A Retrospective Evaluation of Patients with Vitamin B12 Deficiency

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ABSTRACT

A retrospective evaluation of patients with vitamin B12 deficiency

Objective: Vitamin B12 deficiency mainly causes megaloblastic anemia and neurological abnormalities. The purpose of the present study was to evaluate the clinical and laboratory features of patients with confirmed vitamin B12 deficiency, retrospectively.

Material and Methods: Thirty-one patients who were admitted to Department of Internal Medicine of Afyon Kocatepe University Hospital and identified as having vitamin B12 deficiency were enrolled in the study. Data were obtained retrospectively from medical records, including the reason of investigating vitamin B12 levels, comorbidities, concomitant acute infection, hemoglobin level, mean corpuscular volume (MCV), leukocyte and platelet counts, and existence of iron deficiency anemia and folic acid deficiency.

Results: The mean vitamin B12 level was 138.9±30.7 pg/ml, hemoglobin 9.3±2.0 g/dl, MCV 88.2±11.9 fL. Nine patients had iron deficiency anemia. In patients with iron deficiency anemia, MCV was significantly lower (P=0.041). While nine patients (29%) had acute infection, 3 patients presented with pancytopenia. Pancytopenia was significantly higher in patients with acute infection (P=0.023). The relation between B12 levels and other parameters was investigated. Only MCV levels had negative correlation with vitamin B12 levels (r=-0.450, P=0.011).

Conclusion: Macrocytosis in our study group has been found to be low in accordance with previous studies. As in our investigation, although vitamin B12 deficiency may be reason for increased MCV, this rise may not always reach levels for macrocytosis. The concomitant iron deficiency anemia may be responsible for this situation. Consequently, vitamin B12 levels have to be investigated in anemic patients, whether MCV is normal or not.

Key words: vitamin B12 deficiency, macrocytosis, anemia

ÖZET

Vitamin B12 yetersizliği olan hastaların retrospektif olarak değerlendirilmesi

Amaç: Vitamin B12 eksikliği başlıca değişik nörolojik bulgulara ve megaloblastik anemiye neden olur. Bu çalışmanın amacı vitamin B12 eksikliği saptanan hastaların klinik ve laboratuvar özelliklerinin retrospektif olarak değerlendirilmesidir.

Gereç ve Yöntem: Afyon Kocatepe Üniversitesi Tıp Fakültesi İç Hastalıkları Kliniği'ne farklı nedenlerle yatırılan ve vitamin B12 eksikliği tespit edilen 31 hasta çalışmaya alındı. Vitamin B12 düzeyi istenme nedeni, eşlik eden hastalıklar, infeksiyon varlığı, hemoglobin, ortalama eritrosit hacmi (MCV), lökosit, trombosit değerleri ile eşlik eden demir eksikliği anemisi ve folik asit eksikliği retrospektif olarak araştırıldı.

Bulgular: Hastaların ortalama B 12 vitamin düzeyleri 138.9±30.7 pg/ml, hemoglobin 9.3±2.0 g/dl, MCV 88.2±11.9 fL olarak saptandı. Dokuz hastada demir eksikliği anemisi eşlik etmekteydi. Demir eksikliği anemisi olanlarda MCV düzeyleri anlamlı olarak düşüktü (P=0.041). Dokuz (%29) hastada akut infeksiyon mevcut iken, 3 hastada da pansitopeni eşlik etmekteydi ve infeksiyonu olan grupta pansitopeni sıklığı anlamlı olarak daha yüksekti (P=0.023). Tüm grupta B12 vitamini ile diğer parametrelerin ilişkisine bakıldı. B 12 vitamin düzeyi ile sadece MCV düzeyi arasında negatif korelasyon saptandı (r=-0.450, P=0.011).

Sonuç: Olgularımızda makrositoz oranı daha önceki çalışmalara paralel olarak düşük bulunmuştur. Çalışmamızda da bulunduğu gibi, vitamin B 12 düşüklüğü MCV'de artışa neden olsa da, bu artış her zaman makrositoz seviyesine ulaşmayabilir. Demir eksikliği anemisinin eşlik etmesi bu durumdan sorumlu olabilir. Dolayısıyla MCV normal bile olsa anemik hastalarda vitamin B12 düzeyi bakılmalıdır.

Anahtar kelimeler: B12 vitamin eksikliği, makrositoz, anemi

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INTRODUCTION

Vitamin B12, in conjunction with folic acid, is necessary for cell division and proliferation. Vitamin B12 deficiency affects all proliferating and regenerating cells, including hemopoietic cells, gastrointestinal cells, epithelial cells, cervico-vaginal cells, and testicular germ cells. Vitamin B12 stores in the liver can last 2 to 4 years (1,2). Deficiency of vitamin B12 results in megaloblastic anemia. There may be also glossitis, stomatitis, gastrointestinal dysmotility, infertility, lemon-colored skin, hyperpigmentation and neurological abnormalities in deficient patients. Although the prevalance of vitamin B12 deficiency is not well known in the general

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population, its frequency appears to be increased with advancing age, especially in hospitalized elderly patients (3,4). Vitamin B12 deficiency may not be accompanied by anemia and macrocytosis (5,6). In our study, we aimed to investigate the clinical, demographic and laboratory features of hospitalized patients with confirmed vitamin B12 deficiency, retrospectively.

MATERIALS AND METHODS

The study was conducted in the Department of Internal Medicine of Afyon Kocatepe University Hospital. From July 2004 to December 2005, we identified 31 patients with vitamin B12 deficiencies, who were admitted to University Hospital for various medical reasons. Data were obtained retrospectively from medical records, including the reason for measuring vitamin B12 levels, co-morbidities, concomitant acute infection, hemoglobin level, mean corpuscular volume (MCV), leukocyte count, platelet count, iron, transferrin saturation and existence of iron deficiency anemia and folic acid deficiency.

Anemia was defined as a hemoglobin level below 14 g/dl for men and below 11 g/dl for women (<12 g/dl in postmenopausal women). Vitamin B12 deficiency was diagnosed by serum levels of B12 below 197 pg/mL. Leucopenia was defined as a leukocyte count below 4000/mm^3, and thrombocytopenia as a platelet count below 150.000/mm^3.

Quantitative variables were presented as mean ± SD. Categorical variables were presented as absolute numbers and percentages. Relations among quantitative variables or among categorical variables in the study group were assessed using Pearson's and Spearman's correlation analysis, respectively. Mann-Whitney U test was used to compare the parameters between clinical groups, because of unequal distribution of groups with or without iron deficiency anemia, and with or without acute infection. P<0.05 was considered statistically significant.

RESULTS

The mean age of patients (23 females and 8 males) was 57.0±15.8 years (range, 20 to 85 years). All patients except one were initially screened for vitamin B12 deficiency mainly because of anemia and concomitant hematological disorders such as leucopenia and thrombocytopenia. The only exception was the patient with stomatitis. The mean vitamin B12 level was 138.9±30.7 pg/ml (range, 86-194 pg/ml), hemoglobin 9.3±2.0 g/dl (range, 4-13 g/dl), MCV 88.2±11.9 fL (range, 74-120 fL) (Table 1). Macrocytosis was observed in 16.1% of patients.

Tablo 1: Demographic, clinical and laboratory data in patients with vitamin B12 deficiency

	Study group (n=31)
Age (mean, years)	57.0±15.8
Gender (female: male)	23:8
Vitamin B12 (pg/ml)	138.9±30.7
Hemoglobin (g/dl)	9.3±2.0
MCV (fL)	88.2±11.9
Anemia (n, %)	30 (96.8)
Leucopenia (n, %)	7 (22.6)
Thrombocytopenia (n, %)	9 (29.0)
Pancytopenia (n, %)	6 (19.4)
Infection (n, %)	9 (29.0)
Iron deficiency anemia (n, %)	9 (29.0)

Nine patients had iron deficiency anemia, and one had folic acid deficiency. Of the nine patients with iron deficiency anemia (6 female, 3 male), one patient had pancytopenia and another patient had thrombocytopenia. The mean MCV in patients without iron deficiency anemia was 90.4±12.0 fL, whereas the number of patients with MCV above 100 fL was only four (18.2%). MCV was significantly lower in patients with iron deficiency anemia as compared to patients without iron deficiency anemia (P=0.041) (Table 2).

Tablo 2: Comparison of clinical and laboratory data in patients with or without iron deficiency anemia

	Patients with iron deficiency anemia (n=9)	Patients without iron deficiency anemia (n=22)	P
Age (mean, years)	52.2±14.3	59.0±16.3	0.203
Gender (female: male)	6:3	17:5	0.660
Vitamin B12 (pg/ml)	134.7±30.0	140.6±31.5	0.915
Hemoglobin (g/dl)	8.8±2.1	9.4±1.9	0.428
MCV (fL)	82.7±10.0	90.4±12.0	0.041

With regard to the co-morbidities; six patients had various malignancies, eight had type 2 diabetes, four had chronic renal failure, one had amyloidosis, one had

inflammatory bowel disease, and one had IgA nephropathy. In hematological disorders; 21 patients had only anemia, six had pancytopenia, one had anemia and leucopenia, and 3 had anemia and thrombocytopenia. The malignancies observed were colorectal cancer, cervical cancer, meningioma, Burkitt lymphoma, prostate carcinoma and renal cell carcinoma. In the subgroup with iron deficiency, only colorectal cancer and cervical cancer were present.

While nine patients (29%) had acute infection, of these patients, only three had immunosuppressive disorders (one patient with diabetes, chronic renal failure and prostate carcinoma; one patient with diabetes; one patient with Burkitt lymphoma) and three had pancytopenia. In patients with pancytopenia, any disorder predisposing infections was not identified. It was found a significant relationship between pancytopenia and occurrence of infection (rs=0.406, P=0.023). Also frequency of pancytopenia was significantly higher in patients with acute infection (P=0.024).

For entire study group, the relationship between B12 levels and other parameters was investigated. Only MCV levels had a negative correlation with vitamin B12 levels (r=-0.450, P=0.011). The study population was separated into subgroups 1, 2, and 3, representing MCV levels of below 80 fL, between 80 to 100 fL, and above 100 fL, respectively. The total number of patients for these subgroups was 6, 20, and 5 respectively and the number of patients with iron deficiency anemia was 4, 4, and 1.

DISCUSSION

Vitamin B12 deficiency, the prevalence of which is not known in general population, increases with advancing age, and presents with a wide variety clinical manifestations. In our study, the patients admitted with different diagnosis and screened for mainly because of anemia, pancytopenia, thrombocytopenia and stomatitis were retrospectively evaluated. This assessment included demographic characteristics, physical examination, laboratory investigations, and occurrence of concomitant disorders.

In previous studies, the prevalence of anemia in patients with vitamin B12 deficiency has been reported at different rates. Stabler et al. (7), Savage et al. (8), Chan et al. (9), and Rajan et al. (10) have found these rates as 49%, 72%, 61%, and 13% respectively. In present study, the reasons of screening vitamin B12 in our patients were hematological disorders at a rate of 96%, and mainly associated with anemia. Stott et al. (5), Au et al. (11), and Chui et al. (12) have found the rates of concomitant iron deficiency anemia as 34%, 6%, and 9,8% respectively. We found this ratio to be 29% in our study.

In literature, macrocytosis (MCV>100 fL) in subjects with vitamin B12 deficiency has been reported at rates of 36% (7), 23% (5), 12% (11), and 5% (10). Macrocytosis in our study group has been found to be 16,1% in parallel with previous studies. The concomitant iron deficiency anemia in some patients may be responsible for this low rate. Iron deficiency is a condition that complicates diagnosis by masking macrocytosis.

When the subjects with iron deficiency anemia were excluded, the rate of macrocytosis was also low (18.2%). The mean MCV value in this subgroup was within normal limits (MCV=90.4 fL). Whereas MCV in the subgroup with iron deficiency was significantly lower than in the subgroup without iron deficiency anemia. This finding was also parallel with previous literature (12,13).

Even though, in our study, macrocytosis rate was low and mean MCV was within normal limits, there was a negative correlation between vitamin B12 level and MCV. In other words, as vitamin B12 levels decline, MCV values increase. But in anemia caused by vitamin B12 deficiency, the rising in MCV may not always reach levels for macrocytosis. Therefore, even if MCV is within normal limits, blood levels of vitamin B12 should be screened in patients with anemia.

In the study group, nine patients (29%) had an infection. The incidence of pancytopenia was significantly higher among these patients. In addition to pancytopenia, concomitant immunosuppressive disorders such as diabetes, Burkitt lymphoma and malignancies, and defective bactericidal activity and impaired intracellular killing might contribute the high frequency of infection (14, 15).

In conclusion, as vitamin B12 levels decline, MCV values increase. But this increase may not always reach levels for macrocytosis. Therefore vitamin B12 levels should be measured whether MCV is normal or not.

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