

## Hypocalcemic tetany unveiling Vitamin B12 deficiency: A rare manifestation coupled with hyperventilation

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### ABSTRACT

Hypocalcemic tetany is a clinical condition characterized by involuntary muscle contractions and spasms due to low levels of ionized calcium in the blood, commonly associated with conditions such as hypoparathyroidism, Vitamin D deficiency, and chronic kidney disease. We report the case of a 16-year-old vegetarian girl who presented with recurrent episodes of tetany, muscle cramps, and fainting. Initial management with calcium supplementation and anxiolytics provided partial relief. But as tetany was recurrent, respiratory alkalosis was found to be the contributing factor. Anxiety-induced hyperventilation leads to respiratory alkalosis. Despite correction of alkalosis, tetany persisted, and the patient developed gait abnormality. Anxiety and gait abnormality were both found to be due to Vitamin B12 deficiency. Parenteral Vitamin B12 supplementation resulted in complete recovery from tetany, gait disturbance, and anxiety. Hence, this is a rare manifestation of Vitamin B12 deficiency, pertaining to anxiety-induced hyperventilation, leading to respiratory alkalosis and presenting clinically as recurrent tetany. Treatment only by parenteral calcium was not enough, and unmasking the hidden etiology of Vitamin B12 deficiency was key to recovery.

**Key words:** Anxiety, Hyperventilation, Hypocalcemic tetany, Vitamin B12 deficiency

Hypocalcemic tetany is a clinical condition characterized by involuntary muscle contractions and spasms due to low levels of ionized calcium in the blood. It is commonly associated with conditions such as hypoparathyroidism, Vitamin D deficiency, and chronic kidney disease [1]. However, its association with Vitamin B12 deficiency is rare and not well-documented. Vitamin B12, an essential nutrient predominantly found in animal products, plays a crucial role in neurological function and red blood cell formation. Deficiency in Vitamin B12 can lead to a range of neuropsychiatric manifestations, including neuropathy, cognitive disturbances, and psychiatric symptoms [2].

We report a case with persistent tetany, highlighting the complex interplay of Vitamin B12 deficiency, hypocalcemia, anxiety, and hyperventilation without disclosing the identity of the case.

### CASE REPORT


A 16-year-old girl presented in the Emergency Department at Moti Lal Nehru Medical College, Prayagraj, with complaints of facial twitching, abnormal posturing of hands and feet, along with severe generalized muscle

cramps, and pain for 4 h. She had a history of falls and fainting 5 days back in school during ongoing school examinations, for which she received anxiolytics, leading to partial relief.

On examination, pulse rate was 90, blood pressure was 112/78 mmHg, and respiratory rate was 22. Classical tetanic spasm was observed in both her upper and lower extremities. Typical carpopedal spasm was noted, and the trousseau sign was positive.

Urgent serum electrolyte was ordered, and an electrocardiogram (ECG) was done, which showed prolongation of the QT interval  $QTc=QTx.04\text{ s}/\sqrt{R-Rx.04}=11x.04/\sqrt{17x.04}=11x.04/4.12x.2=0.53\text{ s}$ .

Intravenous calcium gluconate was given to relieve tetany. Hypocalcemia was documented with total serum calcium of 8.7 mg/dL and low serum ionized calcium of 1.02 mmol/L. Detailed investigation showed low serum parathyroid hormone (PTH) <4.6. All other investigations, including hemogram, liver function test, kidney function test, serum phosphate, and serum Na/K were normal. Tetanic spasm again reappeared after 4 h, so she was given a repeat dose of IV calcium gluconate. However, recurrent episodes of tetanic spasm continued even after repeated boluses of IV calcium gluconate, so calcium gluconate was started as a continuous infusion. Despite continuous infusion, the patient developed recurrent tetanic spasm.

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For evaluation of the cause of persistently symptomatic hypocalcemia, arterial blood gas (ABG) analysis was done, which showed: pH-7.52, pCo<sub>2</sub>-14.1 mmHg, HCO<sub>3</sub><sup>-</sup>-17.7 meq/L, suggesting primary respiratory alkalosis with compensated metabolic acidosis (Table 1).

The patient was kept on a rebreathing mask for the correction of respiratory alkalosis, which corrected the alkalosis, and no further episode of tetany occurred. The patient was advised to use closed mask ventilation, especially at the time of hyperventilation or anxiety. Oral calcium carbonate and Vitamin D<sub>3</sub> were prescribed along with a mild anxiolytic, and the patient was discharged.

Though tetany improved, the patient noticed difficulty in walking, had muscle cramps, weakness, scary dreams, excessive sweating, and cold extremities. She could not walk without support. Neurological evaluation was completely normal (normal muscle power in all 4 limbs, no sensory deficit, bilateral normal flexor plantar response, all deep tendon reflexes were normal with intact cerebellar function) except for a gait imbalance.

Magnetic resonance imaging brain with seizure protocol was also normal. Her serum total creatine

phosphokinase, Thyroid function test, nerve conduction velocity of all 4 limbs, and visual evoked potential also came normal. For evaluating the cause of anxiety and gait disturbance, serum Vitamin B12 level was also measured, and it was found to be low (146 pg/mL). Serum homocysteine was normal.

She was started on Injectable Vitamin B12 (1000 mcg/day) for 7 days, followed by weekly injections. Along with Vitamin B12, she was continued on calcium and Vitamin D supplementation. On follow-up, serum calcium and serum PTH were normalized. Difficulty in walking improved gradually over a period of 2 months. No further episode of tetany and anxiety noted in follow-up.

## DISCUSSION

Our case presented with hypocalcemic tetany as evidenced clinically with a history of fainting and one episode of fall, facial twitching, abnormal posturing of hands and feet, along with severe generalized muscle cramps and pain, and gait disturbance.

Hypocalcemic clinical features of neuromuscular irritability are paresthesia (usually of fingers, toes, and circumoral regions), tetany, carpopedal spasm, muscle cramps, Chvostek's sign, Trousseau's sign, seizures of all types (i.e., focal or petit mal, grand mal, or syncope), prolonged QT interval on ECG, laryngospasm, and bronchospasm [3]. This case of persistent tetany shows us an interesting interplay of Vitamin B12 deficiency precipitating anxiety-induced hyperventilation leading to respiratory alkalosis, which resulted in ionized hypocalcemia. Hence, here, Vitamin B12 deficiency manifested clinically as hypocalcemic tetany and later gait disturbance.

In this case, a comprehensive search for the cause of hypocalcemia was done, and except for low PTH levels, all other tests, including serum phosphorus and magnesium, were normal. ABG was suggestive of respiratory alkalosis. The most common cause of respiratory alkalosis is alveolar hyperventilation and not underproduction of CO<sub>2</sub> [4]. Hyperventilation is often associated with dyspnea, but not all patients who hyperventilate are dyspneic. Conversely, patients with dyspnea need not be hyperventilating [5]. Anxiety is the most common cause of hyperventilation and respiratory alkalosis [6]. Hence, a diagnosis of "severe anxiety-inducing hyperventilation with subsequent respiratory alkalosis leading to hypocalcemia" was made.

Other causes of hyperventilation and consequent respiratory alkalosis include pain, hypoxia, fever, and aspirin overdose. Usually, hypocalcemia due to respiratory alkalosis has either normal total serum calcium or lower limit of normal calcium levels, but the effective ionized calcium becomes low depending on blood pH. Protein-bound calcium fraction increases as serum pH increases, thus resulting in decreased ionized calcium in spite of normal total calcium. Ionized calcium should be

**Table 1: List of investigation of the patient**

Tests	Patient's value	Normal range
Serum calcium	8.7 g/dL	9–11 mg/dL
Serum ionized calcium	1.02 mol/L	1.13–1.32
Serum phosphorus (%)	3.04 g	3–4.5 g
Serum alkaline phosphatase	56.9 IU/L	350–500 IU/L
Serum PTH	<4.6 pg/mL	14–72 pg/mL
Serum Vitamin D 25 OH	34.3 ng/mL	30–100 ng/mL
Serum magnesium	1.8 mg/dL	1.6–2.5 mg/dL
Serum TSH	2.68 µIU/mL	7–6.4 µIU/ml
Fasting plasma glucose	92 mg/dL	<110 mg/dL
ABG	pH=7.52, pCo <sub>2</sub> =14.1 mmHg, HCO <sub>3</sub> <sup>-</sup> =17.7 meq/L	
Serum Na <sup>+</sup>	136.0 meq/L	135–145 meq/L
Serum K <sup>+</sup>	4.18 meq/L	3.5–5.0 meq/L
Serum Vitamin B12	146 pg/mL	187–883 pg/mL
Serum homocysteine	3.4 µmol/L	3–18 µmol/L
Serum folic acid	20 ng/mL	>5.38 ng/mL
ECG	QTc=0.53 s (prolong)* *QTc=QTx. 04/√R-Rx. 04 s	
MRI brain	Normal	
NCV all 4 limbs	Normal	
VEP	Normal	

PTH: Parathyroid hormone, ABG: Arterial blood gas, ECG: Electrocardiogram, MRI: Magnetic resonance imaging, NCV: Nerve conduction velocity, VEP: Visual evoked potential

unmasked whenever true hypocalcemia is suspected. Out of the total serum calcium, half is ionized calcium that is physiologically active. Even an abnormal serum albumin level must be taken into account for the estimation of effective ionized calcium. In our case, serum albumin was normal, so correction was not needed [7].

As the patient is a vegetarian, had anxiety leading to hyperventilation as the precipitating factor, and later developed gait disturbances, S. Vitamin B12 was also done [8,9], which came extremely low. It has been seen that Vitamin B12 deficiency has varied neuropsychiatric manifestations, including ataxia. As per one recent study of Singh *et al.* in 2022, from BHU, anxiety (83.6%) was the second most common neuropsychiatric manifestation after headache in Vitamin B12-deficient patients [10]. Anxiety disorder was also seen as the prominent neuropsychiatric manifestation related to Vitamin B12 deficiency in a very recent study in North India [11]. Thus, vitamin B12 deficiency is still an underrated entity in spite of its multitude of varied clinical profiles.

Previously, medical literature has shown hypocalcemic tetany in an anxious 24-year-old woman, who required an urgent cesarean delivery [12]. A case has been reported in a previously healthy 51-year-old female without any psychogenic conditions. During spinal anesthesia for lower extremity surgery, the patient landed up in hyperventilation syndrome and developed hypocalcemic symptoms of nausea, headache, paresthesia in the upper extremities, and perioral numbness with carpal spasm in both hands [13].

Our case responded only partially to i/v calcium gluconate, respiratory alkalosis improved with rebreathing mask ventilation, but anxiety was persistent along with the gait disturbance, which recovered fully only after parenteral Vitamin B12 supplementation.

## CONCLUSION

This case highlights an unusual presentation of hypocalcemic tetany secondary to Vitamin B12 deficiency, complicated by hyperventilation-induced respiratory alkalosis in a young vegetarian girl. Despite initial symptomatic treatment for anxiety and calcium supplementation, the persistent and recurrent tetany necessitated a comprehensive evaluation that revealed respiratory alkalosis as a contributing factor. The case underscores the importance of considering Vitamin B12

deficiency in patients presenting with neuropsychiatric manifestations and unexplained hypocalcemia, especially in strict vegetarians. Vitamin B12 deficiency needs to be identified and treated.

## AUTHORS' CONTRIBUTION

A.K.C. and P.G. evaluated, diagnosed, and treated the case. A.K.C and P.G. wrote the manuscript, A.K.C. made table and all reviewed the manuscript.

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