

**Presentation and management of hypoparathyroidism in a paediatric patient - a case report**Kanza Ateeque,<sup>1</sup> Warisha Fatima,<sup>2</sup> Iqra Rehman,<sup>3</sup> Maira Jamal<sup>4</sup>**Abstract**

Hypoparathyroidism occurs due to insufficient parathyroid gland activity leading to abnormal calcium and phosphate levels. The presentation of hypoparathyroidism is rare in adults and mostly encountered in the paediatric population. We present a case of a 3.5-month-old male infant with the presenting complaint of an episode of afebrile generalized tonic-clonic seizure. Haematological, urinary, cerebro-spinal fluid and radiological investigations were unremarkable but a biochemical profile revealed hypocalcaemia, hyperphosphataemia and lowered vitamin D3 levels. Parathyroid hormone profile showed a decreased level, confirming diagnosis of hypoparathyroidism. Intravenous administration of calcium and magnesium in combination with oral activated vitamin D3 and phosphate binders managed to resolve symptoms and maintain normal levels. The rationale of this case is to confirm the necessity of early diagnosis to prevent irreversible sequelae of hypocalcaemia and regular monitoring of treatment to avoid side-effects of medication.

**Keywords:** Child, preschool, Hypocalcaemia, Hyperphosphataemia, Hypoparathyroidism, Seizures

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**Introduction**

Hypoparathyroidism is a rare endocrine disorder involving a deficit in either the production or action of the parathyroid hormone. Since the parathyroid hormone (PTH) is responsible for regulating calcium and phosphate levels in the blood, an imbalance can lead to a spectrum of symptoms resulting from hypocalcaemia, hyperphosphataemia and hypercalciuria<sup>1</sup>. More common symptoms include muscle tetany and seizures, but other

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clinical features have been recorded such as cardiac arrhythmias, renal and brain calcifications, cataracts and altered skeletal development<sup>1</sup>. The only recorded estimates of the prevalence of hypoparathyroidism are of those in America, Denmark and Italy. These amount to 23–37 per 100,000 individuals. However, there is a lack of epidemiological studies available on the prevalence of this disease in Asia.<sup>1</sup> The variation in the clinical presentation depends upon the chronicity of condition, the calcium and parathyroid hormone levels in the blood and aetiology of hypoparathyroidism. Aetiologies range from iatrogenic causes; amounting up to 75% of hypoparathyroidism cases; to more rare genetic or autoimmune conditions and association with other endocrine disorders<sup>1</sup>. Conventional management involves administration of vitamin D, calcium supplements and phosphate binders with careful monitoring to avoid symptoms of hypercalciuria; however due to the uniqueness of such a condition, an ever-evolving discourse on the topic of long-term management is ongoing<sup>2</sup>. This case report aims to describe the presentation of hypoparathyroidism in a paediatric patient and discuss the clinical challenges and outcomes of management of such a rarely reported condition.

**Case Report**

A 3.5 months old male infant presented to the emergency department of Civil Hospital, Karachi on 6th October' 2021 with the complaint of a single episode of afebrile generalized tonic-clonic seizure that lasted for less than five minutes, followed by immediate recovery with no post-ictal drowsiness. The consent of patient's parent was taken for publishing the case. According to the parents, there was no history of prior seizures in the past, neither recent head injury or infectious disease. The infant had an unremarkable perinatal and medical history; he was born full-term weighing 2800g, with an Apgar score of eight in one minute and ten in five minutes. The history revealed normal growth and development. Physical examination and neurological examination showed no abnormality. The visual and hearing ability of the patient was intact and there were no oral lesions; His family history was

positive with his elder female sibling having recurrent episodes of febrile seizures and she expired at the age of 17 months due to such episodes. His vitals and sub-vitals were stable and there were no significant findings in complete blood count, Cerebro-spinal Fluid (CSF) analysis, urine D/R and urine culture and sensitivity. However, biochemical studies revealed severe hypocalcaemia, slightly low serum magnesium values, increased phosphate values and lowered 25-OH vitamin D levels. Creatinine, blood urea nitrogen levels, urine analysis were within normal limits, ruling out renal pathology. Blood glucose was also in the normal range thus excluding hypoglycaemia as the cause of the seizures. The thyroid profile was unremarkable with normal TSH and absent anti-thyroid peroxidase antibodies. The Chest X-ray revealed a normal thymus and isthmus. ECG did not show any significant findings. Based on the report of investigations, hypoparathyroidism was suspected and later confirmed by measuring serum levels of the hormone, which were found to be <3 pg/ml (normal limits 10-55 pg/ml). All biochemical studies and renal function test results have been shown in Table 1.

**Table-1:** Biochemical Studies and Renal Function Test results

| Tests                | Results    | Normal Values   |
|----------------------|------------|-----------------|
| Serum Calcium        | 5.8 mg/dl  | 9-11 mg/dl      |
| Serum Magnesium      | 1.4 mg/dl  | 1.6-2.4 mg/dl   |
| Serum Phosphate      | 8.8 mg/dl  | 4-6.5 mg/dl     |
| Random Blood Sugar   | 92 mg/dl   | 60-100 mg/dl    |
| Serum PTH*           | 3 mg/dl    | 10-55 mg/dl     |
| Serum Vitamin D      | 48 mmol/L  | ≥50 mmol/L      |
| Alkaline phosphatase | 199 U/L    | 150-420 U/L     |
| Serum TSH            | 3.09 mIU/L | 0.58-5.57 mIU/L |
| Serum Creatinine     | 0.3 mg/dl  | 0.2-0.4 mg/dl   |
| Blood Urea Nitrogen  | 14 mg/dl   | 5-18 mg/dl      |

\*PTH- Parathyroid Hormone

Initial treatment was first directed towards acute treatment of severe hypocalcaemia, for which an intravenous (I/V) infusion of calcium gluconate 100mg/kg/24 hour at 6-hour intervals was administered. For concomitant hypomagnesaemia, I/V magnesium sulphate at a dosage of 25 mg/kg every 8 hours was also given. Activated Vitamin D3 was added orally, at a dose of 0.05 mcg/kg daily. Oral calcium-phosphate-vitamin D3 was orally started as well but immediately halted after observing rise in phosphate levels. Continuous electrocardiography (ECG) monitoring was performed during drug administration to watch for any signs of bradycardia. Seven days after admission, the patient developed a second episode of afebrile tonic-clonic seizure with

rolling of eyes, which was treated and managed promptly with standard anti-convulsant therapy. Despite treatment, calcium levels continued to stay low, in the range of 4.7 to 6.9 mg/dl. Magnesium levels were normalised, maintained between 1.5 to 2.1 mg/dl. Meanwhile phosphate levels continually remained in the high range of 8.5-9.0 mg/dl. Due to insufficient response to current supplementation and phosphate levels being greater than 6 mg/dl, administration of oral phosphate binders, namely calcium acetate 667 mg was begun thrice daily with each meal, according to standard guidelines. Regular biochemical profiling was also done to monitor serum calcium, magnesium and phosphate levels to taper drug dosing accordingly and to ensure there were no signs of renal compromise or resultant hypercalcaemia. Consultation with an endocrinologist suggested continued phosphate binder administration until phosphate levels dropped to 5 mg/dl. The addition of oral phosphate binders to the present regimen of I/V calcium, magnesium and oral vitamin D3, managed to increase the patient's calcium levels and decrease phosphate levels. An echocardiography was performed to rule out cardiac defects.

The patient remained admitted for 26 days in the Paediatric ward until calcium and magnesium were under acceptable limits (Calcium-8.9 mg/dl; Magnesium- 2.1 mg/dl). However, phosphate levels were still high at 6.8 mg/dl. Since patient could now be shifted to complete oral supplementation and was asymptomatic, he was discharged, with attendants instructed to continue a regular regimen of oral calcium twice daily, syrup magnesium sulfate orally every 8 hours, oral vitamin D3 once daily and oral phosphate binders twice daily and counselled on the necessity of frequent follow-ups. On first follow-up, which was scheduled 15 days after discharge, physical and neurological examination of the child was normal with no visual and auditory deficits, ultrasound of the kidney was performed-which being normal- ruled out nephrocalcinosis. Biochemical studies showed calcium, magnesium and vitamin D levels to be well controlled while phosphate was still slightly high. Current medication was advised to be continued. A second follow-up scheduled within the next month held similar results and phosphate levels having further dropped. Hence further follow-ups had been scheduled with the plan of tapering drug dosage. However, despite extensive counselling -stressing on the occurrence of similar pathology with the patient's sister and need of surveillance of serum calcium and phosphate levels- and contacting the patient's attendants, they refused continued follow-ups due to their socio-economic restraints. They were also convinced that the patient was in a normal state with current medication and would be

taken to a nearby clinic for future checkups.

## Discussion

PTH is the major regulator of serum calcium; hence iatrogenic or autoimmune damage to the parathyroid gland, or target organ insensitivity to PTH causes deregulated calcium and phosphate retention. The major clinical manifestations of hypoparathyroidism occur due to resultant hypocalcaemia and according to the clinical guidelines this is defined as a serum calcium level of less than 7.5 mg/dl with possible hypomagnesaemia and hyperphosphataemia.<sup>3</sup> An early diagnosis of hypoparathyroidism in the paediatric population is necessary to prevent life threatening manifestations such as seizures and other complications as cerebral calcifications, delayed physical and mental development and cataracts. These can occur as a result of failure to correct deranged serum calcium levels<sup>4</sup>. Tetany, neuromuscular irritability and afebrile seizures are a few of the common initial clinical manifestations of hypoparathyroidism. This has been demonstrated in the case of our patient and further highlighted in similar case presentations by Gkampeta et al.<sup>5</sup> and Hussain et al.<sup>6</sup>; where the presenting complaints of paediatric patients with hypoparathyroidism were seizures. We ruled out initial differential diagnoses of seizures including hypoglycaemia and infectious pathologies like meningitis via biochemical, blood, CSF and radiological investigations. Biochemical studies confirmed severe hypocalcaemia and hyperphosphataemia. Our case just as the one presented by Moon JE et al, also showed the presenting signs of hypomagnesaemia additionally<sup>7</sup>. Furthermore, to establish hypoparathyroidism as the cause of hypocalcaemia, serum PTH were tested which according to diagnostic criteria stated by Brandi et al.<sup>8</sup> should be less than 20 pg/ml. Low PTH levels corresponding to low calcium levels was able to rule out pseudohypoparathyroidism and vitamin D deficiency induced hypocalcaemia. Hypocalcaemia secondary to hypomagnesaemia (HSH) was excluded by the following findings: magnesium levels were above 1.4 mg/dl- as severe hypomagnesaemia (Magnesium<0.8 mg/dl) occurs in HSH and magnesium supplementation by itself was unable to correct hypocalcaemia, similar to the case of Moon JE et al<sup>8</sup>. It is known that magnesium supplementation can correct hypoparathyroid state in HSH.<sup>9</sup> Fits occurring during hospitalization were managed with calcium supplementation and standard anticonvulsant treatment. Seizures in HSH are refractory to such treatment<sup>10</sup>. Depending upon the aetiology, hypoparathyroidism can be divided into primary hypoparathyroidism- arising as a result of defects in the gland itself often due to genetic abnormalities; as seen in Di'George syndrome or calcium channel receptor defects in which hypocalcaemia and

hyperphosphataemia is accompanied with hypomagnesaemia; or autoimmune destruction- and the far more common iatrogenically caused secondary hypoparathyroidism<sup>1</sup>. Di'George syndrome was ruled out by absence of cardiac defects in the echocardiography performed. A positive family history is a strong indicator of familial aetiology such as in the case of our patient having an older sibling with hypocalcaemic fits having begun at the same age. However, due to limited resources of the hospital, genetic testing and 24-hour urinary calcium could not be performed.

Recommendations state that initial treatment involves correction of severe hypocalcaemia with concomitant magnesium and vitamin D3 supplementation<sup>3</sup>. The conventional approach to treating severe calcium depletion; as described in 'The Harriet Lane Handbook'<sup>11</sup> requires intravenous calcium gluconate administration at 100-200 mg/kg/24 hours every 6 hours, for magnesium deficiency I/V magnesium sulphate at 25-50 mg/kg every 4-6 hours and for vitamin D dosing calcitriol 0.02-0.06 mcg/kg/dose per os (PO) once daily. Monitoring treatment for adverse effects is necessary hence, in line with guidelines, continuous ECG monitoring during drug administration for bradycardia was performed<sup>3,4,8</sup>. Although standard treatment regimen resulted in correction of hypocalcaemia and resolution of resultant symptoms in cases described by Gkampeta et al.<sup>5</sup> and Hussain et al.<sup>6</sup>, our treatment course deviated from the standard protocol. Our patient did not respond to calcium, magnesium and vitamin D3 administration, and continued to have heightened phosphate levels and diminished calcium levels, until oral phosphate binders were incorporated into the regimen. Literature guidelines state that for phosphate levels greater than 6.5 mg/dl, phosphate binders can be incorporated into the treatment regimen<sup>9</sup>. The goals of acute treatment involve preventing hypocalcaemic symptoms, maintaining a serum calcium level at the lower end of the normal range to avoid hypercalcaemia induced nephrocalcinosis, and renal calcification<sup>4</sup>. To do so, serum calcium and phosphate levels were continuously monitored to allow for prevention of adverse effects such as hypercalcaemia or renal compromise -especially in phosphate binder use, dose adjustment and, if required, tapering of supplement treatment to prevent future nephrolithiasis and nephrocalcinosis<sup>8</sup>. When signs of hypocalcaemia diminish along with symptoms, the patient can be shifted to a maintenance therapy of oral calcium, magnesium and vitamin D3<sup>3</sup>, which was successfully achieved within our patient. However, phosphate binders had to be continued as, although phosphate levels continued to drop, normal levels were yet to be achieved. Hence this medication was to be continued until phosphate levels were within normal

limits. The goals of follow-ups were to monitor serum calcium and phosphate levels. Addressing safety of the treatment is an important aspect in acute and ongoing treatment as well. Hence follow ups are essential and should include biochemical profiling, ultrasound imaging, ophthalmological and neurological examination for monitoring serum levels for recurrence of hypocalcaemic symptoms, drug induced hypercalcaemia, renal compromise, soft tissue calcium deposition<sup>8</sup>, and to allow for drug dose tapering for prevention of side-effects of such medication. Frequency of follow-ups should be adjusted according to how stable the patient is with ongoing therapy. PTH analogue administration is a recently developed therapy which continues to be developed and debated. A scarcity of enough literature regarding long term side effects of PTH analogue administration; as all cohort studies performed are limited to less than 10 years; along with not being cost-effective have contributed to this mode of treatment which is yet to be established as a mainstay treatment<sup>12</sup>. In addition, PTH administration is only recommended for patients who prove refractory to conventional therapy and patients susceptible to nephrocalcinosis<sup>8,12</sup>. As our patient was successfully managed via conventional treatment, which was more economically feasible for the patient, he did not require PTH analog supplementation. Since our patient presented to the hospital early in the course of this pathology, prompt diagnosis was able to afford a better prognosis. In addition, our report and existent albeit scarce literature suggests such a condition shows a case-to-case variation in presentation and management. Hence more records of such cases, with elaboration on management and challenges, are required to contribute to creating a clearer understanding of how to best manage such a condition with minimal side-effects.

## Conclusion

This case report highlights the importance of an early diagnosis of hypoparathyroidism and how it should always be considered in differentials of a child presenting with fits, especially if a strong family history is present. There is also a

need of extensive literature on management that caters to variations in challenges presented.

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**Conflict of Interest:** None.

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