Sensory Peripheral Neuropathy Aggravated by Vitamin B12 in Elder patient. A Case Report

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Abstract

Background. Vitamin B12 is one of the common drugs used by physicians to treat peripheral neuropathy (PN), although many patients have a good response, however, overdose and toxicity aggravate the condition and worsen the patient's symptoms. The purpose of this paper is to highlight association between Vitamin B12 toxicity and deterioration of PN symptoms.

Case Summary. An elder Sudanese man with acute onset of sensory PN, the patient's symptoms started by tingling sensations and paresthesia affecting both hands and feet. After patient received cobalamin (vitamin B 12) prescribed by his doctor, the patient symptoms were markedly aggravated and his condition worsened to extend that impaired the normal patient ordinary work. No symptoms related to motor system. Other possible etiologies were studied and excluded. Investigations of his condition revealed blood level of B12 was 1900 pg/mL, the patient condition improved dramatically with discontinuation of the drug.

Conclusion Cobalamin toxicity aggravate sensory PN symptoms. Clinicians are advised to adjust the dose and check Cobalamin level before and during treatment to avoid its toxicity.

Keywords: Peripheral Neuropathy, Vitamin B12 toxicity, Cobalamin

Introduction

Peripheral Neuropathy (PN) is a common disorder affect 2-4% of people attending their general practitioner and 8% of people over the age of 55 years.[1] The most common etiology of PN is diabetes, [(1)] other common etiologies are drug induce PN, vitamin deficiencies (like vitamin B12, niacin, thiamine , vitamin E deficiency), toxins (mercury , lead, arsenic toxicity), carpal tunnel syndrome, hereditary neuropathies (Charcot-Marie-Tooth disease, amyloid polyneuropathy), neuropathy from infectious and inflammatory causes Guillain-Barre syndrome, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), HIV associated neuropathy, Leprosy, paraneoplastic neuropathy, toxic neuropathies, Alcohol, Neuralgic amyotrophy and COVID-19.[1]

Objective of study: this is the first case that shows association of high level of vitamin B12 and worsening PN symptoms, also we want to encourage clinicians to adjust the dose and check the level of B12 before and during treatment.

Case Presentation

A 74 years old nonalcoholic male, known case of renal impairment for 10 years, the patient is also known case of diabetes mellitus for four years, the patient is on diet control. He complained of numbness, paresthesia and decrease in sensation in both hands and feet for two weeks. On examination power is grade 5, reflexes and sensation were intact, vibratory sense and joint position were preserved. Sensations of pin prick and light touch were intact. No features suggesting automatic neuropathy. No history of similar condition, family history of similar condition, genetic diseases, hospital admission, or long-term medication apart from Proscar® 4 mg and Finiscar® 5mg for benign prostatic hyperplasia for eight years prior to his disease.

Diabetic neuropathy, Vitamin B12 deficiency, and nerve conduction defect were the differential diagnoses of this case. Investigations revealed, HbA1c = 5.9%, RBG = 160 mg/dl, renal function test: urea = 51mg/dl, creatinine = 1.4 mg/dl, serum K = 4.1 mmol/dl, Na = 140 mmol/l, and PSA = 4 ng/mL. Nerve conduction studies were normal, but basic serum level of Vitamin B12 was not done. Other tumor markers other than PSA were also not done as no significant clinical indication.

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Based on clinical manifestations, empiric treatment was started with six doses of Vitamin B complex injection (Neurobion®) 1000 mcg intramuscularly everyday and 200 mcg orally for one.

After two weeks the patient condition was markedly worsening, he started to develop severe tingling sensation that involve the whole upper limb up to the shoulder and lower limb up to the knees.

Blood Vitamin B12 level was 1900 pg/mL which is markedly elevated. The patient stopped Vitamin B12 and the patient's condition dramatically improved.

Discussion

PN is a common disorder that affects 8% of people over the age of 55 years seen by general practitioners in Italy.[1] Another study conducted in Bombay reported the prevalence of PN is 2-4% among people attending their general practitioner.[1]

A deficiency of vitamin B12 is a known cause of PN, with the deficiency of vitamin B12 causing a defect in myelin formation resulting in degeneration of ascending and descending spinal tracts. Consequently vitamin B12 is widely use in the treatment of PN especially in Asia and its administration improves patients' condition and outcome. This is supported by a study done which showed low level of serum vitamin B12 is associated with PN and are related to both sensory and motor defect.[2]

Vitamin B12 toxicity is an extremely rare abnormality and is clinically underestimated. Toxicity of vitamin B12 is associated with certain disease for instance, solid malignancies, liver diseases, and hematological malignancies. Clinically, vitamin B12 toxicity can also induce PN as reported by Khalid Serraj.[3] He found high serum level of vitamin B12 accompanied by same clinical features of vitamin B12 deficiency. This agrees with the case we report here.

Another study on vitamin B12 level was done in the UK, where they assessed serum vitamin B12 concentration in black and white patients.[4] They found Black patients have significantly higher serum vitamin B12 concentrations across all age groups ($p<0.0001$).

The mechanism by which vitamin B12 toxicity induce PN is unknown. However, we postulate that vitamin B12 can induce PN by impaired myelin sheet functions. More researches are needed in the vitamin B12 toxicity area.

Diabetic PN affects approximately 50% of patients with long term diabetes.[5] Patients with diabetic neuropathy experience significant symptoms such as numbness and paresthesia tingling sensation or complete loss of sensation. These symptoms can develop rapidly in a short period of time, however most of patients' symptoms develop gradually. Diabetic PN is usually symmetrical, affecting hand and feet simultaneously. It contributes in development of serious complication such as chronic ulceration which is a leading cause of infection and amputation. Diabetic neuropathy affects the quality of patients' lives and has a high cost of management. It has bad complications and worse prognosis.[5,6]

The neuropathic complications of diabetes mellitus include distal, symmetric, predominantly sensory neuropathy, autonomic neuropathy, asymmetric proximal neuropathy, and cranial and other mononeuropathies.[1] The incidence of diabetic neuropathy is significantly associated with the duration of the disease. Four per cent of diabetic patients developed PN within five years of their diagnosis, By 20 years after diagnosis, the prevalence has risen to 15%.

In published literatures, drugs have been reported to induce PN. An article reports possible relationship between penicillin and PN.[7] Other antibiotic drugs that were reported are chloramphenicol and metronidazole, nitrofurantoin, dapsone and others.[8]

Several drugs have been reported to cause PN, for example statin and amiodarone that are used in the treatment of cardiovascular disease are reported to induce PN. Gaist et al found that the incidence of PN was higher in patients treated with statins.[9] Amiodarone, an antiarrhythmic drug, is found to induce PN but less frequently than other side effects like hepatotoxicity and thyroid dysfunction.[10]

Anti-tuberculous drugs are also known to cause PN. One of the major side effect of isoniazid is reversible sensory neuropathy that necessitates the use of pyridoxine as a prophylactic. Oxazolidinone linezolid, now a second line treatment for multidrug resistant tuberculosis also produces PN with many studies suggesting it is irreversible PN.[8] Other antibiotics that induce PN are nitrofurantoin, used widely to treat UTI and metronidazole. Prolonged use of metronidazole was reported as a rare side effect. Other antibiotics that may cause PN are pencillins and their derivatives, chloramphenicol, dapsone and tetracycline

Chemo-therapeutic agents that are reported to induce PN are epothilones and laxabepilone that are used in in patients of breast cancer.[8] Sandler SG et al reported that vincristine used in lymphatic malignancies cause PN.[11] Taxanes such as paclitaxel and docetaxel used to treat solid tumors are found to induce loss of pain, temperature sensations, vibration, and position sense.[10] Bortazomib and thalidomide, a combination used for multiple myeloma, were also found to cause dorsal root ganglia neuropathy.[12]

Immunosuppressant agents that were reported to produce PN are tumor necrosis factor-α (TFA-α), inhibitors that are used in the treatment of autoimmune disease. Another one is Interferon β-1-α that are shown to be beneficial in the treatment of multiple sclerosis. Interferon α is a cytokine used in the management of hepatitis B. A third example is leflunomide, which suppresses the proliferation of T-lymphocytes, is used in the treatment rheumatoid arthritis.[10,13,14]

The mechanisms by which these drugs induce PN are not completely understood. However, some authors explain the relation between some drugs and PN. Platinum compounds such as cisplatin, carboplatin and oxaliplatin that are used in colorectal cancer induce neuropathy

through axonal oxidative stress and also induce axonal hyperexcitability and repetitive nerve discharges that contribute in the development of PN.[15] Bortezomib and thalidomide a combination used for multiple myeloma are found to cause dorsal root ganglia neuropathy.[10]

The mechanism of PN in ankylosing spondylitis and inflammatory bowel disease was explained by presence of autoantibodies against myelin and ischemic processes affecting axons. There are numerous pathological mechanisms involved in the development of diabetic neuropathy. Microangiopathy that is caused by thickened basement membrane in diabetic patient causes increased vascular permeability of the capillaries that supply the nerves, leading to direct axonal damage. Persistent intracellular hyperglycemia is another factor that contribute to the PN in diabetic patient. Intracellular glucose is converted to sorbitol by aldose reductase leading to accumulation of sorbitol. This then induces osmotic stress to the nerve. This reaction is mediated by NADPH as a co-enzyme leading to decreased NADP and decreased glutathione, an antioxidant. This makes the neurons vulnerable to oxidative stress.[16]

Patient Perspective. Specified protocol for the treatment of PN is not established in Sudan, however most of patients receive vitamin B12 empirically. Only routine investigations were done for our case, which did not overcome the challenges of the disease. The patient was inconvenienced of his treatment because his symptoms were increased with received drug and reinvestigations revealed a very high level of drug that was prescribed. When patient stopped the drug the condition gradually improved.

Conclusion

Cobalamin (vitamin B12) is a drug that is used in the treatment of PN. We report in this article the association between cobalamin toxicity and aggravation of sensory PN symptoms. Clinicians are advised to adjust the dose and check vitamin B12 level before and during treatment to avoid its toxicity.

Strengths and Limitations: This is a very rare case report the shows PN can be associated with vitamin B12 toxicity. However the lack of basic serum vitamin B12 level provided made some limitations to the early detection of the condition.

Recommendation: Mechanistic studies may be done to understand better how vitamin B12 can cause PN.

Conflicts of Interest: no conflict of interest was declared by authors.

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