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Case Report

CASE REPORT

Neurologic symptoms as the only manifestation of B_{12} deficiency in a young patient with normal hematocrit, MCV, peripheral blood smear and homocysteine levels

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Abstract

B_{12} deficiency is associated with several neurological manifestations. It is well documented that neurologic symptoms due to B_{12} deficiency may sometimes present in the absence of anemia. However, in most cases there are several indicating factors like megaloblastic changes in complete blood count, hypersegmentated neutrophils or macroovalocytes in peripheral blood smear and abnormal homocysteine levels. In this report, we describe a case of a 32-year-old man with neurological symptomatology as the only manifestation of B_{12} deficiency with normal hematocrit, mean cell volume, peripheral blood smear and homocysteine levels. All the above emphasize the point that patients with neurologic symptoms must be screened for B_{12} deficiency even in the absence of any laboratory evidence.

INTRODUCTION

Vitamin B_{12} is important in reactions related to DNA and cell metabolism and its deficiency may lead to several clinical consequences [1]. Conditions associated with vitamin B_{12} deficiency include ineffective erythropoiesis and megaloblastic anemia, neurologic dysfunction, psychiatric manifestations, glossitis, malabsorption, infertility and thrombosis [2].

The full-blown picture of B_{12} deficiency in peripheral blood consists of macrocytic red cells, macroovalocytes, anisocytosis, hypersegmented neutrophils, leukopenia, possible immature white cells, thrombocytopenia, pancytopenia, elevated lactate dehydrogenase level, elevated indirect bilirubin and aspartate aminotransferase levels, decreased haptoglobin level, and elevated levels of methylmalonic acid, homocysteine or both [2].

Neurologic complications of B_{12} deficiency include peripheral neuropathy, lesions in the posterior and lateral columns of the spinal cord and in the cerebrum, and manifestations from the autonomic nervous system [2, 3]. It is well documented that neurologic symptoms due to B_{12} deficiency may be present sometimes in the absence of anemia [4, 5].

In this report, we describe the case of a 32-year-old man, with neurologic manifestations, due to B_{12} deficiency with normal hematocrit, mean cell volume (MCV), peripheral blood smear and homocysteine levels.

CASE REPORT

A 32-year-old man was admitted due to generalized fatigue, weakness in the lower limbs and difficulty in walking for the last 2 months. For the same reasons, he had visited several hospitals during the last month. His symptoms got worse during the last 10 days. His medical history was unremarkable. He denied any alcohol or drug consumption. He was not a

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vegetarian and his family history was negative for any hereditary or metabolic disorders. He was well nourished without any cognitive impairment. During his neurological examination, muscle tone, motor strength and sensory innervation were normal. Romberg sign was negative and cerebellar tests were normal. Patient's deep tendon reflexes were elicited except the abolished patellar and Achilles in both lower extremities. His blood tests revealed the following: Hct = 46.6%, MCV = 85.2 fl, mean corpuscular hemoglubin (MCH) = 29.1 pg and platelets (PLT) = 297.000 K/μl. His basal metabolic panel and thyroid function tests were normal. HIV test was negative. He underwent both a CT and an MRI of the lumbar spine without any pathological results. His brain CT was normal. Lumbar puncture had no pathological finding and both nerve conduction studies and electromyography were normal. His B_{12} level was 143 pg/ml (normal values: 187–883 pg/ml). In the peripheral blood smear examination, both hypersegmented neutrophils and macroovalocytes were absent. In the absence of findings indicating B_{12} deficiency, a serum homocysteine level, which in that case is a sensitive biomarker, was performed. Homocysteine value was 10.06 μmol/l (5–12 μmol/l). In the absence of another diagnosis, explaining his symptomatology, we tried to find a possible cause for B_{12} deficiency. He did not mention any diarrheas, while antiparietal cell antibody (APCA) examination was negative. In order to find the cause for his B_{12} deficiency, he underwent a gastroscopy that revealed edema and diffuse microeruptions both in the stomach as well as in the duodenal bulb. *Helicobacter pylori* testing was negative. Biopsies revealed lesions compatible with chronic gastritis. He was treated with 40 mg esomeprazole once daily and intramuscular hydroxocobalamine (5 mg per injection) for 5 days, followed by one injection weekly for 4 weeks and by one injection monthly thereafter. After 3 months, he was feeling better while during physical examination the previously abolished patellar and Achilles reflexes were elicited.

DISCUSSION

Our patient had no anemia, megaloblastic changes, neutropenia or thrombocytopenia. In previous studies, it was highlighted that neuropsychiatric manifestations of B_{12} deficiency may occur in the absence of anemia, in the absence of megaloblastic changes or in both of them [4, 5]. Lindenbaum *et al* reported that among 141 patients with neuropsychiatric manifestations due to B_{12} deficiency, 34 had normal hematocrit, 25 had normal MCV and 19 had both hematocrit and MCV between normal limits [4]. Likewise Healton *et al* reported that among 153 episodes of B_{12} deficiency involving the nervous system that occurred in 143 patients, hematocrit was normal in 42 (27.4%) and MCV was normal in 31 (23.0%) [5]. In both reports, neutropenia and thrombocytopenia were unusual even in anemic patients.

Moreover our patient did not have hypersegmentated neutrophils or macroovalocytes in peripheral smear. Hypersegmentation is considered more sensitive than MCV in detecting B_{12} deficiency and according to Thompson *et al* among 515 patients with low B_{12} levels, 91% had hypersegmentated neutrophils and 62% had MCV greater than 95 fl [6]. In patients with neuropsychiatric manifestations due to B_{12} deficiency, Lindenbaum *et al* reported that among blood smears obtained from 28 patients with a normal MCV, a normal hematocrit or both, only two had completely normal blood smears. Macroovalocytes were present in 24 of the 28 smears, and hypersegmentation was noted in 26 of the 28 smears [4].

Another point of interest is that our patient did not have elevated homocysteine levels. Usually, in cases of B_{12} deficiency, homocysteine levels are elevated. Actually, among 434 episodes of B_{12} deficiency in a 7-year period, 95.9% of serum homocysteine levels were elevated according to Savage *et al* [7]. Moreover, Lindenbaum *et al* reported that between 34 patients with B_{12} deficiency and neurologic manifestations, with normal hematocrit, one patient had normal and another had slightly elevated homocysteine levels at the time of diagnosis. For the first patient, a peripheral blood smear was not available but he had normal MCV. The second patient had both abnormal MCV and peripheral blood smear [4]. Nevertheless, homocysteine levels are also affected by age [8] and folate status, and is considered a weak marker of vitamin B_{12} status, especially as a stand-alone biomarker [9, 10]. The case we present had normal homocysteine levels but also a clear diagnosis, as plasma vitamin B_{12} indicated the deficiency. However, in the absence of a clear low plasma level of vitamin B_{12}, methylmalonic acid, which is the most sensitive marker of vitamin B_{12} status, or a combination of methylmalonic acid and homocysteine measurement is recommended [9, 10] in subjects with neurological symptoms of unknown etiology.

As it seems from these mentioned above, the combination of the absence of anemia, megaloblastic changes, hypersegmentated neutrophils, macroovalocytes and with homocysteine levels within normal limits, in a patient with neurologic manifestations due to B_{12} deficiency, is quite rare.

In conclusion, neurologic symptoms may be the sole manifestation of B_{12} deficiency, not only in the absence of anemia or megaloblastic changes but furthermore in the absence of hypersegmentated neutrophils or macroovalocytes in peripheral blood smear or with normal homocysteine levels. Patients with neurologic symptoms must be screened for B_{12} deficiency even in cases where no other indicative laboratory finding exists.

CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

Not required

CONSENT

Consent was obtained from the patient.

GUARANTOR

P.V. is the guarantor of this article.

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