

Vitamin B-12 deficiency presenting as bilateral pedal edema; Physiological role of vitamin B-12 in maintenance of vascular smooth muscle tone

VK Tiwari¹, R Mishra², K Kumar¹

¹(Department of Physiology, BRD Medical College, Gorakhpur, India)

²(Department of Pharmacology, All India Institute of Medical Sciences, New Delhi, India)

Abstract: Vitamin B-12 is a water soluble vitamin, found exclusively in products of animal origin. Vitamin B-12 deficiency presents as hematological, gastrointestinal, and neuropsychiatric disorders. Anemia is usually most common presentation of vitamin B-12 deficiency. Neuropsychiatric manifestations are usually late, but irreversible in many cases. Cases of vitamin B-12 deficiency are common in India. Sociocultural practices in Uttar Pradesh make women more vulnerable to vitamin B-12 deficiency. This is a rare case of vitamin B-12 deficiency presenting with bilateral pedal edema, simulating edema of cardiac origin, and without any other clinical manifestation. Patient was prescribed oral cobalamin. Edema started to resolve by second week, and disappeared completely after two months of treatment.

Keywords: Edema, Autonomic neuropathy, Vitamin B-12

I. Introduction

Vegetarian diets are classified as vegan (plant products only), lactovegetarian (plant and dairy products), ovovegetarian (plant products and eggs), and lactoovovegetarian (plant products, dairy products, and eggs). Vitamin B12 is exclusively found in products of animal origin only, colonic bacteria produces vitamin B-12 but it is not sufficient to meet the demand of body [1]. Liver stores 2-5 mg of vitamin B-12 which is sufficient for 3 years, if there is no vitamin B-12 absorption from GIT. Daily absorption of vitamin B-12 is 5 mcg, and daily loss is 3-5 mcg [2]. Recommended daily allowance for vitamin B12 set by Institute of Medicine is 2.4 mcg per day for persons aged 14 years or more [3]. Indians are prone to vitamin B12 deficiency [4]. Vitamin B-12 deficiency has diverse presentation usually presenting with megaloblastic anemia. Anemia presents with macrocytosis, hypersegmented neutrophils, and raised MCV [3]. Hematological presentation may be occasionally in the form of purpura, light headedness, vertigo, tinnitus, palpitation, angina, and symptoms of congestive cardiac failure. Vitamin B-12 deficiency may also present as GIT disorders, and neuropsychiatric diseases. Gastrointestinal manifestation of vitamin B12 deficiency includes smooth beefy red tongue with occasional ulceration on lateral surface, anorexia, weight loss, and diarrhea [5]. Cerebral involvement occurs very late, and permanent if not treated early [3]. Autonomic dysfunction has also been reported in vitamin B-12 deficiency presenting with orthostatic hypotension [6].

II. Case Report

A female Hindu patient aged 32 years came in Medicine OPD at UPRIMS&R (Medical College) with complaints of bilateral pedal swelling for 1 month. She was a house wife and belonged to low socioeconomic status. She told that swelling is increasing day by day; it is minimal in morning, and increases as the day passes. There were no urinary and GI complaints. She has no history of smoking, diabetes mellitus, alcohol, medication, hypertension, heart, and pulmonary disease. She was vegetarian, and was not taking dairy products for last many years. She belonged to a family of farmer and was taking green leafy vegetables on almost daily basis. She had already completed her family and undergone tubectomy five years back.

On examination her built was thin. There was no feature of thyroid disorder, and mild bilateral pitting edema was present over both ankles. Pulse rate was 96 per minute and blood pressure was 96/68 mm Hg. Her chest was clear, heart and breathing sounds were normal, and there was no hepatosplenomegaly.

On examination of nervous system, knee reflexes were normal bilaterally, no sensory impairment in both the legs, position and vibration sense was intact. Romberg test negative, and Planter reflex showed flexor response. Upper limb, cranial nerves and cerebellar functions were normal.

Her laboratory examination revealed hemoglobin 10.2 gm/dl, MCV 108fl, TLC 4200/ μ l, platelets 164000/ μ l. General blood picture showed megaloblastic red cells with hypersegmented neutrophils. Her liver function test, serum creatinine level, and ECG were normal. In view of history and lab results, we proceeded with serum vitamin B-12 level. Serum vitamin-B12 level was low; 148.9 pg/ ml (Normal > 210 pg/ mL). Thus patient was diagnosed as a case of Vitamin B12 deficiency presenting as autonomic dysfunction. She was

treated with oral cobalamin 1500 µg per day for two weeks, followed by 1000 µg per day for 3 months. Two weeks later patient presented with symptomatic improvement, and hypersegmented neutrophils were absent in blood smear. Edema started to disappear after two weeks, and resolved completely in two months. Thus diagnosis was confirmed retrospectively.

III. Discussion

Vitamin B12 plays role in erythropoiesis, synthesis, and maintenance of myelin sheath [3]. Usually anemia is common and early presentation, while neurological complaints are late [3]. Neuropsychiatric manifestations include paresthesias, peripheral neuropathy, demyelination of dorsal column and corticospinal tract, irritability, personality change, dementia, depression, and psychosis [7].

Blood pressure in erect posture in lower limb is blood pressure at level of heart plus pressure due to column of blood in blood vessels between heart and lower limb. Peripheral vascular tone is maintained by sympathetic autonomic fibers. Normally this increase in blood pressure in dependent blood vessels is compensated by increased sympathetic autonomic activity preventing vasodilatation and thus stasis [8]. Vitamin B-12 deficiency causes autonomic dysfunction [6]. So autonomic dysfunction caused by vitamin B-12 deficiency, will lead to vasodilatation in dependent blood vessels with stasis and subsequent increased filtration of fluid [8]. This edema will begin to appear in the morning as the person assumes erect posture, and progressively increases during the day. Edema may disappear overnight during sleep and becomes minimal in morning at the time of rising from the bed due to absence of effect of gravitational forces on blood vessels of lower limb. This explains edema in the patient. Thus Vitamin B-12 plays a key role in maintenance of vascular smooth muscle tone by maintaining the integrity of autonomic functions.

Diagnosis of vitamin B12 deficiency is usually made by serum vitamin B-12 level, whereas increased serum level of methylmalonic acid and homocysteine also help in the diagnosis. [3]. Biopsy and aspiration of bone marrow is not necessary for diagnosing megaloblastic anemia. Imaging of spinal cord is only indicated in the case of severe myelopathy that are not initially recognized as the result of vitamin B12 deficiency. A characteristic hyper-intensity on T2 weighted imaging identified by inverted V-shaped pattern in thoracic and cervical spinal cord is seen in severe myelopathy [9].

Treatment of diagnosed vitamin B12 deficiency may be injectable vitamin B-12, 1000 mcg once a day for 8 to 10 days, followed by 1000 mcg once every three months [9]. Oral replacement therapy of vitamin B-12 is found to be convenient, cost effective, and adequate [10]. Oral therapy comprise single dose of 1000 to 2000 mcg of vitamin B-12 per day for two weeks, followed by 1000 mcg daily dose for life time [9].

IV. Conclusion

Vitamin B12 deficiency may present as isolated autonomic neuropathy. Sociocultural practices of eating at last and preferring vegetarian diet in house wives of lower socioeconomic status, specially married Hindu women in UP, put them at higher risk of developing the vitamin B-12 deficiency. So if any non-pregnant vegan female present with bilateral pedal edema without features of thyroid, cardiac, hepatic, and renal disorders; vitamin B-12 deficiency must be ruled out. There should be high index of suspicion for early diagnosis and prompt treatment to reverse the neurological manifestations, as many of them are inversely proportional to severity and duration of disease.

References

- [1]. I Elmadfa, and I Singer, Vitamin B-12 and homocysteine status among vegetarians: a global perspective, *The American Journal of Clinical Nutrition*, 89(suppl), 2009,1693S-1698S.
- [2]. C.A. Linker, and L.E. Damon, Blood disorders, in S.J. McPhee, M.A. Papadakis (Ed.), *Current medical diagnosis & treatment*, 51 (New York: The McGraw-Hill Companies, 2012) 481-482.
- [3]. D.M.P.U.K. Ralapanawa, K.P. Jayawickreme, E.M.M. Ekanayake, and W.A.T.A. Jayalath, B12 deficiency with neurological manifestations in the absence of anaemia, *BMC Research Notes*, 8(458), 2015, 1-4.
- [4]. G. Santra, R.Paul, S.K. Ghosh, D. Chakraborty, S. Das, S. Pradhan, and A. Das, Generalized hyperpigmentation in vitamin B12 deficiency, *Journal of the Association of Physicians of India*, 62(8), 2014, 714-716.
- [5]. A. Miller, M. Korem, R. Almog, and Y. Galboiz, Vitamin B12, demyelination, remyelination and repair in multiple sclerosis, *Journal of the Neurological sciences*, 233(1-2), 2005, 93-97.
- [6]. M. Beitske, P. Pfister, J. Fortin, and F. Skrabal, Autonomic dysfunction and hemodynamics in vitamin B12 deficiency, *Autonomic Neurosciences: Basic and Clinical*, 97(1), 2002, 45-54.
- [7]. C. Robert, D.L. Brown, Vitamin B12 deficiency, *American Family Physician*, 67(5), 2003, 979-986.
- [8]. J.E. Hall, *Guyton and Hall textbook of medical physiology* (Philadelphia, Elsevier, 2011). p173, 203, 207, 297
- [9]. S.P. Stabler, Vitamin B12 deficiency, *The New England Journal of Medicine*, 368, 2013, 149-160.
- [10]. E. Andres, H. Fothergill, M. Mecili, Efficacy of oral cobalamin (vitamin B12) therapy, *Expert Opinion on Pharmacotherapy*, 11(2), 2010, 249-256.