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Case Report

# FIRST SEIZURE PRESENTATION IN AN ELDERLY WOMAN WITH PRIMARY VITAMIN D DEFICIENCY: A CASE REPORT

## Abstract

Vitamin D insufficiency is common in older people and is associated with several disorders related to aging such as osteoporosis, which leads to a significantly increased risk of bone fractures. This deficiency is more common in Mediterranean countries than in Northern European countries. Hypocalcemic seizures resulting from vitamin D deficiency are rare in adults, and fractures caused by seizures without evidence of direct trauma have not yet been reported. We present an unusual case of secondary right radius fracture caused by hypocalcemic seizures in a 63-year-old Turkish woman with primary vitamin D deficiency. After vitamin D supplementation, increased serum 25-hydroxy vitamin D and calcium levels and decreased parathormone levels were found. The seizures had not recurred. It is important to check for calcium levels in older patients who present with non-febrile seizures. When hypocalcemia was found serum 25-hydroxy vitamin D levels should be measured to find the underlying cause.

***Key Words:*** Hypocalcemia; Seizure; Vitamin D Deficiency; Aged; Bone Fracture.

Olgu Sunumu

# İLK BAŞVURUSU NÖBET OLAN PRİMER D VİTAMİNİ EKSİKLİĞİ OLAN YAŞLI BİR KADIN: BİR OLGU SUNUMU

## Öz

Vitamin D eksikliği yaşlı insanlara sık rastlanmaktadır ve kemik kırık riskinin belirgin artışına yol açan osteoporoz gibi ciddi rahatsızlıklarla ilişkilidir. Bu eksiklik Akdeniz ülkelerinde Kuzey Avrupa ülkelerinden daha yaygındır. Vitamin D eksikliğine bağlı hipokalsemik nöbet erişkinlerde nadirdir ve direkt travma olmadan nöbete bağlı kırık henüz rapor edilmemiştir. Primer vitamin D eksikliğine bağlı hipokalsemik nöbetin neden olduğu sağ Radius kırığı olan 63 yaşında Türk kadın olgu sunmaktayız. Vitamin D replasmanı sonrası, serum 25-hidroksi vitamin D düzeyi ve kalsiyum seviyesinde artış ve parathormon seviyesinde ise azalma görülmüştür. Nöbet tekrarlamamıştır. Nonfebril nöbet ile gelen yaşlı hastalarda kalsiyum seviyesinin kontrolü önemlidir. Hipokalsemi tespit edildiğinde altta yatan nedeni bulmak için serum 25-hidroksi vitamin D düzeyi de bakılmalıdır.

***Anahtar Sözcükler:*** Hipokalsemi; Nöbet; Vitamin D Eksikliği; Yaşlı; Kemik Kırığı.

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## Introduction

Vitamin D is an essential steroid involved in bone metabolism, cell growth, differentiation, and regulation of the minerals in the body. The main sources of this vital vitamin are adequate diet and photosynthesis in the skin. Vitamin D deficiency is common among elderly people and numerous studies have confirmed its high prevalence in both selected and unselected samples (1–4). Vitamin D deficiency is increasing worldwide, and it has been drawing much attention because of its association with various diseases, including osteomalacia. However, there is little information on the prevalence of osteomalacia in elderly people. As osteomalacia is essentially a histological diagnosis, assessment of its true prevalence is difficult, and reported prevalence has varied depending on the diagnostic criteria adopted (5). The main risk factors for vitamin D deficiency in an otherwise healthy person are inadequate exposure to sunlight because of housebound status, insufficient dietary intake, winter season, high latitudes, dark skin and older age, use of antiepileptic drugs, and malabsorption due to inflammatory bowel disease, gastric surgery, and biliary disease (6).

Hypocalcemic seizures resulting from vitamin D deficiency are very rare in adults, and fractures caused by seizures without evidence of direct trauma have not yet been reported.

## Case Report

A 63-year-old Turkish woman was brought to the emergency department after having a first seizure while sitting on an armchair at home. It was witnessed by the patient's daughter and described as a 5-minute generalized self-resolving seizure with rhythmic shaking movements of all extremities and backward rolling of the eyes. It occurred at 1 a.m. after a night without sleep. The patient did not fall from the chair or experience any trauma during the seizure. On arrival at the emergency department, the patient was somnolent but able to answer questions. She complained of pain in her forearm. She reported having felt somewhat weak for the previous few days. Her medical history included subtotal thyroidectomy, no report of seizures, and there were no individuals with seizures in her immediate family.

In the emergency department, her vital signs were: temperature 36.8 °C; heart rate, 106 beats per minute; respiratory rate, 20 breaths per minute; blood pressure, 132/70 mmHg; oxygen saturation, 98% on room air; and pain score, 6/10. Chvostek's and Trousseau's signs were positive. Other physical examination was normal except for the musculoskeletal and neurologic components. Her right forearm revealed contracted muscles and pain on palpation of the wrist. X-ray of the right forearm was taken and fracture was seen on radiography (Figure 1). A splint was placed on the right forearm by an orthopedist. On neurologic examination done by a neurologist, the patient was somnolent but arousable and oriented to person, time and place. Deep-tendon reflexes were brisk all over. Brain computerized tomography (CT) and brain magnetic resonance imaging (MRI) 24 hours later were found to be normal. No additional tests were recommended by the neurologist.

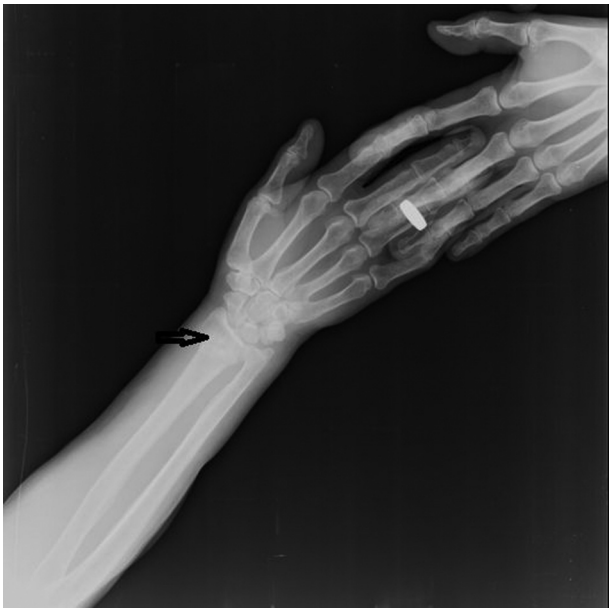

**Figure 1—** Right radius fracture was shown on X-ray (black arrow).

Blood chemistry was significant for a calcium level of 5.8 mg/dL (8.5-10.5 mg/dL) and phosporus level of 2.8 mg/dL (2.5-4.5 mg/dL). Serum albumin level was 3.8 g/dL(3.5-5.2 g/dL). Albumin corrected calcium level was 5.96 mg/dL. Blood urine nitrogen (BUN), creatinine, sodium, potassium and magnesium levels were normal.

An electrocardiogram showed a normal sinus rhythm with a QTc of 405 milliseconds. The patient received intravenous calcium gluconate and was transferred to the endocrinology service. Serum parathyroid hormone (PTH) level was 224 pg/ml (15-65 pg/ml) and serum 25(OH) vitamin D level was 2.5 ng/mL (30-75 ng/mL). Serum alkaline phosphatase (ALP) level was 189 U/L (normal range 60-105 U/L). Serum bone al-

kaline phosphatase level was high (56.6 U/L), above the normal range of 13.0–33.9 U/L. Urinary calcium excretion was low (60 mg/day). Additional workup for malabsorption was negative (negative serology markers for celiac disease and stool negative for fat). We learned from the patient's history that she has been living alone and she had inadequate exposure to sunlight, being housebound for a long time, and had an unbalanced intake of fat-rich foods such as meats, oily fish, and milk. She didn't use any antiepileptic drugs, and she did not have malabsorption due to inflammatory bowel disease, gastric surgery, or biliary disease.

The patient was diagnosed with primary vitamin D deficiency. Vitamin D3 drops 50000 IU/week were given to the patient and she was told to take them for at least 8 weeks; calcium carbonate/vitamin D3 effervescent tablets were also administered. A bone mineral density (BMD) scan was taken and the T-Score from her lumbar vertebra (L2-4) was -2.7 standard deviations (SD), within the range of osteoporosis. Bisphosphonate treatment was postponed because of severe osteomalacia. Serum thyroid stimulating hormone (TSH) level was 6.67 IU/mL (0.4-4.5 IU/mL) , free thyroxine (fT3) and triiodothyronine (fT4) levels were normal, and thought to indicate subclinical hypothyroidism. We administered levothyroxine (LT4) 25 mcg/day to our patient. Her fasting plasma glucose was 200 mg/dl, HBA1C 5.9% and microalbuminuria 76 mg/day. We gave an oral antidiabetic (repaglinide) 0.5 mg/day, angiotensin converting enzyme (ACE) inhibitor (ramipril) 2.5 mg/day, and acetylsalicylic acid (ASA) 100 mg/day. Serum vitamin B12 level was low at 134 mg/dl (220-900 mg/dl) and parenteral vitamin supplementation was given. She was discharged on hospital day 16 with vitamin D3 drops 50000 IU/week, calcium carbonate/vitamin D3 effervescent tablets, ramipril+amlodipin, ASA, LT4 and repaglinide. A diet with increased calcium of at least 2 to 4 servings of dairy per day and daily vitamin D (400 IU) supplementation was recommended. One month after starting vitamin D supplementation, serum 25-hydroxyvitamin D increased to a level of 28 ng/mL and PTH decreased to a level of 119 pg/mL. Serum calcium was measured at 8.5 mg/dL and phosporus at 4.2 mg/dL, within normal ranges. During hospitalization no seizures were observed.

## Discussion

Vitamin D deficiency is common in older individuals. Depending on the country and the definition used, the prevalence of vitamin D deficiency in the older Western population ranges from 0 to 90% (7). Low serum 25-hydroxyvitamin D (25(OH)D) in the elderly is caused by less efficient vitamin D production in the skin, low sunshine exposure and low dietary intake (7, 8). Older individuals often suffer from chronic diseases (9), requiring the frequent use of medication. Previous research, performed in the United States, demonstrated that 23% of women and 19% of men took five or more prescription medicines. In addition, rates of use increased with advancing age (10).

The clinical presentation of osteomalacia in the older population differs from the presentation in younger patients, however more them are asymptomatic. When symptomatic, they tend to present with signs of hypocalcemia such as neuromuscular irritability and, rarely, seizures. Radiographs of the long bones in these patients may not necessarily show radiologic changes of osteomalacia. It is thought that hypocalcemic symptoms secondary to vitamin D deficiency occur largely in patients with rapid growth rates, such as children younger than 1 year and adolescents. In a retrospective review of 65 hospitalized children with vitamin D deficiency in the United Kingdom, Ladhani et al. (11) reported that hypocalcemic symptoms occurred exclusively in children younger than 3 years or older than 10 years. Narchi et al. (12) reported 21 cases of symptomatic rickets in adolescents from Saudi Arabia. Most of their patients presented with carpopedal spasm, limb pain, or weakness. The incidence of seizures in adolescents with vitamin D deficiency is unknown. In the Ladhani et al. series, 16 patients presented with seizures, but it is unclear how many were in the older age group, whereas none of the adolescent patients in the Narchi et al. group had seizures.

Patients with a history of epilepsy seem to be at a higher risk for injuries, including head and dental trauma, lacerations, burns, sprains, and fractures. Surveys and population studies indicate that close to 20% of patients who experience a seizure sustain some kind of injury, and overall, 30% to 35% of patients with seizures have experienced secondary injury as a result of a seizure during their lifetime (13-15).

However, a recent meta-analysis reported that patients with epilepsy are twice as likely to sustain a fracture as patients without epilepsy, which may be a result of 1) increased risk of trauma, 2) decreased bone density caused by the use of antiepileptic drugs, and/or 3) comorbidities (16). Most of the fractures sustained during seizures are caused by direct trauma and typically involve the skull, nasal bones, and clavicles, but in rare instances, fractures can be caused by the muscular tension of the seizure itself. In these cases, the proximal hu-

merus and the shoulder are more commonly affected (17). Radius fractures caused by the muscular tension of a seizure itself seem to be unusual and have not been previously described. To the best of our knowledge, this is the first case of nontraumatic radius fracture in a patient over age 60 resulting from hypocalcemic seizures caused by primary vitamin D deficiency.

Laboratory testing after a first unexplained nonfebrile seizure should be considered, particularly in patients with suggestive clinical findings such as vomiting, diarrhea, or dehydration, failure to return to baseline alertness, or increased muscle tone or fractures such as our patient experienced. The workup should include electrolyte levels, including calcium, magnesium, and phosphorous. Toxicology screening should be considered if there is a question of drug exposure or substance abuse (18). The differential diagnosis of hypocalcemia in adolescence includes vitamin D deficiency, hypoparathyroidism, hypomagnesemia, malabsorption, and renal and hepatic failure, among others (19). Once hypocalcemia is found, additional laboratory investigations such as a basic metabolic panel, liver function tests, and PTH and vitamin D 25-hydroxy and 1,25-dihydroxy levels should be performed. A workup for malabsorption should be undertaken if it is suggested by history or initial laboratory results. The diagnosis of primary vitamin D deficiency is made when low vitamin

D levels along with a compatible history are accompanied by high levels of PTH, in the absence of other metabolic or gastrointestinal abnormalities. Dual-beam radiograph-based photon absorptiometry is the most sensitive routine method of detecting and quantifying

bone loss and may be considered for patients with vitamin D deficiency (20).

Hypocalcemic seizures should be treated with intravenous calcium. In general, calcium gluconate is preferred to calcium chloride because it is less irritating and is less likely to cause tissue necrosis if extravasation occurs. Intravenous therapy with calcium should be continued as long as the patient is symptomatic. Magnesium should be replaced if low levels are identified, and vitamin D replacement in the form of vitamin D3 may be initiated intramuscularly initially, and continued orally as long as the patient does not have malabsorption. Phosphate replacement is usually not necessary for vitamin D deficiency, because low levels are a result of the elevated PTH level, which resolves once adequate calcium and vitamin D are supplied. It is important to monitor serum calcium, phosphate, alkaline phosphatase, PTH, and vitamin D levels and the urinary calcium/creatinine ratio during treatment to assess the response and avoid complications of hypocalcemia or hypercalcemia. Every effort should be made to prevent this disease by encouraging adequate diet, sun exposure, and vitamin D supplementation for patients at risk (21).

In conclusion this case illustrates that emergency medicine physicians should carefully evaluate patients with seizures for secondary injuries, both at presentation and after the patient recovers from the postictal stage. Hypocalcemic seizures resulting from vitamin D deficiency are rare, although the incidence of vitamin D deficiency is increasing. Additional research into primary prevention of primary vitamin D deficiency in this population is warranted.

## Competing Interest

The authors declare that they have no competing interests.

## Contribution of the Authors

Ülkü Yılmaz analyzed and interpreted the endocrinological patient data. Dilek Arpacı was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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