Do low vitamin D-25-OH levels predict a higher likelihood of relapse for acute disseminated encephalomyelitis: A report of 5 pediatric cases

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Background

Vitamin D3, the activated form of which is vitamin 1,25 $(OH)_2$, is recognized as a risk factor in autoimmune diseases. In both murine and rat models, it has been demonstrated to have multiple impacts modulating immune system function to suppress acute activity and reduce risk of relapses in experimental allergic encephalomyelitis. In addition, clinical trials and other observational studies have shown benefit with higher levels of vitamin D3 in reducing risk for relapses in multiple sclerosis, although it has not been extensively studied acutely or subacutely. We describe 3 cases of acute disseminated encephalomyelitis (ADEM) with relapses, all of which had low vitamin D3 levels at presentation or briefly following hospitalization that we suspect may be related to risk for relapses in ADEM. In all 3 of these cases, the patients had vitamin D3 levels < 20 ng/mL either at presentation or shortly following their hospitalization; all 3 of these patients had radiologic and clinical progression of their disease. We contrast these cases with 2 patients with monophasic ADEM: one patient with a normal level and another patient with an initial low level that was normal following supplementation.

Case Summaries

Case 1: Pt #1 was a 2 year old 5 mo female who presented with cerebellar ataxia and sleepiness, found to have brain and cord lesions and was initially treated with IV steroids. She initially responded but later was admitted with worsening of gait and fussiness and received IV steroids, plasma exchange, and then cyclophosphamide and intravenous immunoglobulin. At this visit, her vitamin D3 was noted to be low. She stabilized, and she was sent home with a steroid taper but deteriorated again near the end of her wean. The family was not regularly giving vitamin D3 either. She was re-admitted, received another pulse of steroids and cyclophosphamide and she started to regularly take her vitamin D3. She has stayed in clinical remission since, with a repeat vitamin D3 at 20 ng/mL at 6 mos.

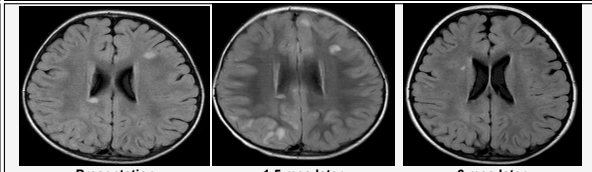
Case 2: Pt #2 was an 8 year old female who had an episode of emesis upon awakening followed by progressive difficulty with walking and altered mental status. She was admitted with noted multifocal brain and cord lesions. She had a course of steroids with minimal improvement and received 7 rounds of plasma exchange, although she still had significant right-sided weakness and we gave her a dose of cyclophosphamide. Her initial vitamin D3 level was 9 ng/mL. Following discharge, the family was noncompliant with her vitamin D3 and she initially was improving until she had an episode of diplopia and worsening of her ataxia. She was admitted about 3 mos after the last attack, and she was given a course of steroids. At the time of this abstract, she was considered multiphasic ADEM, although she later fit a diagnosis of MS. About 5 mos later, with better D3 compliance, her level improved to 24 ng/mL, and her imaging stabilized.

Case 3: The pt was a 4 year old girl who presented with gait abnormality, lethargy, and urinary retention. She had multifocal brain and cord lesions all with faint enhancement. She had a noted initial vitamin D3 level of 14 ng/mL. She responded well to steroids and plasma exchange, although she had noted abnormalities on an eye examination at approximately 3 mos following her initial presentation and swelling of her L chiasmal portion of her optic nerve, which was not affected initially in her first presentation. She had another course of steroids and has stayed in clinical and radiologic remission.

Case 4: The pt was an 11 year old male that woke up sleepy but responsive one morning. A couple of days later, his gait deteriorated and he had new-onset urinary retention. He was admitted and noted to have diffuse brain lesions, both gray and white matter, and he had T2 signal extending down his entire cord. His initial vitamin D3 level was 33 ng/mL. He had an excellent response to high-dose steroids, which he received for 3 days and he had a 2 week taper without problems. He was normal at follow-up at 4 mos and his brain imaging normalized.

Case 5: The pt was an 8 year old female who presented with lethargy, vision loss in her left eye, and parasthesias in her hands. She had a large R temporal lesion, a left optic nerve enhancing lesion, a cord lesion and several scatted smaller brain lesions. She responded well to steroids. Her initial vitamin D3 level was low at 13 ng/mL, but her parents were compliant in supplementation and her repeat level was 90 ng/mL at 4 mos, at which point her exam was normal and her imaging was much improved.

Low Vitamin D3 patients (1-3) vs. Normal Vitamin D3 (4,5)



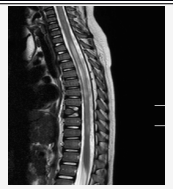
Presentation

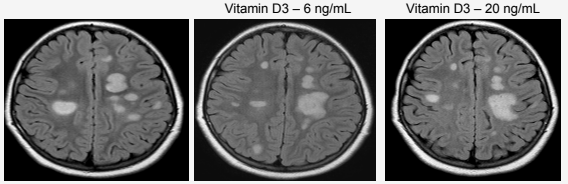
1.5 mos later
Vitamin D3 – 6 ng/mL

6 mos later
Vitamin D3 – 20 ng/mL

#1

Presentation
Vitamin D3 – 14 ng/mL





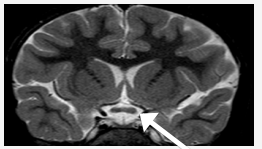
Presentation
Vitamin D3 – 9 ng/mL

3 mos later

5 mos later

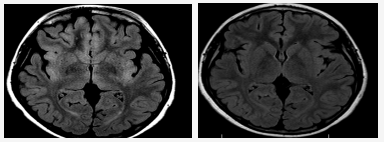
#2

#3



4 mos later

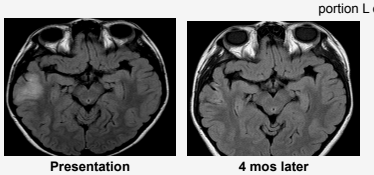
Subtle swelling of chiasmal portion L optic nerve



Presentation
Vitamin D3 – 33 ng/mL

4 mos later

#4



Presentation
Vitamin D3 – 13 ng/mL

4 mos later
Vitamin D3 – 90 ng/mL

#5

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Vitamin D3 mechanisms

- Vitamin D3 may reduce the number of myelin-reactive CD4+ T-cells.
- Vitamin D3 supplementation in mice/rat models have attenuated or abolished the experimental model of MS (EAE).
- Vitaimin D3 levels seem to be inversely proportional to Th1/17 T-cell levels.
- Vitamin D3 may aid to induce apoptosis of auto-inflammatory cells.
- In MS, higher vitamin D3 levels correlate with a lower risk for relapse.

Post-Submission Data

- Out of 5 patients that presented in the past 12 mos with idiopathic transverse myelitis, 3 patients with initial vitamin D3 levels of 7, 12, and 19 ng/mL on presentation had suboptimal outcomes at 3-6 mos despite aggressive treatment.
- 1 other patient with idiopathic transverse myelitis had an excellent outcome with an initial vitamin D3 level of 22 ng/mL
- The last idiopathic transverse myelitis patient that had an good outcome had an initial level of 3 ng/mL but was supplemented to a level of 42 ng/mL by 6 mos
- 3 other ADEM patients, all of whom had excellent outcomes without recurrence, that presented following this submission had initial vitamin D3 levels of 17, 28, and 15 (which was aggressively supplemented to 36 ng/mL within a month) ng/mL.

Conclusions

Acute disseminated encephalomyelitis is typically a monophasic demyelinating disease of the central nervous system. In a limited case series, there may be a suggestion that vitamin D3 levels on presentation and early in a patient's course, as noted in animal models of MS, may have an impact on the likelihood of recurrence. We feel the next step should be a prospective study assessing vitamin D3 levels at regular intervals in acute demyelinating diseases to assess for evidence of an acute and subacute impact.

Disclosures

- Funding for Dr. DeSena's fellowship is provided by the Transverse Myelitis Association.
- Dr. Greenberg has consulted for DioGenix, Elan, and Biogen Idec, has previously given expert testimony, has grants/grants pending with the Accelerated Cure Project, the Guthy Jackson Foundation, and Amplimmune, has received payment for or given lectures for the MSAA and Medilogix, and has stock/stock options with DioGenix.
- Dr. Graves has consulted for Teva Pharmaceuticals and Bayer, has grants/grants pending for Novartis, and has received payment for or given lectures for Teva, Bayer, Novartis, and Pfizer.