Progress in Nutrition 2018; Vol. 20, Supplement 2: 290-293 DOI: 10.23751/pn.v20i2-S.6085

Case report

IgG-NMO status after vitamin D supplementation in patients with NMOSD: a case report and a review of literature

Vahid Shaygannejad[1], Omid Mirmosayyeb[1,4], Gholamreza Askari[2], Mohammad Reza Maracy[3], Mohammad Bagher Maljaei[1,2,5], Sahar Saraf-Bank[2]

[1]Isfahan Neuroscience Research Center and Department of Neurology, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. - Email: mbmaljaie@gmail.com; [2]Food Security Research Center and Department of Community Nutrition, School of Nutrition and Food Sciences, Isfahan University of Medical Sciences, Isfahan, Iran; [3]Department of Epidemiology and Biostatics, Isfahan University of Medical Sciences, Isfahan, Iran; [4]Medical student research Committee, Isfahan University of Medical Sciences, Isfahan, Iran. [5]Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

Summary. *Introduction:* Neuromyelitis optica Spectrum Disorder (NMOSD) is an inflammatory disorder of the CNS that presents typically with relapses of optic neuritis or transverse myelitis, in which IgG autoantibodies against aquaporin-4 water channel protein probably play a pathogenic role. We presented two cases who newly diagnosed with NMOSD that presented alterations in IgG-NMO status after vitamin D supplementation. *Case presentation:* We reported 2 cases, a 36-year-old female and a 27-year-old male newly diagnosed with NMOSD. Cases were stable in remission and experienced no attack and none of them didn't take pulse therapy in the previous 3 months. Vitamin D level and IgG-NMO titration in 36-year-old female were 21 ng/dl and 1/320, and in 27-years-old male were 29 ng/dl 1/100, respectively. As their prescription, they took 50000 IU of vitamin D3 per week for 15 weeks. After 15 weeks vitamin D level raised in both of them and IgG-NMO titration was negative in cases. *Conclusion:* We reported 2 cases with high titration of IgG-NMO whom IgG-NMO status altered after high dose of vitamin D supplementation. Physiological variation in vitamin D may apply a major impact on autoimmune and inflammatory diseases. Further studies with larger sample sizes need to prove these results.

Keywords: Neuromyelitis optica Spectrum Disorder, vitamin D, supplement, Immunoglobulin G

Introduction

Neuromyelitis optica Spectrum Disorder (NMOSD) is an inflammatory disease of the central nervous system that generally affects the optic nerves and spinal cord(1, 2). More than 90% of patients with NMOSD have a relapsing disease with the attacks of myelitis, optic neuritis (ON) or both, occurring unpredictably(3). Aquaporin-4 (AQP4) is the most abundant water channel in the CNS which is confined to astrocytes and ependyma; is enriched at glial–pial and glial– endothelial interfaces; and surrounds nodes of Ranvier and paranodes, adjacent oligodendroglial loops, and synapses(4).

Recently has raised enormous interest among neurologists and researchers, for detection of a highly specific serum immunoglobulin G autoantibody (IgG-NMO) that target astrocytic water channel AQP4 and is a marker for distinction NMOSD from multiple sclerosis(3, 5-7). Today's NMOSD is recognized collectively as IgG-mediated autoimmune astrocytopathy. Before discovery of this antibody, NMOSD were

misclassified as multiple sclerosis variants. IgG-NMO is centrally involved in the pathogenesis and severity of NMOSD (8).

The immunological function of vitamin D was first recognized when the vitamin D receptor (VDR) was identified in lymphocytes (9-11). Vitamin D suppresses B cell proliferation and differentiation to decrease immunoglobulin secretion, affects T cell proliferation and maturation to decrease the numbers of T cells with Th1 and Th17 phenotypes (11, 12). Several studies have shown that vitamin D levels are low in patients with autoimmune disorders, including multiple sclerosis [MS] , systemic lupus erythematous [SLE], rheumatoid arthritis [RA], and type 1 diabetes. In addition, vitamin D levels have been reported to be associated with disease disability or activity in these disorders (13-15).

Some studies have shown reduced levels of vitamin D in patients with NMOSD (16, 17). In another study, it was found that there is an inverse association between levels of vitamin D and disability in these patients (18).

We presented two cases with newly diagnosed of NMOSD that their IgG-NMO titration turned negative after vitamin D supplementation.

Case presentation

A 36-year-old female and a 27-year-old male who newly diagnosed with NMOSD in NMOSD clinic in Ayatollah Kashani Hospital of Isfahan University of Medical Sciences, Isfahan, Iran were studied in June 2015. Subjects diagnosed as having NMOSD and without any medical comorbidities or any other major chronic diseases. Cases were prescribed oral Azathioprine. They did not consume cholecalciferol, calcium, multi-vitamin or mineral supplementation, or vitamin D-fortified foods during the previous 3 months and were of Iranian ethnicity and had lived in Isfahan city since their birth (latitude: 26˚42'N). Vitamin D was assessed with LIAISON® method (LIAISON® 25 OH Vitamin D TOTAL Specimen Diluent Set, REF 310602). IgG-NMO determined in the serum of the patients by indirect immunofluorescence (EUROIMMUN IIFT, Germany) on a cell line which had been molecular biologically modified (AQP4 transfected cells) to produce large quantities of AQP4 at Milad laboratory in Isfahan. Baseline vitamin D level and IgG-NMO titration in 36-year-old female were 21 ng/dl and 1/320, and in 27-years-old male were 29 ng/dl and 1/100, respectively. A supplementation of 50000 International Unit (IU) of vitamin D3 per week for 15 weeks started. They were in a stable status and none of them didn'ttake any pulse therapy of corticosteroids or other oral medication during 15 weeks of intervention. After 15 weeks of supplementation vitamin D level and IgG-NMO titration determined. Vitamin D level in 36-year-old female was 48 ng/dl and in 27-years-old male was 64 ng/dl. In addition, IgG-NMO titration reported negative in both cases.

Discussion and conclusion

Our study is the first report of vitamin D effect on IgG-NMO titration in NMOSD patients. There are some studies about the effects of vitamin D on IgG autoantibodies in other diseases. In a study it was demonstrated that Vitamin D supplementation in tetanic mice induce monocytes and decrease IgG with suppress of T and B lymphocytes proliferation (19). In another study with long term vitamin D supplementation in mice, total IgG concentration elevated in intervention group in comparison with control group(20). But in controversy, some studies have shown inverse correlation between vitamin D level and total IgG in human; for example Vogt et al showed that 25OH vitamin D correlated negatively with IgG level in patients with relapse-onset multiple sclerosis (21). In addition, Pincikova et al demonstrated an inverse correlation between vitamin D level and total IgG in cystic fibrosis patients that supports the proposed role of vitamin D in the immune system during infection (22). Also, Decard et al have shown that low levels of vitamin D may correlate with level of IgG and Epstein-Barr virus markers that may elevate risk of MS (23).In a recent study, Rosjo et al demonstrated that high dose of vitamin D supplementation can affect on IgG antibody against Epstein-Barr virus in patients with relapsing-remitting multiple sclerosis and vitamin D can affect humeral immune responses against Epstein-Barr virus (24). Many previous studies suggest that 1,25OHD3 inhibit B cell proliferation (11). There are some studies

in controversy of our study that shown no correlation between vitamin D and IgG that suggest vitamin D induce Th2 cells and increase IgG synthesis (25).

We presented two cases a 36-year-old female and a 27-year-old newly diagnosed NMOSD. They were stable in remission and experienced no attack and none of them didn't take pulse therapy in the previous 3 months that their IgG-NMO titration turned negative after vitamin D supplementation.

Further studies with larger sample sizes need to prove these results.

Acknowledgement

This study was extracted from M.sc dissertation which was approved by School of Nutrition and Food Sciences, Isfahan University of Medical Sciences (code number 393886).

References

1. Ketelslegers I, Catsman-Berrevoets C, Neuteboom R, Boon M, van Dijk K, Eikelenboom MJ, et al. Incidence of acquired demyelinating syndromes of the CNS in Dutch children: a nationwide study. Journal of neurology. 2012;259(9):1929-35.
2. Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinshenker BG. The spectrum of neuromyelitis optica. The Lancet Neurology. 2007;6(9):805-15.
3. Jarius S, Franciotta D, Bergamaschi R, Wright H, Littleton E, Palace J, et al. NMO-IgG in the diagnosis of neuromyelitis optica. Neurology. 2007;68(13):1076-7.
4. Nielsen S, Nagelhus EA, Amiry-Moghaddam M, Bourque C, Agre P, Ottersen OP. Specialized membrane domains for water transport in glial cells: high-resolution immunogold cytochemistry of aquaporin-4 in rat brain. The Journal of neuroscience. 1997;17(1):171-80.
5. Lennon VA, Kryzer TJ, Pittock SJ, Verkman A, Hinson SR. IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel. The Journal of experimental medicine. 2005;202(4):473-7.
6. Lennon VA, Wingerchuk DM, Kryzer TJ, Pittock SJ, Lucchinetti CF, Fujihara K, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. The Lancet. 2004;364(9451):2106-12.
7. Paul F, Jarius S, Aktas O, Bluthner M, Bauer O, Appelhans H, et al. Antibody to aquaporin 4 in the diagnosis of neuromyelitis optica. PLoS Med. 2007;4(4):e133.
8. Hinson S, Pittock SJ, Lucchinetti CF, Roemer S, Fryer J, Kryzer T, et al. Pathogenic potential of IgG binding to water channel extracellular domain in neuromyelitis optica. Neurology. 2007;69(24):2221-31.
9. Provvedini D, Tsoukas C, Deftos L, Manolagas S. 1, 25-dihydroxyvitamin D3 receptors in human leukocytes. Science. 1983;221(4616):1181-3.
10. BHALLA AK, AMENTO EP, CLEMENS TL, HOLICK MF, KRANE SM. Specific high-affinity receptors for 1, 25-dihydroxyvitamin D3 in human peripheral blood mononuclear cells: presence in monocytes and induction in T lymphocytes following activation. The Journal of Clinical Endocrinology & Metabolism. 1983;57(6):1308-10.
11. Chen S, Sims GP, Chen XX, Gu YY, Chen S, Lipsky PE. Modulatory effects of 1, 25-dihydroxyvitamin D3 on human B cell differentiation. The Journal of Immunology. 2007;179(3):1634-47.
12. Boonstra A, Barrat FJ, Crain C, Heath VL, Savelkoul HF, O'Garra A. 1α, 25-Dihydroxyvitamin D3 has a direct effect on naive CD4+ T cells to enhance the development of Th2 cells. The Journal of Immunology. 2001;167(9):4974-80.
13. Smolders J, Menheere P, Kessels A, Damoiseaux J, Hupperts R. Association of vitamin D metabolite levels with relapse rate and disability in multiple sclerosis. Multiple Sclerosis. 2008.
14. Mok C, Birmingham D, Ho L, Hebert L, Song H, Rovin B. Vitamin D deficiency as marker for disease activity and damage in systemic lupus erythematosus: a comparison with anti-dsDNA and anti-C1q. Lupus. 2012;21(1):36-42.
15. Rossini M, Bongi SM, La Montagna G, Minisola G, Malavolta N, Bernini L, et al. Vitamin D deficiency in rheumatoid arthritis: prevalence, determinants and associations with disease activity and disability. Arthritis research & therapy. 2010;12(6):1.
16. Jitprapaikulsan J, Siritho S, Prayoonwiwat N. Vitamin D level status in Thai neuromyelitis optica patients. Journal of neuroimmunology. 2016;295:75-8.
17. Tüzün E, Küçükhüseyin Ö, Kürtüncü M, Türkoğlu R, Yaylım α Reduced serum vitamin D levels in neuromyelitis optica. Neurological Sciences. 2015;36(9):1701-2.
18. Min J-H, Waters P, Vincent A, Cho H-J, Joo B-E, Woo S-Y, et al. Low levels of vitamin D in neuromyelitis optica spectrum disorder: association with disease disability. PloS one. 2014;9(9):e107274.
19. Heine G, Drozdenko G, Lahl A, Unterwalder N, Mei H, Volk H-D, et al. Efficient tetanus toxoid immunization on vitamin D supplementation. European journal of clinical nutrition. 2011;65(3):329-34.
20. Smith E, Frankenburg E, Goldstein S, Koshizuka K, Elstner E, Said J, et al. Effects of long-term administration of vitamin D3 analogs to mice. Journal of endocrinology. 2000;165(1):163-72.
21. Vogt MH, ten Kate J, Drent RJ, Polman CH, Hupperts R. Increased osteopontin plasma levels in multiple sclerosis patients correlate with bone-specific markers. Multiple sclerosis. 2010.
22. Pincikova T, Nilsson K, Moen IE, Karpati F, Fluge G, Hollsing A, et al. Inverse relation between vitamin D and serum total immunoglobulin G in the Scandinavian Cystic Fibrosis Nutritional Study. European journal of clinical nu-

trition. 2011;65(1):102-9.
23. Décard BF, von Ahsen N, Grunwald T, Streit F, Stroet A, Niggemeier P, et al. Low vitamin D and elevated immunoreactivity against Epstein–Barr virus before first clinical manifestation of multiple sclerosis. Journal of Neurology, Neurosurgery & Psychiatry. 2012;83(12):1170-3.
24. Røsjø E, Lossius A, Abdelmagid N, Lindstrøm JC, Kampman MT, Jørgensen L, et al. Effect of high-dose vitamin D3 supplementation on antibody responses against Epstein–Barr virus in relapsing-remitting multiple sclerosis. Multiple Sclerosis Journal. 2016:1352458516654310.
25. Holmøy T, Lossius A, Gundersen T, Moen S, Castellazzi M, Fainardi E, et al. Intrathecal levels of vitamin D and IgG in multiple sclerosis. Acta Neurologica Scandinavica. 2012;125(6):e28-e31.

Correspondence:
Mohammad Bagher Maljaei, Ph.D student
Department of Nutrition, School of Public Health,
Iran University of Medical Sciences, Tehran, Iran
E.mail: mbmaljaie@gmail.com