ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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HEMATOLOGICAL FINDINGS IN CHILDREN WITH VITAMIN B12 DEFICIENCY

B12 VİTAMİN EKSİKLİĞİ OLAN ÇOCUKLARDA HEMATOLOJİK BULGULAR

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Öz

Amaç

Vitamin B12 eksikliği çocukluk çağında sık görülen bir durumdur ve eksikliğine bağlı olarak çeşitli nörolojik, hematolojik ve dermatolojik bulgular görülebilmektedir. Çalışmanın amacı B12 vitamini eksikliği tanısı alan çocuklarda hematolojik bulguları değerlendirmektir.

Gereç ve Yöntem

Çocuk Hematoloji Bölümü'nde B12 eksikliği tanısı ile izlenen hastaların hematolojik verileri geriye dönük olarak incelendi.

Bulgular

Çalışmamızda yüz yirmi dört hastanın hematolojik verileri değerlendirildi. Kırksekiz hastada anemi, 8 hastada trombositopeni ve 6 hastada lökopeni tespit edildi. İki süt çocuğu uzamış sarılık ve hemolitik anemi ile başvurdu. Hastaların ortalama vitamin B12 düzeyleri 97.3±30.6 (5-140) pg/ml idi.

Sonuç

Vitamin B12 eksikliği gelişmekte olan ülkelerde sık görülen bir hastalıktır ve çoğunlukla annedeki eksiklikten kaynaklanır. Çalışmamızda 52 bebekten 42'sinin (%80) annesinde B12 vitamini eksikliği saptandı. Buda gebelerde B12 vitamini düzeyinin belirlenmesinin ve eksiklik durumunda tedavisinin önemini açıkça göstermektedir. B12 vitamini eksikliği olan hastalar çeşitli nedenlerle hastaneye başvurabilirler. Bu nedenle özellikle uzamış sarılık ve hemolitik anemi ile başvuran hastalarda B12 vitamini eksikliğinin neden olabileceği akılda tutulmalıdır.

Anahtar Kelimeler: Çocuklar, Hematolojik bulgular, Vitamin B12 eksikliği

Abstract

Objective

Vitamin B12 deficiency is a common condition in childhood and various neurological, hematological, and dermatological findings could be seen due to its deficiency. The aim of the study is to evaluate the hematological findings in children diagnosed with vitamin B12 deficiency.

Materials and Methods

Hematological data of children with B12 deficiency who were examined in Pediatric Hematology Department were retrospectively reviewed.

Results

Hematological data of one hundred twenty-four patients were assessed in our study. Anemia, thrombocytopenia and leucopenia were detected in

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48 patients, 8 patients and 6 patients, respectively. Two infants presented with prolonged jaundice and hemolytic anemia. The mean vitamin B12 levels of the patients were 97.3±30.6 (5-140) pg/ml.

Conclusion
Vitamin B12 deficiency is a common disease in developing countries and it is mostly of maternal origin. In our study, vitamin B12 deficiency in mothers of 42 out of 52 infants (80%) were discovered. This percentage clearly shows the importance of the vitamin B12 level determination in pregnant women and its treatment in case of deficiency. Patients with vitamin B12 deficiency might be admitted to the hospital for various reasons. Therefore, it is recommended to keep in mind that vitamin B12 deficiency might be the base of various diseases, especially for patients presenting prolonged jaundice and hemolytic anemia.

Keywords: Vitamin B12deficiency, hematological findings, children, Turkey.

Introduction

Vitamin B12 deficiency is commonly seen in children of developing countries and its frequency increases in infancy and adolescents. Various neurological, hematological and dermatological disorders could be seen due to vitamin B12 deficiency. Here, maternal vitamin B12 deficiency is a major cause of neonatal deficiency. Other reasons of this deficiency could be inadequate consumption of animal foods, vegetarian or vegan diets and vitamin B12 absorption disorders (1-4). The aim of our study is to detect hematological findings in children diagnosed with vitamin B12 deficiency and to evaluate their response to the treatment.

Material and Methods

Records of 124 patients between 1 month and 17 years of age admitted to the Pediatric Hematology Department between June 2014 and June 2015 and diagnosed with vitamin B12 deficiency were analyzed retrospectively. Patients' medical history, complaints and physical examination findings were recorded also with measurements of the following parameters: complete blood count, peripheral smear, serum vitamin B12 and folate levels, iron and iron binding capacity, ferritin levels, and vitamin B12 levels of the mothers of infancy. After evaluation of these parameters, the study continued with patients having a serum vitamin B12 level less than 200 pg/ml. The type of treatment given to these patients, and their vitamin B12 levels before and after the treatment were noted.

The study was conducted in accordance with the Helsinki Declaration principles and approved by Turgut Özal University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 10.08.2015, Number: 999506691/73).

Statistical Analysis

All analyses were performed using IBM SPSS version 21 (SPSS IL, USA) and Graph Pad Prism 6 (San Diego, USA) software. The normality of variables was tested using aD'Agostino-Pearson omnibus normality test. On the other hand, categorical variables were compared using the chi-square test and Fisher's exact test. Student's t test was also used to compare variables between groups. A nonparametric test (Mann–Whitney U test) was used if the variables did not have Gaussian distribution. In this assessment, P value<0.05 was considered statistically significant.

Results

A total of 124 patients with vitamin B12 deficiency between the ages of 1 month and 17 years were included in the study. Fifty-six patients were girls and sixty-eight patients were boys. Their mean age was 6.5±5.9 years (1 month-17 years). Ninety-three of the 124 patients were either adolescents or infants. Fifty-two patients were infants and forty-one patients were adolescents in this category. The mean age of infants were 10.3±6.8 months (1-24 months), and the mean age of adolescents were 14.0±1.7 years (11-17 years). The patients were admitted to our clinic with complaints pallor (n: 17), growth retardation (n: 6), upper respiratory tract infection (n: 6), abdominal pain (n: 3), constipation (n: 2), syncope (n: 2), seizure (n: 1), difficulty in perception (n: 1), recurrent aphthous stomatitis (n: 1), palpitations (n: 1) and epistaxis (n: 1). The following diseases were identified in these children who has B12 deficiency: thrombocytopenia in four, prolonged jaundice in two, splenomegaly in two and hepatomegaly in one. Other patients were diagnosed during the routine control. All patients under 6 months in infancy were fed breast milk and those over 6 months were fed breast milk and additional foods.

Laboratory findings of the patients are shown in Table-1.

Anemia in 48 patients, thrombocytopenia in 8 patients, and pancytopenia in 5 patients were detected, respectively. The demographic and laboratory characteristics of the patients having pancytopenia are shown in Table-2. The mean hemoglobin values of the patients with anemia were 8.3±1.8 (3.6-10.9) g/dL. Twenty patients had high mean corpuscular volume (MCV) values, and the mean was 96.5±6.6 (90-116) fL.

Mean vitamin B12 levels were 97.3±30.6 (5-140) pg/mL. Iron deficiency were detected in 38 patients. Folate deficiency was not found in our patients. Two of these patients had prolonged jaundice and anemia. They were 1.5 months old and their mothers had low vitamin B12 levels. Both patients had negative direct coombs, high reticulocyte count and hemolysis findings in their peripheral smear. There were no blood group and subgroup incompatibility between mothers and babies. Thyroid function tests, G6PD and pyruvate kinase enzyme levels were in normal ranges. Patients' urine analysis were normal and

Table 1 Laboratory findings of the patients

	Mean±SD	Min-max (SD)
Vitamin B12 (pg/mL)	97.3 ± 30.6	5-140
Haemoglobin (g/dL)	11.2±2.7	3.6-16.1
MCV (fL)	79.1±13.3	45.0-116.0
MCH (pg)	25.1±5.6	12-41
MCHC (g/dL)	31.4±2.7	25.0-39.8
WBC (103/µL)	8983±4549	2736-41230
Platelet (/mm3)	362.7±15.5	13.9-916.0
Iron (µg/dL)	55.6±49.6	2-255
Total iron-binding capacity (µg/dL)	318.8±91.6	81-505
Ferritin (ng/mL)	41.8±71.1	0.8-546.0

Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; WBC, white blood cell.

Table 2 Demographic and laboratory characteristics of patients presenting with pancytopenia

Case	Gender	Age (year)	VİTAMİN B12 (pg/mL)	WBC (10^3/µL)	Hb (gr/dL)	MCV (fL)	MCH (pg)	MCHC (gr/dL)	Platelet (/mm3)
1.†	male	1	38	3130	3.6	69	27	39	140000
2.	male	0.8	83	3900	6.5	91	30	33	146000
3.	male	10	97	3400	6	116	41	36	58100
4.	female	0.3	5	3870	5.7	96	32	34	101000
5.‡	female	0.8	124	3560	10.3	74	24	33	13900

Abbreviations:Hb, haemoglobin; MCH, mean corpuscular hemoglobin;
MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; WBC, white blood cell.
† The case has accompanying thalassemia trait
‡ The case has accompanying iron deficiency

urine cultures were sterile. One patient's mother had accompanying thrombocytopenia and anemia. Transfusion was performed before cesarean delivery. Vitamin B12 deficiency was detected in the mother of 42 out of 52 (80%) infants.

All of the patients had received intramuscular (IM) treatment. In the first month of treatment, it was observed that vitamin B12 levels returned to normal, and anemia, thrombocytopenia and leucopenia improved. It was noticed that blood values of the mothers with thrombocytopenia and anemia returned to normal in the first month of treatment. Vitamin B12 treatment and iron treatment were given to patients with iron deficiency. The bilirubin levels of two infants who presented with hemolytic anemia and jaundice decreased to normal limits in the first month of the treatment, their hemolysis findings were completely recovered and hemoglobin values increased.

Discussion

Although the frequency of vitamin B12 deficiency is not known exactly, it is more common in infancy and adolescence. The biggest factor in infants is of maternal origin (5). In the study conducted by Koç et al. (6) on 180 mothers and newborns in the Southeastern Anatolia Region, the frequency of vitamin B12 deficiency was found to be 72% in mothers in the immediate postnatal period and 41% in newborns, it was emphasized that the deficiency in babies was arised from the maternal originand that their mothers could be given vitamin B12 prophylactically.

Çoban et al. (7) in a study they conducted with 240 infants and their mothers, found cobalamin deficiency with a rate of 60.8% in infants and 76.7% in their mothers.

In our study, all patients under 6 months in infancy were fed breastmilk, and those over 6 months were fed breastmilk and additional foods. Vitamin B12 deficiency was detected in the mother of 42 out of 52 infants (80%).

In other studies conducted in our country, similar rates to our study is observed and the importance of determining the vitamin B12 level in pregnant women and its treatment in case of vitamin B12 deficiency is clearly seen (6-8). Especially in vegetarian or vegan pregnant women, vitamin B12 level and iron parameters are recommended to be checked before pregnancy and treatment should be started for deficient vitamins.

Hematological, neurological and dermatological findings are common in vitamin B12 deficiency. There are publications and case reports in the literature indicating that it progresses with neutropenia, macrocytosis, macrocytic anemia, thrombocytopenia, and pancytopenia (6, 8-10). In a study involving 201 adults with vitamin B12 deficiency, it was found that approximately 10% of patients showed life-threatening hematological symptoms. These included pancytopenia (5%), severe anemia (defined as hemoglobin level <6.0 g / dL; 2.5%), and hemolytic anemia (1.5%) (11). We detected anemia in 48 (38.7%), thrombocytopenia in 8 (6.4%), pancytopenia in five (4%) and hemolysis in two (1.6%) of our patients. 20 patients had high MCV values. Findings were similar to rates reported in theliterature (6, 8-10). It has been reported that vitamin B12 deficiency may be among the causes of prolonged jaundice (12).

In our study, hemolytic anemia and prolonged jaundice were found in two infants. No abnormality was observed except for vitamin B12 deficiency in the examination results of these two patients for prolonged jaundice. Hemolysis of the patients improved in the first month of vitamin B12 treatment. Thrombocytopenia and anemia due to vitamin B12 deficiency were detected in the mother of one of the patients and she received transfusion before delivery. Iron therapy and vitamin B12 treatment were initiated due to accompanying iron deficiency.

Hematological values were within normal limits in the first month of vitamin B12 treatment. Accompanying iron deficiencies are common and should be evaluated in all patients. We found iron deficiency in 38 patients (30.6%). Folate deficiency was not found in our patients, and the rate of iron deficiency was not different from the literature (6, 8-10).

Although previous studies have shown palpable splenomegaly as a common finding in megaloblastic anemia, the exact prevalence of hepatosplenomegaly in severe vitamin B12 deficiency is not known (13,14). Two of our patients had splenomegaly and one had hepatomegaly.

Vitamin B12 deficiency may present with findings mimicking acute leukaemia (ie, pancytopenia and organomegaly), so it is important in differential diagnosis.

Conclusion

Vitamin B12 deficiency is still a common health problem in our country. Especially in pregnancy and

infancy, it is very important to determine vitamin B12 level and to treat it quickly in case of deficiency. Patients with vitamin B12 deficiency may present with different clinical findings. It is recommended to keep in mind in patients presenting with prolonged jaundice and hemolytic anemia might have vitamin B12 deficiency.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
The study was conducted in accordance with the Helsinki Declaration principles and approved by Turgut Özal University, Faculty of Medicine, Clinical Research Ethics Committee (Date: 10.08.2015, Number: 999506691/73).

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