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Case Report

Persistent hypocalcemia: an interesting maze!!

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ABSTRACT

A 2 months old child was brought with c/o arching of back and fisting present since day 15 of life, which was increased during feeding and h/o not gaining weight since birth. They were evaluated at a local doctor where the child was started on calcium syrup and the child is taking the medications for 1 month. Despite the treatment, the child was still having the similar complaints. Now the child has been brought to the hospital with multiple episodes of breath-holding spells, convulsions, and not feeding well, with significant weight loss and lethargic. After clinical evaluation, various laboratory investigations were carried out which led us to even better diagnosis. The blood calcium levels were found to be persistently low. We did multiple investigations, keeping the physiology of calcium and vitamin D metabolism in mind and arrived at a conclusion.

Keywords: Hypocalcemia, Hypoparathyroidism, Convulsions

INTRODUCTION

Most body calcium is stored in the bone and is in constant equilibrium with serum calcium. Parathyroid hormone (PTH), vitamin D and calcitonin are the key regulators of calcium metabolism.

Sunlight is the major source of vitamin D. Increased PTH levels stimulate the osteoclastic activity of the bone and helps restore blood calcium levels to normal. PTH leads to concomitant loss of phosphate from the kidney leading to low serum phosphate levels. Hypocalcemia (total calcium <8 mg/dl) important metabolic disorder. Ionic calcium levels also have to be low.[2]

Rickets is a disease of growing bones. Vitamin D deficiency leads to hypocalcemia which stimulates the parathyroid gland to secrete parathormone.[1] Increased PTH levels stimulate the osteoclastic activity of the bone and helps restore blood calcium levels to normal.[5] Rickets that does not respond to treatment of nutritional rickets is called refractory rickets. Reduced levels of serum calcium, normal to low phosphate and elevated alkaline phosphatase are characteristics. Blood levels of $25(OH)D_3$ are normal and $1,25(OH)_2D_3$ is decreased despite hypocalcemia.[2]

Vitamin D-dependent rickets type-1 (VDDR1) is an autosomal recessive disorder characterised by onset of rickets by 2 years of age, accompanied by poor growth and hypotonia, muscle weakness, seizures, hypocalcaemia with secondary hyperparathyroidism, hypophosphataemia and normal plasma 25-hydroxyvitamin D ($25(OH_2)D$) concentration that distinguishes VDDR1 from vitamin D deficient rickets.[12] VDDR1 is caused by loss-of-function mutations of the 25-hydroxyvitamin D 1-alpha-hydroxylase gene, also referred to as cytochrome P450 family 27 subfamily-B member-1 *(*CYP27B1), and this explains the occurrence of low plasma $1,25(OH_2)D$ concentrations, despite the normal 25(OH)D and elevated PTH concentrations.[13]

CASE REPORT

A 2 months old male child, born of a consanguineous marriage, full term section, 2.5 kg birth weight, cried immediately after birth, with no h/o neonatal intensive care unit (NICU) admission and normal will 15 days of life, however, there was no weight gain present even after 10 days of life and on day 15 the weight of the baby was 1.9 kg. After 15 days of life, the mother noticed that the child had posturing and clonic movement of the hand which increased during feeding, followed by bluish discolouration of the skin which lasted for 5–7 mins. The child was referred for similar complaints and the local doctor started the child on calcium medications, the symptoms did not reduce and the child used to have such episodes which increased during feeding. After admission, the child had history of eye fluttering movement, lip smacking behaviour, which increased during feeding and was followed by cyanosis for 1-2 mins (d/t laryngospasm).

Investigations were done and the child was found to have persistent hypocalcemia, serum calcium was persistently low since birth. Ionic calcium also was persistently low. Despite giving IV calcium in the fluids, we witnessed the eye fluttering and lip-smacking episodes present when the child was feeding followed by fall in saturation with tachycardia (subtle seizure). So basically, the IV calcium therapy wasn't working out and we were forced to think about something else. If it were a basic case of hypocalcemic seizures, the child would have been absolutely normal post the correction of the calcium levels, just as a case of late onset hypocalcemia would act. Due to the persistent episodes of seizures, child was kept nil by mouth. Increasing distress was present and the child was put on oxygen for the same.

Prior to this admission, detailed history helped us find out that the child is taking syrup calcium since 1 month. Other two siblings are normal and no h/o seizure disorder in the family. Developmentally, the child has no startle response, no fixation or following movements

Child was given top feed along with expressed breast milk since birth. Weight of the child currently is the birth weight; it is below third percentile. And microcephaly is present. Sutural ridging was present.

On central nervous system (CNS) examination, hypotonia was present in all the limbs with normal reflexes and extensor plantar. Superficial reflexes were normal. On further evaluation, we found blood calcium levels low, along with high phosphorus levels, liver function test (LFT) normal, urinary calcium was high with urine calcium: creatinine ratio high, vitamin D2 levels were normal, Parathormone levels were borderline low. Thyroid function tests: normal. We wanted further evaluation of the cause of the hypocalcemia despite medical management so the further investigations were carried out.

Computed tomography (CT) brain showed frontal and parietal lobe calcification.

Ultrasonography (USG) abdomen showed nephrocalcinosis. Magnetic resonance imaging (MRI) brain was normal.

Electroencephelography (EEG) showed complicated epileptiform wave pattern.

Chest X-ray was normal. USG neck shows normal thyroid gland and no parathyroid seen on USG neck.

2D ECHO was done to rule out cardiac abnormalities (suspected Di-George syndrome).

Maternal parathyroid and calcium levels were done which was normal (rule out transient cause).

So, we took a trial of tablet rocaltrol (calcitriol: active form of vitamin D) and we gave it for a week followed by repeat blood levels of calcium which showed increase in the serum calcium levels.

Repeated follow-up after 15 days also showed increased in the serum and ionic calcium levels. After ruling out the multiple diagnosis, we came to a diagnosis of vitamin D Dependent type 1 rickets.

Figure 1: Focal movement during the episode.

DISCUSSION

In the article discussed, it has been jotted down how to proceed with such a case, although not all cases are going to be the same.[3] But the eyes-only searches what the mind knows, so it is a better option to get to the end of the maze and evaluate the case which comes up with the most common finding of hypocalcemia.[6]

Severe hypocalcemia in the clinical setting is most commonly seen in the post thyroidectomy patient because

of transient/permanent hypoparathyroidism because of intraoperative injury.[11]

Sometimes it is seen as part of an autoimmune polyendocrine syndrome.[12] Rarely is it seen as a part of PTH receptor resistance.

Rickets affects an estimated 1 in 200,000 children. The condition is most often caused by a lack of vitamin D in the diet or insufficient sun exposure rather than genetic mutations. Genetic forms of rickets, including vitamin D-dependent rickets, are much less common. Rickets is a disease of growing bones. Vitamin D deficiency leads to hypocalcemia which stimulates the Parathyroid gland to secrete parathormone.[1] Increased PTH levels stimulate the osteoclastic activity of the bone and helps restore blood calcium levels to normal.[3] Rickets that does not respond to treatment of nutritional rickets is called refractory rickets.[5]

When this baby came with refractory seizures, and a low calcium, despite of treating hypocalcemia medically, the calcium levels did not pick up.

The various differentials that we tried to evaluate based on the clinical findings: hypoparathyroidism, pseudo-hypoparathyroidism, and vitamin D dependent rickets type 1.

CONCLUSION

Based on the above case, after evaluation thoroughly we came to a conclusion that not all vitamin D deficiency can present as a direct untwisted presentation. And not all the low calcium can be attributed to correcting calcium levels.

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