Consultant360 Multidisciplinary Medical Information Network

CASE IN POINT

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Hypocalcemic Seizures in an Adolescent With Autism Spectrum Disorder

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A 14-year-old boy with autism spectrum disorder (ASD) was brought to the emergency department by his grandparents for increased agitation and aggressiveness for 1 week. While being evaluated, the boy developed a generalized tonic-clonic seizure lasting approximately 3 minutes. After initial stabilization, further history was elicited.

History. He had been afebrile and in his normal state of health prior to this presentation. He was on sertraline, 10 mg daily, which he had not taken in 2 weeks. He had no personal or family history of seizures. Review of his diet revealed that he is a very picky eater and that in the 4 months preceding this admission, his diet had consisted exclusively of chips and juice. He was being taken care of by his elderly grandparents because of parental neglect and a history of psychological trauma. Due to these social issues, his psychological well-being was paid more attention than was his nutritional status. He attends a special school and receives speech, occupational, and behavioral therapies.

Physical examination. Examination findings were significant for a nonverbal, noncooperative boy whose weight and height were in the 10th and 5th percentile, respectively. He had bad dentition with multiple cavities.

Diagnostic tests. Laboratory evaluation included a complete blood cell count with differential, electrolyte tests (including calcium and magnesium), a hepatic panel, a prolactin test, a thyrotropin test, and neuroimaging. Most of the findings were negative except for undetectable calcium levels (<5 mg/dL; reference range, 8.2-10.2 mg/dL), low 25-hydroxyvitamin D (5.6 ng/mL; reference range, 30-100 ng/mL), and elevated alkaline phosphatase levels (430 U/L; reference range, 117-390 U/L).

Further investigation to identify the cause of hypocalcemia was done. Serum magnesium and albumin levels were normal. Parathyroid hormone (PTH) levels were elevated (638 pg/mL, reference range, 15-65 pg/mL) along with an elevated phosphorus level (4.9 mg/dL; reference range, 2.7-4.5 mg/dL). The urine calcium to creatinine ratio was normal. Radiographs of the wrist showed no signs of rickets (**Figure 1**).

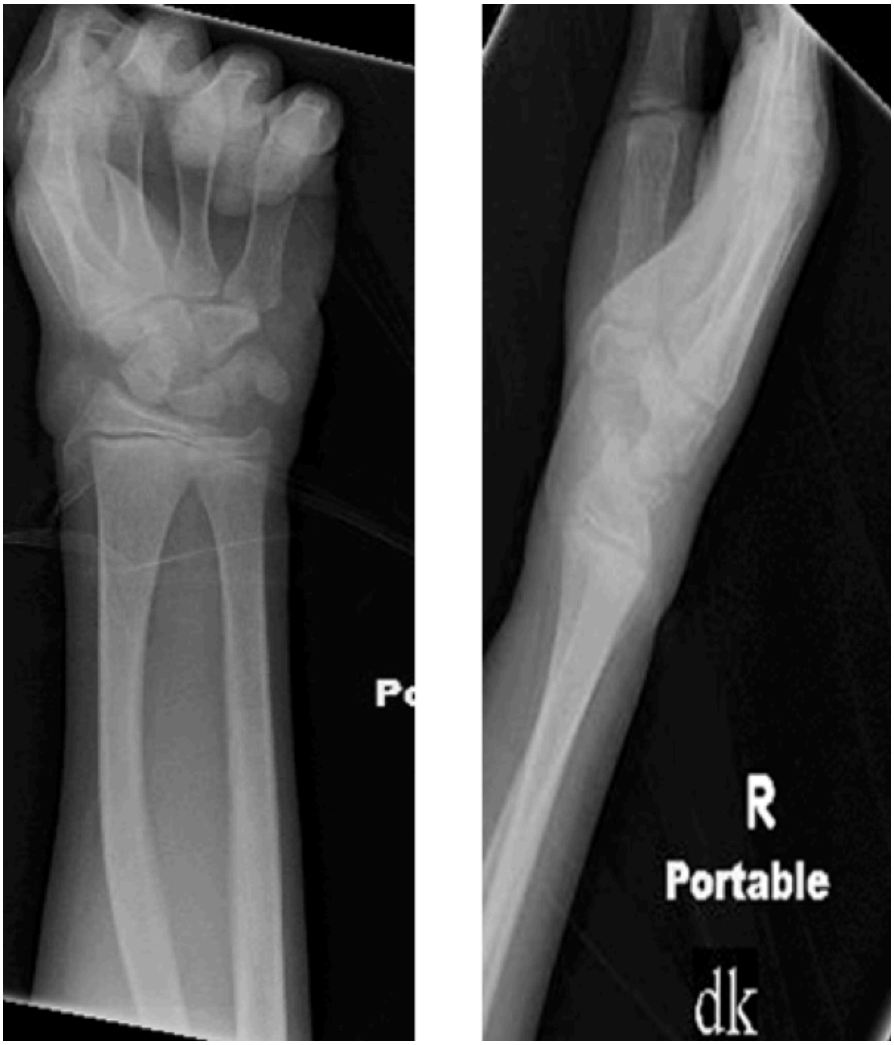

Figure 1. *Anteroposterior and lateral radiographs of the right wrist demonstrated no definitive radiographic evidence of rickets.*

Treatment. The patient was managed in the pediatric intensive care unit. He was given intravenous infusions of calcium gluconate along with vitamin D supplementation. Oral intake of calcium was encouraged. His diet was slowly transitioned to calcium-fortified snacks, juices, PediaSure, and finally a varied diet. Calcium, phosphorus, and PTH levels promptly normalized (**Figure 2**). He remained asymptomatic for the rest of his hospital stay.

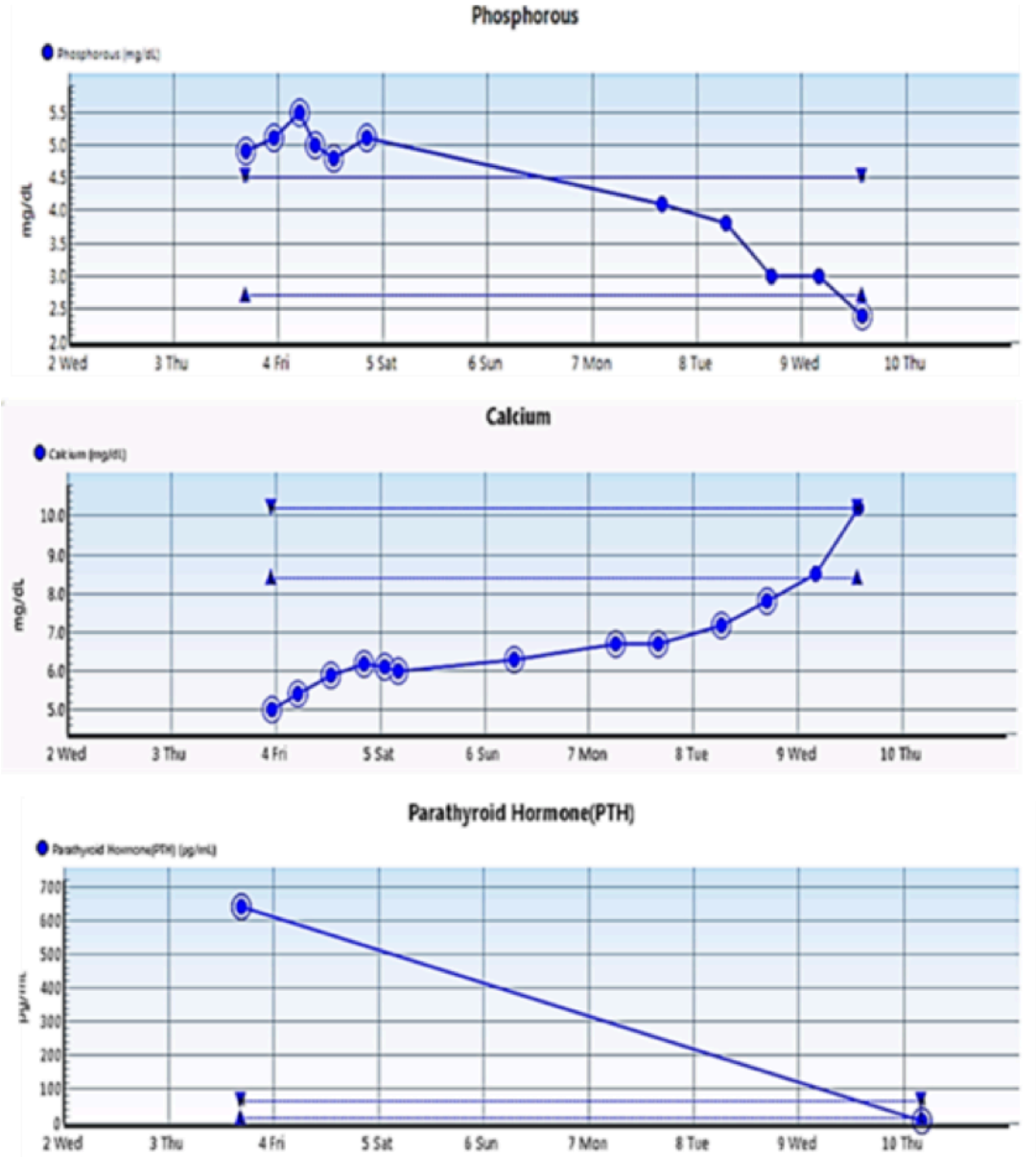

Figure 2. *Progression of laboratory values for phosphorus, calcium, and PTH from admission.*

Diagnosis. The differential diagnosis for hypocalcemia in an adolescent is broad and includes vitamin D disorders, parathyroid disorders, and disorders of the calcium-sensing receptors. In this case, the initial laboratory test results suggested pseudohypoparathyroidism (PHP) in conjunction with 25-hydroxyvitamin D deficiency, but the complete normalization of all laboratory parameters with calcium and 25-hydroxyvitamin D supplementation led to a diagnosis of nutritional deficiency due to his extremely restricted diet.

Outcome of the case. The patient was followed up in the pediatric clinic after 3 months. He had been on a varied diet, and his calcium, vitamin D, and PTH levels were within normal limits.

Discussion. Nutritional rickets is a disorder of defective chondrocyte differentiation and mineralization of the growth plate and defective osteoid mineralization.[1] It is caused in children by vitamin D deficiency and/or low calcium intake. The current recommendations are for children to consume at least 300 to 500 mg of calcium and 400 to 600 units of vitamin D daily.[1]

Severe hypocalcemia and vitamin D deficiency have been reported in several developing countries such as India, Bangladesh, and Nigeria.[2,3] Low socioeconomic status contributes to limited or no access to dairy and fortified foods. Children in these circumstances can present with nutritional rickets (osseous and nonosseous signs), suggesting significant contribution of low dietary calcium intake. Children with rickets respond better to a combination of calcium and vitamin D, or even calcium alone, as opposed to vitamin D supplementation that is more familiar in the Western world. Low calcium intake (<300 mg/d) is associated with the development of rickets irrespective of vitamin D levels.[2,3]

Biochemical changes consistent with PHP (low calcium, high phosphate, and elevated serum PTH) were noted in vitamin D-replete children with very low dietary calcium intake.[4] These abnormalities correct quickly with calcium supplementation, as they did in our patient's case.

Nutritional rickets due to hypocalcemia is very uncommon in the United States. It is usually seen in immigrants from developing countries. However, patients with extremely restricted diets such as our patient can present with a similar picture.

ASD is a neurodevelopmental disorder characterized by persistent deficits in social communication and interaction along with restricted, repetitive patterns of behavior, interests, or activities. Patients with ASD can have food neophobia, a limited food repertoire, rigid diets, and sensory issues that contribute to oral aversions. Because no definitive cure exists for ASD, parents often employ alternatives such as casein-free or gluten-free diets in order to improve behavioral or gastrointestinal tract problems that can exacerbate nutritional deficiencies.

Recently, several studies investigated the nutritional status of children with ASD.[5] No deficiencies in caloric intake were identified, but significant problems were noted with vitamin and micronutrient intake, especially calcium, vitamin D, folate, and vitamin B_{12}. The main source of calcium and vitamin D in the United States is dairy and fortified foods; most of the children with ASD were averse to dairy products.[5]

The prevalence of ASD continues to rise in the United States, with recent estimates as high as 1 in 68 children. It is important for clinicians to screen these nutritionally vulnerable children on a regular basis and intervene when necessary by diversifying the diet or adding fortified foods

or nutritional supplements. However, a recent study concluded that the use of multivitamins in these children might not mitigate the nutritional deficiencies, especially of calcium and vitamin D.[6] Special focus must be paid to these nutrients, since they contribute to bone health, growth and development.[6,7]

While there are no definitive guidelines for nutritional screening or supplementation in children with ASD, it is important to keep in mind that every child with ASD has a unique diet, and that occasionally the diet might be extreme. Such children may benefit from an early referral to a dietitian to plan an appropriate dietary intervention and prevent clinical manifestations of these deficiencies.

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