

## Hypocalcemic Seizure Due to Severe Vitamin-D Deficiency in an Adolescent with Obesity and Autism

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### Abstract

Hypocalcemic seizures due to Vitamin D deficiency are rare in children beyond the neonatal period. In this case, a 12 year old female adolescent with intellectual disability, autism, obesity and a very restricted diet presented with hypocalcemic seizure secondary to Vitamin D Deficiency. A higher level of alertness about nutritional deficiencies must be maintained in the presence of dietary restrictions, particularly in children with developmental disabilities.

**Keywords:** Hypocalcemia; Seizures; Obesity; Autism spectrum disorder; Vitamin D deficiency; Developmental disabilities; Nutritional deficiencies

### Introduction

A 12-year-old Hispanic girl with severe autism spectrum disorder (ASD), intellectual disability, and obesity presented to the emergency department (ED) in the middle of winter with an episode of unprovoked, tonic-clonic seizure that lasted 8 minutes. Upon arrival to the ED she was afebrile 97.6°F, pulse 110/min, respiratory rate 20/min, blood pressure 103/56 mmHg, O<sub>2</sub> Sat 97% on room air, weight was 63.6 kg (95%), height was 155 cm (61%) and Body Mass Index (BMI) was 26.4 (96%). During examination she was alert and awake. There was no facial dysmorphism and no findings of rickets. The neurological exam showed no focal deficits, tremors, or other involuntary movements. Tanner stage of puberty was 4. She showed limited social interactions and her communication skills were limited to use of short phrases and significant echolalia.

### Case Presentation

Past medical history was remarkable for being the product of a twin pregnancy and premature delivery at 24 weeks of gestation. Since the patient was 3 years old, her diet consisted exclusively of french fries with ketchup and Doritos® (corn chips), water and Sunny-Delight® (an orange flavored, sugar-containing beverage). For years, the mother had unsuccessfully made numerous attempts to expand the child's diet. Because of this limited intake a nutritional drink (Pediasure®) was used as a supplement for several years. It was discontinued two years prior to this episode because of the child's worsening obesity. Her exposure to sunlight was limited because of her difficult behaviors coupled with long harsh winters. The laboratory evaluation was remarkable for severe hypocalcemia, very low levels of Vitamin D and secondary hyperparathyroidism (Table 1). The rest of the blood work was within normal limits.

Test Parameters	On admission	Normal values
Calcium (mg/dL)	6	8.4 - 10.5
Ionized Calcium(mg/dL)	3.4	4.5 - 5.3
PTH (Pg/ml)	309.9	14 - 72
Vit D (ng/dl)	< 0.4	30 - 100
Magnesium (mg/dL)	2	1.6 - 2.5
Phosphorus (mg/dL)	4.1	2.7 - 4.5
TSH (IU/ml)	3.31	0.27 - 4.20
Albumin (g/dL)	2.7	3.7 - 5.1
Total Protein (g/dL)	5.2	6.3 - 8.2
ALT (U/L)	30	13 - 56
AST (U/L)	22	15 - 37
Hemoglobin (g/dL)	12.7	12 - 15
Hematocrit (%)	37.2	35 - 49
RDW (%)	14.2	12 - 15

**Table 1:** Laboratory evaluation parameters.

She received IV infusion of Calcium gluconate followed by oral calcium gluconate 150 mg TID (115 mg/5 ml) and ergocalciferol 8,000 IU daily. She was responsive to the management and remained seizure-free without anticonvulsants.

Upon discharge, Vitamin D and calcium were mixed with ketchup. Her diet, which continued to consist of fries, Doritos® and Pediasure®, was restarted. Behavioral interventions continued to be used to expand the repertoire of food. Upon follow up 3 weeks later, Vit D was 20.7 ng/ml; the rest of the laboratory tests were within normal limits, and she remained asymptomatic.

## Discussion

Autism spectrum disorder (ASD) is a group of complex, heterogeneous neurodevelopmental conditions characterized by impairments in social interaction and social communication, starting in early childhood, in the first 3 years of life. There is an increase in prevalence of this disorder since it was first described by Kanner in the 1940s and first introduced in the DSM III (Diagnostic and Statistical Manual III) in 1980. The latest data from the Centers for Disease Control (CDC) is 1 of every 68 children has an autistic spectrum disorder [1]. The etiology of ASD is not known but multifactorial, based on the interplay of genetic predisposition and environmental influences. Among the environmental influences, recent studies report that Vitamin D deficiency is common in children with autism and its correction improves their behavior [2].

ASD is usually diagnosed in early childhood when the developmental trajectory of the child becomes atypical. For an autism spectrum disorder to be diagnosed, the child must fulfill criteria based on the DSM 5 (Diagnosis and Statistical Manual version 5) [3]. There must be persistent deficits in social communication and social interaction across multiple contexts including:

- Deficits in social-emotional reciprocity,
- Deficits in nonverbal communicative behaviors used for social interaction and
- Deficits in developing, maintaining, and understanding relationships.

The child must also show at least 2 features of restricted, repetitive patterns of behavior, interests, or activities, presenting as:

- Stereotyped or repetitive motor movements, use of objects, or speech;
- Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior;
- Highly restricted, fixated interests that are abnormal in intensity or focus and
- Hyper or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment [3].

This last feature, hypo or hyper reactivity to sensory inputs is commonly seen in ASD, and has become a diagnostic criterion since it was included in the DSM 5. Among a wide range of atypical behaviors, children with ASD often have atypical feeding behaviors, of which food selectivity is the most common [4-6]. For the most part, even autistic children with food selectivity achieve growth adequacy [4]. Children with more severe autism and challenging behaviors may have increased food selectivity and this can cause significant stress for the families [4,6]. Food selectivity may include food refusal, eating a decreased variety of food, or a high frequency of a single food. Diets may be selectively rich in protein or starch or have sensory aspects like particular textures or flavors [7]. There are many theories about the possible reasons for selective diets, including sensory sensitivity [5]. These feeding difficulties may lead to nutritional deficiencies, including Vitamin D Deficiency (VDD) and iron deficiency anemia [8].

VDD during pregnancy or early childhood has been proposed as a possible environmental trigger in the pathogenesis of ASD [9,10]. Specific genetic polymorphism found in some children with ASD encodes the vitamin D binding protein. Several clinical trials have demonstrated that Vitamin D supplementation can improve core symptoms in children with ASD [11].

Vitamin D is a pro-hormone, a normal level of which is necessary for adequate calcium absorption from the gut. In a vitamin D deficient state, the intestinal absorption of calcium decreases significantly causing hypocalcemia. Phosphate absorption decreases with calcium absorption too. When ionized calcium decreases, it stimulates Parathyroid Hormone (PTH) secretion which increases calcium reabsorption from the renal tubules and activates 1- $\alpha$ -hydroxylase enzyme increasing an active version of 1,25(OH)<sub>2</sub> vitamin D. Hyperparathyroidism also increases the loss of renal phosphorus. Decrease in calcium-phosphorus product results in decreased bone mineralization leading to osteopenia, which increases the risk for bone deformities and fractures.

Skin is a major contributor of circulating vitamin D, which is synthesized from its exposure to ultraviolet B (UV-B) radiation. So natural sunscreen, melanin pigmentation, and the use of artificial sunscreen affects its production. Other causes of decreased skin production of vitamin D include skin covering such ethnic clothing, limited exposure to sun in winter months, or to fear of skin cancer. Vitamin D is present in oily fish, cod liver oil, dairy products, and vitamin D fortified food or drinks. Children and adolescents who avoid nutrition rich in vitamin D naturally become at high risk for its deficiency. The suggested requirement for Vit D is 400 IU/d (IU=25 ng) in infants 0 to 1 year old, and 600 IU/d in children older than 1 year.

The current Endocrine Society clinical practice guideline [12] recommends screening for VDD in at-risk individuals such as obese children; African-American and Hispanic children; pregnant and lactating women; children with physical findings of rickets, chronic kidney disease, hepatic failure, malabsorption syndromes; and patients on medication like anticonvulsants, glucocorticoids, antifungals such as ketoconazole, and medications for AIDS. ASD and other developmental delays are not quoted as risk factors for VDD screening. The recommended screening method is to measure serum circulating 25-hydroxyvitamin D 25(OH)D level by a reliable assay [12]. Vitamin D deficiency is defined as a 25(OH)D below 20 ng/ml and insufficiency as a 25(OH)D of 21 to 29 ng/ml [12].

The prevalence of vitamin D deficiency increases with weight: among healthy-weight, overweight, obese, and severely obese children was 21%, 29%, 34%, and 49%, respectively [13]. VDD is also often decreased in children with autism and other neurodevelopmental conditions like epilepsy [14,15]. In addition, lack of sun exposure on the eastern coast of North America during winter puts children at higher risk for Vitamin D deficiency [16].

Clinical features of vitamin D deficiency range from asymptomatic to bone pain, irritability, delay in motor development, rickets in growing children or osteomalacia in adults. Hypocalcemic seizures as a presenting sign of VDD is commonly reported in infancy [17] but rarely seen in adolescents [18], periods of higher metabolic demand of calcium.

An extreme deficiency of Vitamin D, after the calcium storage has been depleted, can lead to hypocalcemic seizures. These occur mostly in the newborn period. A case of hypocalcemic seizure in a girl with Down syndrome, celiac disease and VDD secondary to malabsorption was also reported recently [19].

Seizures as an initial presentation of Vitamin D Deficiency are uncommon in older children [20], and are rare overall: a recent British publication reports a frequency of 3.49 per million children ages 0-15 (95% CI: 2.81-4.26) in the UK and Ireland [20]. In this study, South Asian and Black ethnic groups were at the highest risk of symptomatic

VDD, but autism with a restricted diet was also noted in only 2 white adolescents with hypocalcemic seizures [20].

Our case is a rare case of a first afebrile seizure as a manifestation of hypocalcemia secondary to severe vitamin D deficiency in a light-skin adolescent female with autism, intellectual disability, and obesity with food restrictions. Since her diet was extremely restricted, the use of a nutritional supplementation was likely the main or only food source of Vitamin D for this child. Our speculation is that discontinuation of the nutritional supplement (Pediasure), her only source, lead to vitamin D deficiency and eventually caused a hypocalcemic seizure. There are no records of previous Vit D levels in the patient before she presented to our emergency department. Her diet had not improved with the behavioral approaches informally tried by the family and school. However, there are studies reporting that interdisciplinary feeding programs successfully improve challenging feeding behaviors [21] and this was offered to the mother. Since this patient was lost to follow up, we are not able to report on changes in her behavior after the treatment of Vitamin D deficiency.

## Conclusion

Hypocalcemic seizures due to Vitamin D deficiency secondary to dietary restriction are rare in children beyond the neonatal period. A higher level of alertness must be maintained in the presence of dietary restrictions in children with developmental disabilities. Current endocrine society practice guidelines do not include autism or other developmental disorder as an indication for screening for VDD. Further studies are therefore needed to establish the connection between autism spectrum disorder and Vitamin D deficiency.

## Conflict of Interest

None declared.

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