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Case Report

# Vitamin D Deficiency in the Setting of Multiple Sclerosis - A Case Report and Literature Review

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## Abstract

**Introduction:** Multiple sclerosis (MS) is a chronic idiopathic inflammatory disorder of the central nervous system, characterized pathologically by demyelination and subsequent axonal degeneration. The disease commonly presents in young adults and affects twice as many women as men. Clinical presentation include numbness, weakness, visual impairment, loss of balance, dizziness, urinary bladder urgency, fatigue, and depression among many other unspecific symptoms. A higher MS risk in individuals with low vitamin D intake or low circulating 25-dihydroxyvitamin D as well as a reverse correlation between vitamin D levels and MS activity have been reported and suggest that vitamin D is related to the disease process that leads to and perpetuates MS. In this case report, we present a patient with MS and low levels of Vitamin D.

**Case Presentation:** A 35-year-old female was seen in the Emergency room complaining of 3 days of acute polymyalgia and worsening chronic right-sided hemiparesis. Her past neurological history is significant for acute right-sided hemiplegia during the 2nd trimester of her third pregnancy in 12-24-2013 when she was admitted to the hospital and -according to the patient- diagnosed with possible Multiple sclerosis according to a Cerebral spinal fluid (CSF), Neurology evaluation and ophthalmologic evaluation confirming Optic Neuritis. On her day of admission, her labs were unremarkable except for a Vitamin D level of 10 ng/mL. Her work-up at that time was limited due to her pregnancy.

**Conclusion:** MS patients who present with Vitamin D deficiency should be closely monitored to prevent the aforementioned deficiency. Additionally, the risk of developing MS could be reduced by upholding optimal vitamin D levels in the healthy population. Further randomized interventional trials are definitely required to elucidate the therapeutic effect of vitamin D in MS.

***Keywords:*** *Multiple sclerosis (MS); Central Nervous System (CNS); Vitamin D*

## Introduction

Multiple sclerosis (MS) is an autoimmune chronic inflammatory/demyelinating disease of the Central Nervous System (CNS) accompanied by gliosis and neuronal loss; the course can be relapsing-remitting (most common) or progressive. Lesions of MS typically develop at different times and in different CNS locations (dispersed in time and space). About 340,000 individuals in the United States and over 2 million individuals are affected globally. The clinical course can be variable, ranging between a benign condition and a rapidly progressive and debilitating disease requiring significant lifestyle changes. Increasing evidence associates sunlight or vitamin D as a crucial environmental factor in etiology. It has been hypothesized that this environmental candidate might interact with inherited factors and sought responsive regulatory elements in the MHC class II region [1].

## Case Summary

A 35-year-old female assisted to the emergency room with a history of acute polymyalgia and worsening chronic right-sided hemiparesis. Her past medical history is remarkable for an acute right-sided hemiplegia during the 2nd trimester of her pregnancy when she was admitted to the hospital and diagnosed with possible multiple sclerosis. Her workup at that time was limited due to her pregnancy, but the patient's CSF was studied and suggested a possible MS, although the patient does not have certainty if the findings in CSF were Oligoclonal bands, myelin basic protein or other findings. She lost follow-up and her deficits recovered notably apart from chronic residuals of quadriparesis, more notable on the right side, clumsiness and heaviness that have not affected her work. She further related chronic right-sided intermittent visual obscuration, brightness and fuzziness since 2004 attributed to bilateral optic neuritis which were confirmed at the onset by Neurology and Ophthalmology. One week before her admission, the patient presented right painful leg swelling for which arterial doppler was ordered and was concerning for Peripheral artery disease. Hence, the patient had a CTA which demonstrated a congenital vascular abnormality of anterior and posterior tibial arteries. Several hours after the procedure, patient experienced severe muscle aches of her entire body including arms, legs and torso. The aches progressed to the point that it almost caused hemiplegia and interfered with her ability to move and stand.

Patients vital signs were: Blood pressure: 122/67, Respiratory rate: 20, Heart rate: 74, Weight: 107 kg, Temperature: 37.1°C, $SpO_2$: 97%.

The work-up for the patient included a:

Complete blood cell count with:

- WBC: 16.600, Neutrophils: 67.4%, Lymphocytes: 25.1%
- RBC: 4.59 x 103
- Hemoglobin: 13.7
- Hematocrit: 41.7%
- MCV: 90.8
- MCH: 29.8
- Platelets: 309.000.

Glucose levels: 143 mg/dL

Creatinine: 0.8 mg/dL

Sodium 137 mmol/L

Potassium: 3.6 mmol/L

Chloride: 102 mmol/L

$CO_2$: 29 mmol/L

Anion Gap: 10 ratio

Calcium: 8.2 mg/dL

Globulin: 3.9 g/dL

Albumin: 3.1 g/dL

Total Protein: 7gr/dL

CK: 21 unit/L

hCG urine: Negative

CT scan of the brain showed no acute intracranial abnormalities

Vitamin D: 12 ng/mL.

Patient was evaluated by the Neurologist who performed a complete Cranial nerve examination from II to XII and was normal. Motor examination showed a quadriparesis more notable on the right, the findings were: hemiparesis 4/5 in right arm, 3/5 in right leg and 4/5 in the left side. Coordination showed slow fine motor and rapid alternating movements. No pronator drifts. There were no dysmetric movements. Deep tendon reflexes: symmetric in the arms and legs grade 1+ bilaterally. Flexor plantar response. Gait and station were not evaluated because the patient could not stand or walk due to her weakness. Sensory examination was diminished to light touch, pin prick of the right arm, leg and cheek.

A cardiology evaluation included a transthoracic echocardiogram that was normal, showing an Ejection fraction of 55 - 60% with a Pulmonary peak pressure of 22 mmHg.

More studies included a CT scan of the head that showed no acute abnormality. MRI of the neck with and without contrast displayed no hemodynamically significant stenosis identified in the carotid arteries bilaterally. Vertebral arteries within normal limits bilaterally. MRI of the brain with and without contrast showed no acute process or significant intracranial abnormality. No evidence to suggest acute ischemia/infarction. MRI of the spine with and without contrast with no significant disc bulge, spinal canal, or neural foraminal stenosis. No significant abnormality appreciated in the cervical spine on this examination. Bilateral Ultrasound of the carotids with bilateral carotid atherosclerosis with sonographic findings compatible with less than 50% stenosis involving bilateral internal carotid. Grossly patent antegrade flow involving bilateral vertebral arteries.

Rheumatologic studies included: ANCA screen negative, Myeloperoxidase antibody < 1, Proteinase-3 Antibody < 1, DNA antibody < 1, SM Antibody < 1, SM, RNP Antibody < 1, Sjogren Antibody (SS-A) < 1, Sjogren Antibody (SS-B) < 1.

The patient was then seen by a Neurologist who reviewed the entire case, considering Sarcoidosis as a possible differential diagnosis, in the absence of written evidence of the findings suggesting MS. Although Sarcoidosis was considered at one point, the patient's statement that she had MS findings in a CSF and was confirmed by Neurology and Ophthalmology (bilateral Optic Neuritis), were considered remarkable and important at the time to treat the patient.

Her last study was a Nerve conduction study which could not determine any nerve damage or any abnormality.

When patient was seen by Internal Medicine on her first hospital admission, she received an aggressive treatment with Vitamin D presenting rapid improvement. But she presented for a second hospital admission due to a flare-up. This time the improvement was seen

thanks to a rapid onset of treatment with oral Vitamin D and administration of Steroids (Dexamethasone 8 mg daily for 7 days). It is important to mention that in-between hospitalizations, she had four relapses, all of them presenting as moderate muscle pain and weakness, each presenting with low levels of Vitamin D and requiring the same steroid treatment mentioned above. Patient's symptom-free states happened with a maintenance of high normal levels of Vitamin D.

## Discussion

MS may be sudden or insidious. Symptoms may range between mild to severe, in occasions, mild enough that a patient does not seek medical care for a long time. The severity of symptoms depends on the severity of the lesions found within the CNS. At the post-mortem stage, approximately 0.1% of life-time asymptomatic individuals will be found, unpredictably, to have pathologic evidence of MS. Radiologic studies such as MRI scans (gold standard) indicated for other reasons different from MS, at times, may show evidence of asymptomatic MS [2]. Neurologic dysfunction on asymptomatic locations may be evident on examination.

There are no clinical findings that are unique to MS, but some are highly characteristic of the disease. Common manifestations of MS include sensory symptoms in limbs or face, unilateral visual loss, acute or subacute motor weakness, diplopia, gait disturbance and balance problems, Lhermitte sign (electric shock-like sensations that run down the back and/or limbs upon flexion of the neck), vertigo, bladder problems, limb ataxia, acute transverse myelitis, and pain. Charcot's neurologic triad in MS consists of three classic symptoms: Scanning speech, Intention tremor (also Incontinence and Internuclear Ophthalmoplegia) and Nystagmus. Presentations due to cortical syndromes such as aphasia are rare. Presenting symptoms and signs may be either monosymptomatic or polysymptomatic [3,4].

The typical patient presents as a female Caucasian young adult with one or more clinically distinct episodes of central nervous system dysfunction with at least partial resolution. While most MS cases follow a relapsing-remitting course, approximately 10% of MS cases are characterized by steadily increasing neurologic disability independent of relapses, which is termed primary progressive MS. In our case report, the patient is epidemiologically characteristic of a MS patient (Caucasian, young adult, female) who presented with Vitamin D deficiency and also had multiple flare-ups, all of which coincidentally had low Vitamin D levels.

Some cases of MS may be presaged by a radiologically isolated syndrome (as in our patient's first presentation), which is defined by incidental brain or spinal cord MRI findings that are highly suggestive of MS in an asymptomatic patient lacking any history, symptoms, or signs of MS [5,6].

Typical findings on brain MRI in patients with MS include hyperintense white matter lesions on T2 sequences in characteristic locations (periventricular, cortical or juxtacortical, infratentorial, and spinal cord), as described elsewhere.

There is no specific test to diagnose MS. Clinically, we may find some diagnostic criteria indicating that MS requires evidence of more than two episodes of signs and symptoms that suggest presence of the disease in anatomically noncontiguous white matter tracts of the Central Nervous System [7]. These symptoms should last more than 24 hours and ensue as different episodes that are separated by more than a month. If during a neurological examination a patient only presents with one sign (Clinical Diagnosis), an abnormal test such as a MRI or evoked potentials should be considered. In the same way, Radiologic findings on a MRI consisting of either: development of focal new white matter lesions or simultaneous presence of both an enhancing lesion and a non-enhancing lesion in an asymptomatic location may be acceptable as a diagnosis of MS [8].

MS therapy may be divided into several categories: 1. Treatment for acute attacks/flare-ups (IV Steroids), 2. Treatment with disease-modifying agents (B-interferon, Glatiramer, Natalizumab) that reduce the biologic activity of MS, and 3. Treatment of symptoms (Neurogenic bladder, spasticity and pain) [9].

Treatments that help remyelinating or repairing neurons do not exist at the moment, but several promising approaches are being actively investigated [10].

In our case, this patient had only unspecific clinical signs and symptoms related to Multiple Sclerosis, although several tests performed did not show signs of the disease at the moment. She did state having a CSF highly suggestive of the disease, but she does not mention any specific finding and was then lost to follow-ups. Throughout her hospital admissions, her Vitamin D levels were always below the normal value.

However, published studies are not as homogeneous as it has been indicated in some protocols. In the study by Kampman., *et al*. [11] the weekly supplements of 20,000 IU of Vit. D3 did not show an improvement in the activity of the disease measured by clinical outbreaks, functional tests or intensity of fatigue. Neither Stein., e*t al*. [12] found improvement in MRI studies comparing groups of patients treated with high doses of Vit. D2 and Vit. D3. In the SOLAR study [13], a double-blind study was carried out on 229 patients who received 14,000 IU of Vitamin D3 or placebo as a treatment added to interferon, and no difference was observed between the two groups when measuring absence of outbreaks, progression of disability and activity in MRI. Similar results were published later by Camu., *et al*. [14] in a study in 129 patients who received 100000 IU weekly of Vitamin D3 or placebo.

Sintzel., *et al*. [15] published an exhaustive review of all the studies that have been conducted and conclude that although there is increasing evidence that low levels of Vitamin D are associated with an increased risk of MS and with greater clinical activity on MRI (in cases already established), the impact of Vitamin D on the activity of MS is not adequately investigated.

## Conclusion

Given that the geographical distribution of MS is related to a lower exposure to sunlight, which is the main source of vitamin D in humans, studies suggest that one of the modifiable risk factors that can play a role in the development of MS is the deficit of vitamin D [16].

Although there is suggestive evidence from the ecological, epidemiological, clinical and biomedical point of view, a review of 5 studies of Vitamin D supplementation in MS found no beneficial effect in 4 of the 5 studies. However, the heterogeneity of the doses and outcome variables, small sample size and possible biases mean that conclusive evidence on the usefulness of Vitamin D supplementation as adjuvant therapy in MS is not available at the moment [17].

We can conclude that there are data that suggest some role of Vitamin D in the development and flare-ups of MS and in a clinical and radiologic improvement when Vitamin D supplements are used. However, the contradictory results that have been observed in certain studies and the lack of knowledge regarding potential side effects of dose supplements maintained over years suggest the need to be cautious and to treat each patient individually. Only and only then, we may be able to respond three fundamental questions: 1. Does Vitamin D prevent MS? 2. Does Vitamin D impact disease activity? 3. Does Vitamin D modify disease progression?

Our case represents an epidemiologically characteristic patient with MS who had flare-ups that coincided with low Vitamin D levels, which leads us to the conclusion that Vitamin D deficiency does play an important role in Multiple Sclerosis.

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