was 50.9, ferritin:357, folate:4.9ng /dl and vitamin B12 <83pg/dl. Bone marrow aspiration revealed no megaloblastic changes. Stool microscopy revealed abundant leukocytes. No growth was observed in stool culture. Immunoglobulin levels were age–appropriate, and TORCH IgM (-) was determined. Lymphocyte subgroups were within normal levels. Sweat test value was 28 mmol/l.

The patient was started on fluid administration through the intravenous route. The antibiotic therapy he was receiving was maintained. Erythrocyte suspension was transfused at a level of 10 cc/kg, and control Hb was determined at 9.7 g/dl. Albumin was administered iv at a dose of 1 g/kg. Low vitamin B 12 levels were determined. Vitamin B12 was administered daily for 1 week at 100 µg im, and then on alternate days for another week. No fever was observed at follow-up, diarrhea resolved, skin findings improved and the patient's interest in his surroundings increased. Post-treatment Hb was11.3 g/ dl, Htc: 33.5%, WBC: 13,400/mm³, PLT: 557,000 /mm³, MCV:95fL and RDW:21.3 fL.The patient's appetite improved. He began receiving supplementary foods and gained weight. He was discharged on the 12th day of hospitalization to attend check-ups at the hematology clinic with a recommendation of monthly vitamin B12 injection.

Fig 1, 2. Hyperemic, occasionally crusty cutaneous lesions were observed in the perioral, cervical and pelvic region.

DISCUSSION

Vitamin B12 deficiency and associated megaloblastic anemia is generally a problem involving children, pregnant women and the elderly in developing countries. Vitamin B12 deficiency in early childhood is frequently seen in babies born to mothers with vegetarian diets and vitamin B12 deficiency. During pregnancy, vitamin B12 is actively transmitted from the mother to the baby via the placenta. Babies born to mothers with no deficiency are born with a 25-50 mcg reserve of vitamin B12, enough to meet the baby's needs for 6 months to 1 year. Vitamin B12 deficiency is therefore rarely seen under the age of 4 months [3].

Development of the brain, and particularly the cortex, is very rapid in the first 2 years. Myelination, which begins in the second half of pregnancy and continues to puberty, is most intensive in the first 2 years and is adversely affected by vitamin B12 deficiency. Compromise of fetal brain development is less severe than postnatal brain maturation compromise. In infantile vitamin B12 deficiency, myelination slows down, and cerebral atrophy and diffuse EEG deceleration occur. Vitamin B 12 deficiency leads to compromise of nervous functions through consecutive demyelination in the nervous system, axonal degeneration and neuronal death. This finally results in mental and motor development retardation. If infantile B12 deficiency is diagnosed and treated early neurological symptoms resolve in as little as 3-6 months, while in cases diagnosed late neurological findings take at least 6 months to improve, and the process may sometimes take years. Cases of pronounced vitamin B12 deficiency-related cortical atrophy have been reported [4]. Schneck et al. reported complete resolution in 16 out of 24 cases of physical, mental and motor development retardation with vitamin B12 deficiency, while neurological improvement was not complete in another six cases due to late diagnosis although physical development was normal [5]. In addition to neurological symptoms such as hypotonia, tremor and convulsion, findings such as abnormal pigmentation, sparse and dull hair, lack of appetite, vomiting, diarrhea, glossitis, oral moniliasis, hepatomegaly, splenomegaly, rejection of solid foods and growth retardation may be observed [6]. Lack of appetite, rejection of solid food, diarrhea, glossitis, cutaneous

lesions, hepatomegaly and neuromotor development retardation were also present in our case. VitaminB12 and folate deficiency can also lead to depression in adults. The probable mechanism involves an increase in homocysteine levels in patients with vitamin deficiency.

Findings ranging from mild anemia to pancytopenia, hypogammaglubulinemia and proteinuria may be determined at laboratory examination. High plasma homocysteine levels are observed [7]. Anemia, thrombocytopenia and leukopenia were present in our case. Immunoglobulin values were normal and no proteinuria was determined.

In a study of 1120 schoolage children from Denizli, Turkey, Balci *et al*. reported that 5.6% of children were anemic. While iron deficiency was determined in 59% of those, both iron and vitamin B12 deficiencıes were present in 41% [8]. Another study from Diyarbakır determined a vitamin B12 deficiency level of 2.2% among school age children [9]. In a similar study from Şanlıurfa, Koç et al. assessed 203 children aged 9-12. Anemia was determined in 4.9%, of whom 10.8% also had vitamin B12 deficiency. Additionally, vitamin B12 levels were significantly lower among children with helminthes identified at stool examination compared to those with no helminthes [10].

Pregnant women and newborns represent a significant risk group for vitamin B12 deficiency in developing countries. In a study of 250 mothers and term babies from Istanbul, Önal *et al*, observed vitamin B12 insufficiency in 81.6% of mothers and 42% of babies [11].

In terms of treatment, 100 µg dose must be administered im daily for 1 week. The same dose must be administered on alternate days in the second week and once monthly thereafter. Hematological parameters improve very quickly after treatment. However, vitamin B12 deficiency can lead to permanent neurological injury in patients diagnosed late. Response to treatment was achieved within a few days in our case, and anemia, thrombocytopenia and leukopenia all resolved. Cutaneous findings and apathy improved, and the patient's interest in his surroundings increased.

In conclusion, vitamin B12 deficiency must be considered in patients presenting with cytopenia and neuromotor retardation. Early diagnosis and treatment is important in terms of preventing permanent neurological damage. At risk pregnant women must be identified, and vitamin B12 replacement must be administered throughout pregnancy and breastfeeding.

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