A case report of tetanic crisis from acute severe hypocalcemia secondary to hypovitaminosis D: analysis of risk factors for vitamin D deficiency between 1 and 18 years

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ABSTRACT

Background: Hypocalcemia is one of the most common disorders of metabolism in children. One of the most known causes is hypovitaminosis D, an extremely widespread condition in the world, both in developed and developing countries.

Etiology is related to poor exposure to sunlight and inadequate diet, especially in subjects with dark skin or exclusively breastfed or born to mothers with vitamin D deficiency by ethnic and cultural reasons.

Case Presentation: We report a case of a teenager from Morocco, who presented a tetanic crisis in the course of influenza B. The laboratory tests showed severe hypocalcemia and low serum vitamin D concentration with increased parathyroid hormone value. The administration of calcium and vitamin D normalized the clinical and laboratory parameters.

Conclusions: Adolescents of ethnic groups at risk frequently find themselves in a chronic situation of altered metabolism deriving from vitamin D deficiency. Hence, a simple insult, as influenza B virus, can lead to severe pathological manifestations.

Keywords: Hypovitaminosis D risk factors, hypocalcemia, influenza B, adolescent, case report.

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Background

Hypocalcemia is one of the most common disorders of phosphorus and calcium metabolism in children. In pediatric age, it is defined as the concentration of total serum calcium below 8.8 mg/dl (calcium ion <2.2 mmol/l) [1].

Various factors regulate calcium homeostasis. The parathyroid glands produce the parathyroid hormone (PTH), which promotes: bone resorption, releasing calcium and phosphorus; in the kidney, calcium reabsorption, phosphorus excretion and renal activation of 1,25-dihydroxy vitamin D. The last mentioned increases the absorption of intestinal calcium. The synthesis of 1,25-dihydroxy vitamin D requires an adequate amount of the vitamin D precursor from diet or UV exposure [2].

The impairment of any of these systems can alter the normal balance of vitamin D, with the risk of causing serious consequences.

Case Presentation

A 13-year-old boy, born in Morocco and transferred to Italy at the age of 6, without a major medical history, came to the emergency department. For the past 2 days, the boy presented with rhinitis, asthenia, nausea, abdominal pain, and low-grade fever and, for about 24 hours, burning pain in both hands, such as to disturb sleep and not responsive to paracetamol or ketoprofen. The physical examination revealed an inflammation of the upper airway, whereas the neurological state did not show any pathological data. In the suspicion of peripheral neuropathy, he was admitted to the pediatric ward. After a few hours, it occurred a rapid deterioration of his conditions, and the pain was getting worse and extending also to the lower limbs and face. At the physical examination, he presented with a muscular spasm of the hands with the fingers in the shape of cones as an "obstetric hand." Blood tests revealed normal blood count, slightly increased C-reactive protein (0.99 mg/dl), mild compensated respiratory acidosis, severe hypocalcemia (serum calcium 5.4 mg/dl and calcium ion 0.56 mmol/l), hyperphosphatasemia (7.8 mg/dl), high levels of alkaline phosphatase (457 U/l), lactic dehydrogenase (LDH, 329 U/l), and creatine phosphokinase (CPK, 700 U/l). The patient began intravenous infusion with 10% calcium gluconate with a progressive increase in speed from 0.5 mg/kg/hour to 2 mg/kg/hour, and the contextual serial controls of calcium ion associated with cardiac activity monitoring by electrocardiogram. The clinical conditions rapidly improved, and the values of serum and calcium ion gradually increased to allow, on the third day of hospitalization, there was a transition to oral supplementation

with calcium carbonate (about 60 mg/kg/day). Laboratory tests for the evaluation of calcium metabolism showed a severe deficiency of 25-hydroxy D-vitamin (4.2 ng/ml) and hyperparathyroidism (PTH 336 pg/ml). Body mass index was 15.1, in the underweight category. The adolescent started oral supplementation with vitamin D (about 3,600 U/day of cholecalciferol). Meantime, the pharyngeal swab was positive for influenza B virus. Bone densitometry (lumbar spine *Z*-score = 0.0 and femoral neck *Z*-score = −1.8) and the upper and lower limbs' X-rays excluded osteopenia and signs of rickets.

Furthermore, the other main secondary causes of hypocalcemia were excluded: malabsorption (celiac and inflammatory bowel diseases), renal and hepatic insufficiency, hypogonadism, hypercalciuria, and hyperphosphaturia.

Treatment with calcium carbonate has been continued for 3 months and therapeutic dose D vitamin D for 6 months with rapid normalization of serum calcium, PTH, CPK and LDH; clinical and laboratory stability even after stopping of therapy.

Discussion

Several factors responsible for the patient's clinical manifestations emerge from the case report. The first is hypocalcemia secondary to vitamin D deficiency. It occurs when one or more factors alter calcium homeostasis. The earliest manifestations are the perioral and extremity paresthesia, but the most typical picture is represented by the tetany. The tetanic crisis is characterized by one or more of the following symptoms: spasms of the musculature of face and limbs, the hand with a "hand-held obstetrician" attitude, laryngeal spasm, convulsive crises, and cardiovascular manifestations. Many patients have an atypical tetanic pattern, especially in the early stages, characterized by asthenia, headache, paresthesia, and abdominal pain [3].

One common cause of hypocalcemia is hypovitaminosis D, an extremely widespread condition in the world, both in developed and developing countries.

In the past, vitamin D deficiency had almost disappeared in industrialized countries through exposure to sunlight or supplements to prevent rickets. In recent years, secondary to immigration route, we are assisting to the recurrence of this disease, particularly in children from Africa and the Middle East. The inadequate diet is the main cause; especially, in subjects with dark skin or exclusively breastfed or born to mothers who for ethnic and/or cultural reasons (clothes that cover entirely the body) are also deficient. Other important etiological factors are poor exposure to sunlight and widespread use of sunscreen [4].

The most involved age is childhood. Symptomatic hypocalcemia consequent to hypovitaminosis D occurs more rarely in adolescence or adulthood; for this reason, the cases of adolescents described in the literature are absolutely rare.

The only similar case was published in 2012 by Martínez et al. [5]. A 13-year-old adolescent of Pakistan origin had absolutely similar symptoms and laboratory tests that normalized after the administration of calcium and vitamin D as well as with dietetic corrections.

In adolescence, the pubertal spurt occurs (maximum growth acceleration) and inevitably requires a greater need for calcium to satisfy the increased metabolic demand. A study carried out in collaboration between three London hospitals (Newham General Hospital, Royal London, and King's College Hospital) demonstrates that hypocalcemia can appear before the rickets changes in the age of rapid growth (childhood and adolescence) and that vitamin D administration alone leads to healing [6].

The last consideration regards the infection in course, influenza B, which, in the described case, could have represented the trigger and altered the weak balance of calcium metabolic homeostasis. Influenza B virus produces an inflammation that causes tissue damage (muscle, kidneys, and liver) [7]. Muscle damage increases the release of phosphorus and CPK in blood. Consequently, hyperphosphatemia causes the deposition of calcium phosphate in destroyed muscle cells and other tissues. For this reason, hypocalcemia and hyperphosphatemia occur in the initial stages of damage. In this case, the initial rhabdomyolysis by influenza B virus has exasperated hypocalcemia [8,9].

Thus, in short, the risk factors for hypovitaminosis D between 1 and 18 years of age are represented by: non-Caucasian ethnicity with dark skin pigmentation, reduced sunlight exposure and/or constant use of sunscreens, international adoption, obesity, inadequate diets, chronic kidney disease, hepatic failure and/or cholestasis, malabsorption syndromes, chronic therapies, anticonvulsants, systemic glucocorticoids, antiretroviral therapy, and systemic antifungals.

The prevention can be carried out through
vitamin D supplementation in adolescents and the risk categories, apart from the other pediatric age classes. The recommended vitamin D supplementation is performed with vitamin D metabolites. The dose varies from 600 IU/day up to 1,000 IU/day. It increases at least 2–3 times in individuals with chronic therapies [10,11].

Conclusions

This is the second case report of an adolescent with a manifestation of hypocalcemia, secondary to hypovitaminosis D. The rarity of the presented case consists of the simultaneous presence of multiple triggers, which have shown the underlying hypocalcemia, making evident the weak balance in individuals at risk for vitamin D deficiency. Thus, a simple insult, such as influenza B, can lead to severe pathological manifestations that can be avoided administering vitamin D supplementation in prevention.

The hypocalcemia finding in subjects at risk must always be attributed to vitamin D deficiency in the first

hypothesis, possibly confirmed by the exclusion of other secondary causes.

What is new?

This is the second case report, reported in the literature, of an adolescent with a manifestation of hypocalcemia, secondary to hypovitaminosis D. The rarity of the case consists of the simultaneous presence of multiple triggers, which have shown the underlying hypocalcemia, making evident the weak balance in individuals at risk for vitamin D deficiency. Hence, the authors show the relevance of the vitamin D supplementation in adolescents and subjects at risk.

List of Abbreviations

CPK Creatine phosphokinase
LDH Lactic dehydrogenase
PTH Parathyroid hormone

Consent for publication

Informed consent was obtained from the patient's parents included in this study.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	A 13-year-old male
2	**Final diagnosis**	Tetanic crisis from acute severe hypocalcemia due to hypovitaminosis D triggered by influenza B virus
3	**Symptoms**	Mild respiratory symptoms, paresthesia, muscular spasm of the hands
4	**Medications**	Intravenous infusion with 10% calcium gluconate; oral supplementation with calcium carbonate and Vitamin D
5	**Clinical procedure**	Clinical examination, laboratory tests, bone densitometry, upper and lower limbs X-rays
6	**Specialty**	Pediatrics