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CASE REPORT

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Pseudotumor cerebri with status epilepticus in a child: A rare presentation of vitamin D deficiency

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Key Clinical Message

Pseudotumor cerebri (PTC) encompasses a constellation of symptoms caused by elevated intracranial pressure of unclear etiology. Various associations have been described, rarely hypovitaminosis D. Vitamin D deficiency should be considered as a potential etiology of neurological manifestations like PTC and seizures in children. Early diagnosis and correction of vitamin D deficiency is key to preventing morbidity and achieving good outcomes.

KEYWORDS

case report, elevated intracranial pressure, pseudotumor cerebri, status epilepticus, vitamin D deficiency

1 | INTRODUCTION

Vitamin D deficiency is an important and growing public health problem and has a wide range of clinical manifestations.[1] Vitamin D deficiency is defined by serum levels of 25-dihydroxyvitamin D ($25[OH]_2$ Vitamin D) of <20 ng/mL.[2] Pseudotumor cerebri (PTC) syndrome encompasses a constellation of symptoms caused by elevated intracranial pressure of unclear etiology with normal brain parenchyma and cerebrospinal fluid (CSF) constituents.[3] PTC syndrome is classified as primary, when no underlying cause is identified, and it includes Idiopathic Intracranial Hypertension (IIH). Secondary PTC syndrome is associated with various conditions like cerebral venous thrombosis, medical conditions, and medications.[4] Vitamin deficiencies like hypovitaminosis A have been described with this condition and rarely, hypovitaminosis D.[5] Status epilepticus is a life-threatening condition with a mortality rate of around 3%. In the pediatric group, infections and febrile illnesses contribute to the majority of its causes. Status epilepticus secondary to hypocalcemia due to vitamin D deficiency is a rare presentation and is sparsely reported in the literature.[6] The presence of both PTC syndrome and status epilepticus is an exceedingly rare presentation of this common nutritional deficiency and we aim to describe it with this case report. This case report is written in line with the CARE guidelines.[7]

2 | CASE HISTORY/EXAMINATION

An 11-year-old neurodevelopmentally normal boy was brought to the emergency department following two episodes of seizure-like symptoms, a few hours prior to the presentation. Both the episodes were described as stiffening and jerky movement of bilateral upper & lower limbs with loss of consciousness, up-rolling of eyes, frothing from mouth, and fisting with urinary incontinence. Each episode, according to a bystander, was

about 2 min with regaining consciousness. According to his father, the child was also having a runny nose with a non-productive cough for 5 days with fever during the first 2 days which resolved with antipyretics. The child is also a known case of tetralogy of fallot diagnosed at 18 months of age and underwent intracardiac repair at the age of 19 months. No history of altered sensorium, headache, blurring of vision, trauma, loose stool, skin rashes, or burning micturition, no history of seizure disorder in the past or in the family. He was born of a non-consanguineous marriage and his birth and developmental history were normal. During assessment at the emergency department, the boy sustained an episode of a generalized tonic–clonic seizure. The patient was managed by securing his airway and administering Midazolam IV stat and oxygen via facemask. However, the seizure reappeared after 10 min with no gain of consciousness. He was managed in the line of status epilepticus with Phenytoin loading dose IV over 30 min. The child gained consciousness after 30–45 min and was shifted to the pediatric ICU. The patient had postictal drowsiness of around 1 and half an hour and also developed irritability. On arriving at PICU his GCS was 15/15, bilateral pupils were equal and reactive to light with no signs of meningeal irritation. Vitals: T 99.5°F, RR 32/min, BP 94/50 P 100/min SpO2 96%. His height and weight were −1SD for age and BMI was −3SD for age. Neurological and other systemic examinations were unremarkable apart from a pan systolic murmur on auscultation. Chvostek and Trousseau's signs were negative.

3 | METHODS

3.1 | Differential diagnosis

Differential diagnosis of meningitis, seizure secondary to metabolic derangement, intracranial space occupying lesion and IIH was made.

3.2 | Investigations

Initial blood workup revealed a normal complete hemogram including total and differential leucocyte counts, normal renal and liver function tests, corrected Calcium: 6.08 mg/dL, Phosphorus: 7.14 mg/dL, Magnesium 2.17 mg/dL (Table 1). Arterial blood gas analysis was normal. Fundoscopic examination revealed bilateral Grade

TABLE 1 Laboratory investigations.

Investigations	Results	Reference Range [8]
Total leukocyte count	3300/mL	4000–10,500/mL
Differential leukocyte count	N60, L35	N 54%–62%, L 25%–33%
Platelets	160,000/mL	150,000–400,000/mL
Sodium	139 mmol/L	135–145 mmol/L
Potassium	3.6 mmol/L	3.3–4.6 mmol/L
Urea	18 mg/dL	5–18 mg/dL
Creatinine	0.7 mg/dL	0.31–0.88 mg/dL
Total bilirubin	0.2 mg/dL	<1.0 mg/dL
Direct bilirubin	0.07 mg/dL	<0.3 mg/dL
Aspartate aminotransferase	46.1 U/L	10–40 U/L
Alanine aminotransferase	48.9 U/L	5–45 U/L
Alkaline phosphatase	178 U/L	140–560 U/L
Total cholesterol	235 mg/dL	<170 mg/dL
HDL	59.7 mg/dL	>45 mg/dL
LDL	123.9 mg/dL	<110 mg/dL
Triglyceride	244.7 mg/dL	<150 mg/dL
Serum Ca	6.08 mg/dL	8.4–10.2 mg/dL
Serum Mg	2.17 mg/dL	1.5–2.5 mg/dL
Serum phosphorus	7.14 mg/dL	3.7–5.6 mg/dL
Serum albumin	4.65 g/dL	3.5–5.6 g/dL
Vitamin D ($25[OH]_2$ vitamin D)	12 ng/mL	20–60 ng/mL
PTH	252 pg/mL	51–217 pg/mL

III papilledema. A contrast CT scan of the head was taken which showed no evidence of space-occupying intracranial lesion, mass effect, hemorrhage, or infarction. A lumbar puncture was performed which showed opening pressure of 30 cm H_2O. CSF parameters (Table 2) showed no evidence of infection.

An MRI of the brain was also taken and was unremarkable. Intravenous calcium gluconate was administered for hypocalcemia. Further evaluation revealed Vitamin D ($25[OH]_2$ vitamin D) levels at 12 ng/mL and parathyroid hormone (PTH) levels at 252 pg/mL. A diagnosis of PTC with status epilepticus secondary to vitamin D deficiency was made.

3.3 | Treatment

The patient was treated with antiepileptics, acetazolamide, calcium, and vitamin D supplementation. Daily serum calcium levels were studied which normalized on the 5th day of admission. The child remained seizure free throughout his hospital stay. He was discharged on antiepileptics, acetazolamide, calcium, and vitamin D supplements.

4 | OUTCOME AND FOLLOW-UP

At 2 months follow-up, he was symptom-free and doing well. The serum levels of calcium, PTH, phosphorus and vitamin D were normal. Fundus examination showed bilateral Grade I papilledema, signifying improvement in comparison to the findings at admission.

5 | CONCLUSION

Vitamin D deficiency should be considered as a potential etiology of neurological manifestations like PTC and seizures in children. Early diagnosis and correction of vitamin D deficiency is key to preventing morbidity and achieving favorable outcomes. Appropriate screening and timely treatment of vitamin D deficiency, especially in developing countries, can prevent deadlier complications resulting from the common and undermined nutritional deficiency. Further research is needed to elucidate the exact mechanism of vitamin D deficiency-induced PTC and its association with status epilepticus.

6 | DISCUSSION

Vitamin D, a fat-soluble vitamin, not only functions to maintain calcium homeostasis in the body but has now been established to play other important roles such as regulating cell proliferation, the functioning of adaptive and innate immune system, regulation of blood pressure, and normal neuromuscular function.[9]

Vitamin D deficiency has been acknowledged to have a global extent in recent review papers with the highest prevalence in Asia, Middle East, and Africa with lower average levels in women and girls than male counterparts. Nutritional rickets which can also be used to evaluate the burden of Vitamin D deficiency is also higher in these regions with a prevalence of 1%–24% in children. This has also recently re-emerged in the high-income countries with prevalence figures ranging from 3 to 120 per 100,000 children.[10]

Although the active form of vitamin D is 1,25 dihydroxy vitamin D, blood level of 25 hydroxy vitamin D ($25\text{-}(OH_2)D$) is considered the best indicator of vitamin D sufficiency. [a] It has a long half-life in the body, is relatively stable and responsive to recent endogenous vitamin D production and exogenous intake. Vitamin D deficiency is now defined as circulating $25[OH]_2$ Vitamin D levels of 20 ng/mL or less.[2]

In a systematic review and meta-analysis study on high burden of hypovitaminosis D among the children and adolescents in South Asia, it was found that the overall pooled prevalence of hypovitaminosis D in the study groups was 61% with a burden of 35% and a weighted mean vitamin D level of 25.96 ng/mL among studies conducted in Nepal. The study inferred that the prevalence of hypovitaminosis was 85% in neonates, 55% in the age group 1 month to 5 years, and 57% in the age group 6–18 years.[11] In another study on vitamin D deficiency in South-East Asia region children, the prevalence of vitamin D deficiency ranged from 0.9% to 96.4% with female sex and urban living being the most common determinants.[12]

Vitamin D deficiency can present as rickets in infants and children and osteomalacia in all age groups to tetany and seizures associated with hypocalcemia. One of the rarer manifestations of its deficiency is a syndrome known as PTC which refers to a spectrum of clinical features of raised intracranial pressure without focal neurological deficit.[13] An elevated CSF pressure in lumbar puncture, with normal CSF study, points by exclusion to the diagnosis of PTC.[2]

Primary PTC is also known as IIH whereas secondary PTC can be ascribed to numerous causes such as cerebral venous abnormalities, medications, hypervitaminosis A, vitamin D deficiency, some endocrine and genetic comorbidities. The annual incidence of PTC in the general population is variable with an average of approx. 0.5–2 per 100,000 and is in a rising trend.[14–16] It affects women unjustifiably more than men, and with elevated BMI. In children, however, both genders are equally affected.[14,16]

TABLE 2 CSF parameters.

Parameters	Observed values	Reference range
Opening pressure	30 cm H_2O	<28 cm H_2O
Protein	29.2 mg/dL	20–45 mg/dL
Glucose	51.2 mg/dL	>50 mg/dL
Acid fast bacilli	Negative	
Gram stain	Negative	
C/S	No growth	
WBC	No cells	

TABLE 3 Revised diagnostic criteria for pseudotumor cerebri [4].

Diagnostic criteria for pseudotumor cerebri syndrome
1. Required diagnosis of pseudotumor cerebri syndrome[a]
a. Papilledema
b. Normal neurologic examination except for cranial nerve abnormalities
c. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (female and obese), and MRI, with and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used
d. Normal CSF composition
e. Elevated lumbar puncture opening pressure (≥250 mm CSF in adults and ≥280 mm CSF in children (250 mm CSF if the child is not sedated and not obese) in a properly performed lumbar puncture)
2. Diagnosis of pseudotumor cerebri syndrome without papilledema
In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if b-e from above are satisfied, and in addition the patient has a unilateral or bilateral abducens nerve palsy
In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if b-e from above are satisfied, and in addition at least three of the following neuroimaging criteria are satisfied
(i) Empty sella
(ii) Flattening of the posterior aspect of the globe
(iii) Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
(iv) Traverse venous sinus stenosis

[a]A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria a-e. The diagnosis is considered probable if criteria a-d are met but the measured CSF pressure is lower than specified for definite diagnosis.

In a study by Babikian et al. 1994, it was observed that IIH was more common after the age of 10 years.[17]

The clinical features of PTC syndrome include headache, visual symptoms such as blurring, obscurations of vision, and lateral diplopia. Nausea and vomiting are common at the time of the first presentation. When it is associated with vitamin D deficiency, the patient can present with other manifestations linked to the activity of vitamin D such as hypocalcemia-associated seizures due to dysregulation in calcium homeostasis in the gut, kidney, and bone. These all together make PTC a sight-threatening disease alone and a life-threatening one in conjunction with status epilepticus.

The modified Dandy criteria was used for the diagnosis of IIH; however, due to the fact that IIH in young children appeared to be different compared to adults, a new diagnostic criterion (Table 3) was proposed for IIH in children.[4]

The key to the management of a patient of PTC syndrome is recognition and treatment of the underlying cause. Treatment of patients with this condition is generally with lumbar punctures, weight loss, and acetazolamide. Surgical procedures such as lumboperitoneal shunt, ventriculoperitoneal shunts, subtemporal decompression, venous sinus stenting have also been used effectively along with optic nerve sheath fenestration to prevent visual loss when aforementioned approaches are unsuccessful.[8,13] Prognosis is variable with some patients stabilizing after a single lumbar puncture, while others with persistent symptoms for many years. It can be a self-limited condition, but optic atrophy and blindness are the most significant complications of untreated PTC.[13]

Salaria et al. have reported a case of 4-month-old infant with vitamin D deficiency rickets with hypocalcemic convulsions.[18] This case is very similar to our case but in an infant, who responded well to acetazolamide and vitamin D and calcium supplementation and remained asymptomatic after treatment. DeJong et al reported PTC in two children with vitamin D deficiency rickets each with the clinical picture of bulging fontanelle persisting for several months even after ongoing treatment; our case is of a 11-year-old boy with neurological complications that resolved after treatment.[19] Hanafy et. al reported 10 children aged 5–10 months with PTC in vitamin D deficiency rickets associated with malnutrition which did not respond to either vitamin D or vitamin A therapy, whereas our case did respond well to vitamin D therapy.[20] Since malnutrition or hypocalcemia alone can lead to PTC, it isn't clear if the cause of PTC syndrome is vitamin D deficiency in patients with generalized malnutrition including vitamin D deficiency rickets. The BMI of our patient was ≥3SD for given age, indicating undernutrition. Recent flu like illness could have been the most likely trigger in this child.

The pathophysiology of PTCS is complex. It is basically attributed to abnormal CSF dynamics, either impaired CSF outflow, or aberrant CSF production, or both.[21] The mechanism by which vitamin D deficiency leads to PTCS is not fully known. However, hypocalcemia appears to play a role. In a patient with primary hypoparathyroidism induced hypocalcemia,[22] Sambrook et al. studied the plasma absorption of CSF using radioiodinated serum albumin (^{131}I RISA) cisternography. Their study showed that CSF absorption was greatly reduced which returned to normal after correction of hypocalcemia. In a study done on squid axons,[23] Baker et al. demonstrated that efflux of intracellular sodium is decreased in the setting of hypocalcemia. Increased intracellular sodium is implicated with disturbance in absorption of CSF through the arachnoid villi.

The spectrum of clinical manifestation of hypocalcemia can range from paresthesia and muscle cramps to heart failure, tetany, bronchospasm, and life-threatening seizures. Low concentration of ionic calcium in the CSF has a convulsive effect and seizures can occur even without tetany in hypocalcemic patients.[24] In a retrospective study done in 19 children with IIH, 26.3% of them had hypovitaminosis D. Most cases reported in the literature include vitamin D deficiency rickets; just like our case did.[5,19,25]

This case report highlights that vitamin D deficiency, a common and undermined nutritional deficiency especially in developing countries, can lead to life threatening complications. The authors recommend appropriate screening and timely treatment of vitamin D deficiency.

AUTHOR CONTRIBUTIONS

Soumya Pahari: Conceptualization; supervision; writing – original draft; writing – review and editing. **Prakash Kunwar:** Writing – original draft. **Subi Acharya:** Writing – review and editing. **Pallavi Rauniyar:** Writing – original draft. **C. K. Sagar Bahadur:** Conceptualization; supervision; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest or financial disclosures to declare.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article or in the data repositories listed in References.

CONSENT

Written informed consent was obtained from the parents to publish this report in accordance with the journal's patient consent policy.

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