

MEGALOBLASTIC ANEMIA PATIENT ADMITTED WITH PANCYTOPENIA AND WALKING DIFFICULTY WITH NORMAL VITAMIN B12 AND MCV LEVELS

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ABSTRACT

Vitamin B12 deficiency may cause hematologic, gastrointestinal, psychiatric and neurological symptoms. Sub-acute combined degeneration of spinal cord, which develops in the deficiency of vitamin B12, may be reversible in case of early diagnosis and treatment. We describe the management of a 50-years old female who got admitted with pancytopenia and elevated LDH, with walking difficulties since last 15 days. B12 and folic acid levels were found in normal ranges. Megaloblastic changes were observed in the bone marrow examination. Abnormal hyperintense signal changes were observed in T2-weighted cervical spinal cord Magnetic Resonance Imaging in posterior row. Due to the high homocysteine level, treatment with parenteral B12 vitamin was initiated. Following the 3-months treatment, hematologic counts and neurological symptoms of the patient were found to be completely recovered at the control visit. Vitamin B12 deficiency should be considered for the patients with pancytopenia, elevated LDH levels and neurological symptoms, even if vitamin B12 and MCV levels are in normal ranges. Vitamin B12 deficiency should be confirmed with the additional assays, such as, the assessment of serum homocysteine and methylmalonic acid levels, and the treatment should be started promptly.

KEY WORDS: Vitamin B12, Pancytopenia, Subacute Combined Degeneration.

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INTRODUCTION

Vitamin B12 and folate are two major vitamins for nucleotide synthesis, genomic and non-ge-

nomonic methylation, providing the transformation of homocysteine to methionine, with the help of methionine synthase. Megaloblastic anemia, caused by B12 and folate deficiency, can not be differentiated morphologically. In addition, as these two vitamins have major important roles in central nervous system (CNS) functions, undistinguished neuro-psychiatric syndromes may arise in case of their deficiency. It is known that vitamin B12 and folic acid treatments are effective in the prevention of CNS diseases and dementia (especially Alzheimer disease and vascular dementia), particularly in the elderly patients.¹

Myelopathy, caused by vitamin B12 deficiency is called "sub-acute combined degenera-

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tion" (SCD). SCD, commonly involves posterior and lateral columns of spinal cord and results in neuropathic changes that occurs with vacuolization of white substance. Ataxic walking, disbalance on sub extremities and mental changes are some of the symptoms of neurological disturbance. Elevated signal intensity is observed in T2-weighted cervical spinal cord Magnetic Resonance Imaging (MRI). After vitamin B12 replacement treatment, observed clinical recovery is accompanied by MRI proven improvement.^{2,3} If diagnosis is delayed, neurological defects may be irreversible. Vitamin B12 deficiency can not always be diagnosed with low B12 levels and mean corpuscular volume (MCV) measurements. In the literature, it was reported that, vitamin B12 deficiency might be present even though with normal B12 and MCV levels measurement and additional assays (elevation of homocysteine and blood methylmalonic acid levels, bone marrow and MRI evaluations) should be followed for differential and certain diagnosis.^{4,5}

CASE PRESENTATION

Our patient was a fifty (50) years-old female diagnosed with pancytopenia; suffering from fatigue, lack of appetite, weight loss and particularly difficulty in standing up and walking in the last 15 days. It was determined that the patient was not currently taking any oral or parenteral vitamin B12 and/or folic acid. Vitamin B12 level was measured in normal limits by two different laboratories using two different assays. During physical examination, skin color was seen in citrine. Icterus in sclera and atrophy of tongue papillae was detected. In systemic examination, maximum pulse rate was 110/min and 2/6 mid-systolic murmur in the apex was detected. In neurological examination, deterioration was observed in vibration and in position sense. Macroovalocytosis and hypersegmented neutrophils were observed in peripheral blood smear. Evaluation of viral markers, ANA and Anti-ds DNA due to pancytopenia revealed to be negative. In bone marrow aspiration and biopsy, significant changes in erytroid, myelogramulocytes, and megakaryocytes series, significant elevation espe-

cially in erytroid series, nucleocytoplasmic disosiation and giant metamyelocytes were observed (Figure 1,2). Other laboratory findings are summarized in Table-I. In T2-weighted cervical spinal cord MRI imaging, abnormal hyperintense signal change was detected at posterior row. According to cranial MRI results, elevation of T2 intense in cerebral white substance was detected.

Vitamin B12 treatment (cyanocobalamine 100mcg/day, i.m) was initiated. Following the 10-days of treatment, recovery in blood hemogram and biochemistry levels and in clinic symptoms were observed. Chronic atrophic gastritis was diagnosed with gastroscopic evaluations and biopsies. Due to the positive *Helicobacter pylori* test result, eradication treatment was prescribed. After three months of treatment, blood assessments and neurological examinations were considered as normal. The control MRI revealed an almost complete recovery, achieved in pathological signal intensities, which was detected in the first diagnosis.

DISCUSSION

Intrinsic factor deficiency and gastrectomy operations are accepted to be the most common reasons of vitamin B12 deficiency. Myeloneuropathy development was reported 20 years after partial gastrectomy.⁶ It was reported that vitamin B12 deficiency may cause several neuropsychiatric disorders, i.e. cognitive and behavioral dysfunctions, and in such

Table-I: Laboratory findings

	<i>Findings</i>	<i>Normal Range</i>
WBC (x10 ⁹ /l)	3.1	(4.4-11.3)
Hb (g/dl)	5.0	(14-17.5)
Platelet (x10 ⁹ /l)	120	(150-450)
Neutrofil (%)	28	(37-73)
MCV (fl)	95	(78-101)
AST (U/l)	80	(10-34)
Indirect Bilirubin (mg/dl)	3.6	(0.2-0.7)
Total Bilirubin (mg/dl)	4.7	(0.2-1.3)
LDH (U/l)	2700	(125-243)
Ferritin (ng/ml)	235	(13-150)
Folic Acid (ng/ml)	6	(3-17)
Homocysteine (µmol/l)	26	(5.5-14)
Vitamin B12 (ng/l)	195	(190-900)

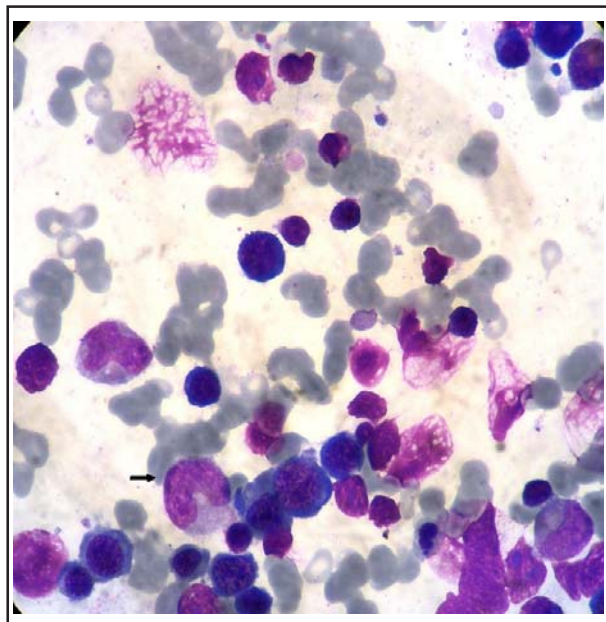


Figure-1: Giant metamyelocyte in bone marrow. (Giemsa, x100)

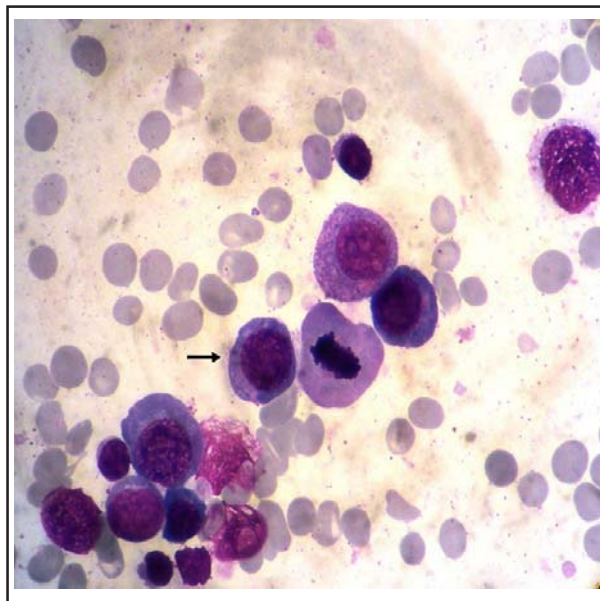


Figure-2: Megaloblast in bone marrow. (Giemsa, x100)

situations neuropsychiatric test results may improve after vitamin B12 treatment, similarly to our case.⁷

In another study, a case with neurological symptoms deriving from Vitamin B12 deficiency was investigated and myeloneuropathy, cognitive dysfunction, peripheral neuropathy, neuropsychiatric symptoms and dementia were determined. In all cases, megaloblastic changes were observed in bone marrow. About 17% of all cases were observed to have normal levels of either hemoglobin or MCV. Following the parenteral vitamin B12 treatment, improvement was observed in 54% of the cases in follow-up visits that was performed at least semi-annually. It was noted that, despite normal levels of MCV and hemoglobin, B12 deficiency should be investigated in the presence of cognitive function loss and neuropathy.⁸

Neurological symptoms arising from vitamin B12 deficiency, can be determined in early period with MRI, and after treatment significant recovery is observed in neurological view.^{9,10}

In our case, although vitamin B12 levels were detected in the normal ranges, according to the elevation in homocysteine levels and other clinical and laboratory findings, vitamin B12 defi-

ciency was diagnosed. Response to the treatment, measured with clinical and laboratory assessments, confirms the diagnosis. Therefore, it was thought that the lower limits for vitamin B12 deficiency should be changed to an upper level.

As a result, despite normal ranges of vitamin B12 and also MCV levels, if pancytopenia, neurological symptoms, elevated LDH levels were present, vitamin B12 deficiency should be considered in differential diagnosis. For further investigation; serum and urine methylmalonic acid levels, homocysteine levels and bone marrow assessments should be performed for confirmation and B12 vitamin treatment should be initiated promptly.

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AMNIOTIC BANDS

I am presenting the rare pictures possibly of amniotic band seen after the delivery of placenta. The patient was a multipara who presented in third trimester to maternal day assessment unit with the complaint of fall over her abdomen in third trimester. She had a normal 20 week anomaly scan. After this event a thin line was picked up on ultrasound scan possibly raising the suspicion of amniotic band. However this patient was discharged home later as CTG, fetal movements and other scan findings were normal. She had a spontaneous labour at term and she delivered a healthy normal baby without any fetal abnormalities. In figure-I a very thick band of amniotic band (black arrow) can be seen. In figure 1 (red arrow) and in figure 2 (Blue arrow) shows a sheet of amniotic membranes "glued together" toward the fetal side of cord. Placenta was complete and normal.

Amniotic bands are rare, affecting 1 in 1200 (0.08%) of all pregnancies¹ and there are very few case reports available in the English literature. Amniotic bands are fibrous strands of membrane stretching from the outer membrane surface into the amniotic cavity. There are different theories but according to Torpin et al, the primary event could be a rupture of the amniotic membrane and its detachment from the chorion with amniotic fluid leaking through the tear. As a result, the fetus can move digits or limbs through this tear and exit the amniotic cavity

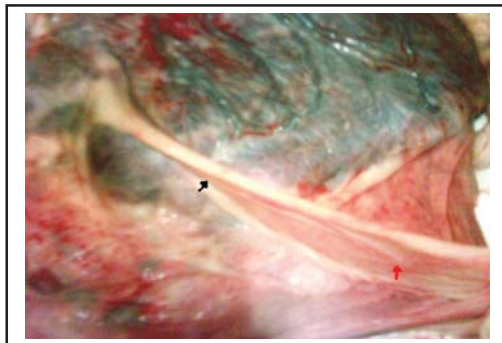


Fig 1: Amniotic band (black arrow); Fused membranes (red arrow)

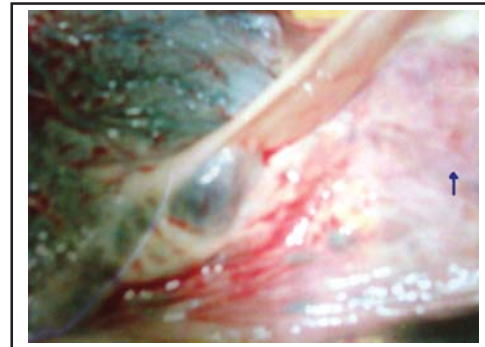


Fig-2 : Thick fused / "glued membranes" toward fetal side (Blue arrow) (partially or completely). The outer surface of the amnion, and to a lesser degree the naked chorion, produce mesodermic fibrous strings which may entangle and entrap different fetal organs, leading to constriction and amputation anomalies.¹

On ultrasound the bands appear as thin, mobile lines, which may be seen attached to or around the baby. About 70% of amniotic bands disappear on follow-up ultrasound, presumably due to rupture or compression. Secondly if there is no evidence of any abnormality, other than the amniotic band, at the time of the scan then there appears to be little risk to the baby. Other reassuring factors are normal fetal movement and the band not being attached to the baby. In this case they are called 'innocent amniotic bands.'² This explanation is consistent with the findings of our case where in spite of thick amniotic band neither there were any fetal deformities nor any complaints of decreased fetal movements. Fetal movements can be decreased if fetal parts are badly entangled in amniotic bands. These bands may constrict the base of the cord at the placental attachment which can be lethal.

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