Acta Neurologica Belgica (2020) 120:413–414
https://doi.org/10.1007/s13760-018-0919-7

LETTER TO THE EDITOR

Pyridoxine-induced sensory ataxic ganglionopathy: a case report and literature review

Elia Malek[1] · Hassan Doumiati[1] · Johnny S. Salameh[1]

Received: 13 March 2018 / Accepted: 4 April 2018 / Published online: 28 April 2018

Keywords Vitamin B6 · Pyridoxine · Sensory ganglionopathy · Sensory neuronopathy

Vitamin-B6, a water soluble vitamin, cannot be synthesized by mammals. They consume its inactive form as pyridoxine, pyridoxal and pyridoxamine. These are converted to pyridoxal phosphate (active ingredient) [1]. Pyridoxine is unsaturable and can be absorbed excessively [2]. Vitamin B6 is involved in the synthesis of neurotransmitters, thus affecting neuronal function [1].

We report a case of 54-year-old, right-handed man presented for insidious, progressive numbness and imbalance for 12 years. Past medical history was pertinent for depression on escitalopram. He is a non-smoker and works as energy consultant with no history of exposure to hazardous substances, no history of heavy alcohol intake or substance abuse. Family history was non-contributory.

First evaluation performed 9 years after symptom onset. Then, he underwent brain magnetic resonance imaging revealing no abnormalities. Otorhinolaryngology specialist ruled out vestibular causes. Video nystagmography did not reveal evidence of peripheral vestibular dysfunction. Blood studies including complete blood count, C-reactive protein, thyroid-stimulating hormone, vitamin D, glucose, liver transaminases, and renal function tests were normal.

He presented after 10 years of symptom onset complaining of progressively worsening gait instability while walking at night, on uneven surfaces, and climbing stairs. He reported feeling "near falls", but never actually fell down. No history of motion sensitivity and weakness. Eyeglasses corrected vision. No history of hearing symptoms. Examination revealed positive Romberg test, decreased vibratory sense distally, and absent deep tendon reflexes. Clinical diagnosis of sensory ataxia was made.

Patient was referred to undergo nerve conduction studies, electromyography (EMG), and somatosensory-evoked potentials (SSEP). These revealed diffusely absent sensory responses in bilateral sural, median and ulnar nerves with normal motor responses in tibial, fibular, median and ulnar nerves. Abnormal tibial SSEP responses were noted with absent cortical responses on the left and severely delayed cortical responses on the right. EMG of proximal and distal muscles was normal. Electrophysiological evaluation suggested the presence of severe, generalized, and non-length-dependent sensory neuronopathy/ganglionopathy.

Blood studies including vitamin B12, folate, glycated hemoglobin, erythrocyte sedimentation rate, angiotensin converting enzyme, antinuclear antibodies, Anti-Sjögren's syndrome related antigens A/B, rheumatoid arthritis latex, venereal disease research laboratory test, P/C Anti-neutrophil cytoplasmic antibodies, anti-endomysial-IgA antibodies, anti-gliadin antibodies, anti-Hu antibodies, serum protein electrophoresis and serum immunofixation were normal. Patient was offered physical therapy.

On follow-up, patient complained of worsening imbalance and described loss of lower limb coordination especially on quick turns. Patient was able to climb stairs holding to rails, but felt as if falling backwards. No voice changes, vertigo, visual symptoms, loss of upper limb coordination, bladder/bowl symptoms, tremor, headache or neck pain. Examination revealed intact cranial nerve function, preserved motor power, the absence of hand ataxia or dysdiadochokinesia, difficulty standing on one foot, impaired tandem gait, with no sensory changes, and the absence of deep tendon reflexes. Patient was diagnosed with idiopathic

✉ Johnny S. Salameh
js73@aub.edu.lb

Elia Malek
eliamalek@gmail.com

Hassan Doumiati
hd32@aub.edu.lb

[1] Department of Neurology, American University of Beirut Medical Center, PO box: 1107 2020, Cairo Street, Beirut, Lebanon

pan-sensory neuronopathy. Additional tests were ordered: treponema pallidum hemagglutinin assay, myelin-associated glycoprotein antibodies, GM1/2 antibodies, GD1a/b antibodies, GQ1b antibodies, copper, and heavy metal screening came negative. Vitamin-B6 level reported: 60.2 ng/ml (reference range was 3.6–18 ng/ml). After thorough questioning, patient reported used self-prescribed medication containing pyridoxine. Intake of pyridoxine reached up to 30 mg/day. Patient also mentioned heavy consumption of various energy drinks containing high amounts of pyridoxine. Medication and energy drink consumption were stopped. Vitamin B6 level was normal after 1 month (20.9 ng/ml, reference range 5–30 ng/ml). Patient was diagnosed with pyridoxine-induced diffuse sensory ganglionopathy, and remained stable after 18-month follow-up.

First case of pyridoxine-induced polyneuropathy was reported more than 3 decades ago [3]. Papers followed reporting patients with sensory symptoms and ataxia. Electrodiagnostic studies showed pure sensory polyneuropathy with preserved motor components, with high vitamin B6 serum levels, and no other causes [4, 5]. The condition reported irreversible, even after stopping vitamin B6. Various pyridoxine doses reported to cause neuropathic symptoms (50–100 mg daily) [5]. The European Scientific Committee for Food recommended the tolerable upper intake adult level of 25 mg/day [6]. Animal studies revealed high doses of vitamin B6 caused degenerative changes and necrosis in sensory neurons, mainly dorsal root ganglia and large diameter neurons. Myelin was irregularly fragmented with axonal swelling and vacuolation [7].

Pyridoxine is used as vitamin B6 supplementation source. Clear dose-dependent relationship for the development of pyridoxine-induced neuropathies was reported. Paradoxically, pyridoxine was suggested to act as competitive inhibitor on vitamin B6 active form (pyridoxal-5-phosphate) by inhibiting pyridoxal-5-phosphate-dependent enzymes. The result is a condition similar to vitamin B6 deficiency [8].

No treatment options reported to date. Animal study showed that glutamate carboxypeptidase-II (GCP II) inhibitors may induce neuroprotective effects against pyridoxine-induced neuronal injury [9]. This was based on the high availability of GCP-II in dorsal root ganglia, and possible neuroprotective mechanism by decreasing glutamate-induced excitotoxicity and increasing *N*-acetylaspartylglutamate levels which is inhibited by GCP-II [10].

Previously, it has been reported that pyridoxine can cause sensory neuronopathy [5], yet electrophysiological studies did not reveal the typical findings of diffuse non-length dependent sensory neuronopathy. We report the first case of diffuse sensory ganglionopathy, after chronic ingestion of high doses of pyridoxine, confirmed by electrophysiological studies.

Funding This paper did not receive any funding.

Compliance with ethical standards

Conflict of interest Elia Malek M.D. declares that he has no conflict of interest. Hassan Doumiati, M.D. declares that he has no conflict of interest. Johnny Salameh, M.D. declares that he has no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from the individual (reported case observation) included in this paper.

References

1. Stover PJ, Field MS (2015) Vitamin B-6. Adv Nutr 6(1):132–133
2. Said HM (2011) Intestinal absorption of water-soluble vitamins in health and disease. Biochem J 437:357–372
3. Schaumburg H, Kaplan J, Windebank A, Vick N, Rasmus S, Pleasure D et al (1983) Sensory neuropathy from pyridoxine abuse. A new megavitamin syndrome. N Engl J Med 309(8):445–448
4. Dalton K, Dalton MJ (1987) Characteristics of pyridoxine overdose neuropathy syndrome. Acta Neurol Scand 76(1):8–11
5. Kulkantrakorn Kongkiat (2014) Pyridoxine-induced sensory ataxic neuronopathy and neuropathy: revisited. Neurol Sci 35:1827–1830
6. European Food Safety Authority (EFSA), Parma, Italy (2016) Draft scientific opinion. Scientific opinion on dietary reference values for vitamin B6. EFSA panel on dietetic products, nutrition and allergies (NDA). EFSA J 43:10–11
7. Perry TA, Weerasuriya A, Mouton PR, Holloway HW, Greig NH (2004) Pyridoxine-induced toxicity in rats: a stereological quantification of the sensory neuropathy. Exp Neurol 190:133–144
8. Vrolijk MF, Opperhuizen A, Jansen EHJM, Hageman GJ, Bast A, Haenen GRMM (2017) The vitamin B6 paradox: supplementation with high concentrations of pyridoxine leads to decreased vitamin B6 function. Toxicol In Vitro 44:206–212
9. Potter MC, Wozniak KM, Callizot N, Slusher BS (2014) Glutamate carboxypeptidase II inhibition behaviorally and physiologically improves pyridoxine-induced neuropathy in rats. PLoS One 9(9):e102936
10. Zhang W, Murakawa Y, Wozniak KM, Slusher B, Sima AA (2006) The preventive and therapeutic effects of GCPII (NAALADase) inhibition on painful and sensory diabetic neuropathy. J Neurol Sci 247:217–223