

Many Faces of Vitamin B12 Deficiency

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Vitamin B12 deficiency is common. Pernicious anemia is the most common cause of severe vitamin B12 deficiency worldwide [1]. Clinical spectrum of vitamin B12 deficiency may range from asymptomatic subclinical state to megaloblastic anemia to demyelination of the cervical and thoracic dorsal and lateral columns of the spinal cord and demyelination of the white matter in the brain (subacute combined degeneration).

Hematologic parameters of vitamin B12 deficiency also vary widely. Dyssynchrony between the maturation of cytoplasm and that of nuclei leads to macrocytosis, immature nuclei, and hypersegmentation in granulocytes in the peripheral blood [2]. Megaloblastic anemia, however, is not always seen. More than 25% of patients with neurologic manifestations of vitamin B12 deficiency have either a normal hematocrit or normal mean corpuscular volume (MCV), or both². In a study of 100 patients with an MCV greater than 115 fl, only 50% had subnormal values of vitamin B12 or folate deficiency [3]. In another study in patients with confirmed vitamin B12 deficiency, only 51.5% of the patients were found to be anemic. Leukopenia and thrombocytopenia was found in 16% and 11% respectively. 10.8% of patients had pancytopenia 1.9% hemolytic anemia [4].

Intramedullary hemolysis due to ineffective erythropoiesis may give a picture of microangiopathic hemolytic anemia with elevated lactate dehydrogenase [5]. Bone marrow may be hypercellular and dysplastic mimicking acute leukemia.

Tanyildiz et al. have reported a case of vitamin B12 deficiency mimicking acute leukemia in a child in this issue. Vitamin B12 is a cofactor for two enzymes: methionine synthase and L-methylmalonyl-coenzyme A mutase and is essential for DNA synthesis [6]. The presence of megaloblastic changes in the marrow usually implies a diagnosis of vitamin B12 or folate deficiency but similar changes may be found in some myelodysplastic disorders. Case reports of vitamin B12 deficiency mimicking Myelo Dysplastic Syndrome (MDS) or acute leukemia have been published before. Interestingly, some of these patients also had distinct cytogenetic and flow cytometric abnormalities mimicking MDS, making it difficult to differentiate vitamin B12 deficiency from MDS/leukemia [7]. In another report of three children with severe vitamin B12 deficiency, spontaneous chromosomal breakage, chromosomal rearrangement and deletions were found and were mistakenly diagnosed with clonal chromosomal abnormality suggestive of a neoplastic process [8].

Thymine is required for DNA synthesis. The major source of thymine in the bone marrow cells is by de novo synthesis from deoxyuridine, which requires vitamin B12 and folate. Deoxyuridine cannot be efficiently converted to thymine in the absence of vitamin B12/folate and this may be the reason for cytogenetic abnormalities seen in severe vitamin B12 deficient patients.

MDS is a fatal hemopoietic disorder characterized by ineffective hematopoiesis, bone marrow dysplasia and frequent evolution to acute myeloid leukemia. Vitamin B12 deficiency, on the other hand, is easily cured. It is therefore important to differentiate the two conditions before the start of treatment. Vitamin B12 assay along with total plasma homocysteine (tHcy) and/or methylmalonic acid (MMA) should be measured. Vitamin B12 assay alone is not sensitive enough to rule out vitamin B12 deficiency. tHcy is more sensitive and MMA more specific

for vitamin B12 deficiency but both can be high in renal impairment. Defer treatment for MDS if diagnosis is uncertain since it will avoid unnecessary cytotoxic drug therapy with its concomitant morbidity and mortality [9].

The case presented by Tanyildiz et al. [10] has once again shown that vitamin B12 deficiency can present in many ways, both clinically and by hematological parameters. Clinicians should remain alert this and should have a low threshold for checking the vitamin B12 status in patients with suspicious features.

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