VITAMIN D INTOXICATION IN A PATIENT WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS – CASE REPORT

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ABSTRACT
Lately, vitamin D has been a hot topic among multiple sclerosis specialists. Vitamin D supplementation is being thoroughly researched in order to establish whether or not it is useful in the treatment of multiple sclerosis. We present the case of a patient with multiple sclerosis, who, after searching online, decided to administer vitamin D supplements in high doses; subsequently he was admitted to our clinic for symptoms consistent with vitamin D intoxication.

Keywords: vitamin D, toxicity, multiple sclerosis, relapsing-remitting

INTRODUCTION
Multiple sclerosis is the most common chronic demyelinating disease, and the second most common cause of disability in young people. (1) The etiology of this disease is still unknown, but some authors believe vitamin D, through its immunomodulatory role, might be a key component in the treatment of this disease, due to the discovery that a significant number of MS patients have vitamin D deficiency. (2) Vitamin D toxicity was once considered to be rare, but incidence numbers are rising due to the growing reports of disease improvement after dietary supplementation. Symptoms of acute intoxication are due to hypercalcemia and include confusion, polyuria, polydipsia, anorexia, vomiting, and muscle weakness. (3)

CASE REPORT
We report the case of a 32 year old male, with a history of relapsing-remitting multiple sclerosis, who was admitted in our clinic for generalized paresthesias, weight loss and loss of appetite after ingesting massive doses of vitamin D daily for 5 months.

The patient is right handed and works in engineering. He has no known family history of multiple sclerosis or other autoimmune diseases. The diagnosis of relapsing-remitting multiple sclerosis was established in 2014, but clinical onset was in 2013 consisting of left sided paresis of the abducens nerve. Prior to 2013, the patient has no significant medical history.

In October 2014, when diagnosis was established, the patient was admitted in our clinic for thoracic pressure and discomfort at T11-T12 level (MS girdle) and lower limb paresthesias, treated with methylprednisolone pulse-therapy during 5 days with total recovery. In December 2014 the patient was admitted for a second relapse with similar symptoms, and after a new cure of methylprednisolone, it was decided to initiate interferon beta-1a (Rebif) treatment. At the time of treatment initia-
tion EDSS score was 2.0. Patient outcome was favorable, without relapses until June 2015, when he came to consult claiming a polymorphic symptomatology, consisting of weight loss, loss of appetite, generalized paraesthesia, fatigue.

Medical history revealed the patient has been included in a clandestine clinical study with vitamin D supplementation that he has found online. He buys vitamin D supplements online upon instruction from a person claiming to be a physician from the U.S. and takes 70,000 IU daily without council or consent from his treating physician.

General clinical examination was unremarkable. Neurological assessment upon admission found right Claude Bernard-Horner syndrome (miosis, ptosis and enophthalmus), ataxia of the left limbs, brisk reflexes and absent abdominal reflexes; EDSS score was 2.0. Blood panel found hyperkalemia, biologic inflammatory syndrome with high fibrinogen, PCR and ESR and normocytic anemia. He was tested for serum 25-OH-vitamin D levels and findings showed levels of 560 ng/ml (lab ranges between 30-100 ng/ml). However, the levels of serum calcium (9.85 mg/dL [RI, 8.6 to 10.2 mg/dL]), magnesium (1.93 mg/dL; 1.6 to 2.6 mg/dL) and phosphate (3.89 mg/dL; 2.7 to 4.5 mg/dL) were normal.

Glucocorticoid treatment was initiated with i.v. Methylprednisolone 1,000 mg daily for 5 days after which the patient showed significant clinical improvement. The patient was asked to discontinue administration of vitamin D supplements, to maintain adequate hydration and to keep a calcium restricted diet. The patient was advised to repeat testing of his vitamin D levels after 6 months.

**DISCUSSION**

Multiple sclerosis (MS) is the most common chronic inflammatory demyelinating disease of the central nervous system with an autoimmune component. It is the second leading cause of severe disability and early retirement after head trauma in young adults. MS is more prevalent in women and although it was previously thought that men are more severely impacted by the disease, further studies have found that sex or age of onset are not independent prognostic factors. (1,2,4,5)

In 1960 Acheson suggests an association between MS incidence and solar radiation exposure. Research into this hypothesis isn’t showing any favorable results; the data supporting the idea of a latitude gradient is obtained from prevalence studies but it is in fact incidence studies that offer a clearer picture. Furthermore, recent MS data is show in the risk of relapse. (11,12)

On the other side there are numerous studies published that haven’t obtained such positive results after increasing serum levels of 25(OH) vitamin D. Such a study was reported by a norwegian group led by Kampman which, after prescribing supplementation with 20,000 IU of vitamin D, did not find any positive results on annual relapse rates, EDSS score and other clinical measurements. (13)

Summarizing, current data on the matter is contradictory, some results support a protective effect of vitamin D, but the nature of this effect and its mechanism are not yet fully understood. (14,15)

The human body is capable to synthesize vitamin D after exposure to sunlight, thus research on this topic has been challenged with two caveats, one regarding dose requirements in patients with no exposure to sunlight and the second determining the relationship between serum 25-hidroxi vitamin D and systemic effect. The Institute for Medicine advises use of vitamin D supplements with doses ranging between 400 and 4,000 IU daily. Selected populations of patients can receive up to 50,000 IU but only under strict medical supervision. Normal ranges for serum 25-hidroxy vitamin D have also sparked controversy, the Institute of Medicine concluded that 20 ng/ml (50 nmol/L) is optimal for normal individuals, while other institutions suggest that older individuals with risks of orthopedic problems should have at least 30 ng/ml (75 nmol/L). (9,16)

Regarding vitamin D toxicity, data in the literature is mostly through case reports due to the fact that clinical trials on the subject are unethical. Once vitamin D supplementation became a popular subject among several medical specialties, data started to be published regarding dosage and toxicity respectively. One such case, published by Chakraborty et al, showed the case of a female patient who was prescribed 60,000 IU once weekly. The patient misinterpreted the dose and took 60,000 IU daily for 4 months. She had no symptoms, the diagnosis of vitamin D toxicity (746 ng/ml) was made upon re-evaluation of vitamin D levels. Like our patient, she did not have elevated levels of serum calcium, magnesium or phosphate. A similar case was described by Kumar et al. but in this case the patient was an elderly, illiterate woman who presented with severe hypercalcemia and deranged renal function. Calcium homeostasis is maintained by two mechanisms, firstly through the increase of intestinal absorption and secondly through bone resorption; the latter is implicated in cases of hypercalcemia. (17-19)
CONCLUSIONS

Vitamin D is considered to be a very good candidate for treatment improvement in several diseases. Results so far haven’t shown definitive proof of its efficacy in multiple sclerosis but monitored supplementation in patients less exposed to sunshine or with documented vitamin D deficiency might prove to be useful in lowering relapse rates and development of new lesions of MRI. Patients should be counseled not to take dietary supplements without medical council so as to avoid cases like our patient.

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REFERENCES