Case Report

Neonatal idiopathic primary hypoparathyroidism: A rare cause of neonatal seizures
Shabbir Hussain, Moin-ud-Din Sabir, Mubaral Ali, Syed Awais-ul-Hassan Shah

ABSTRACT
Etiology of neonatal seizures (NNS) is diverse and hypocalcemia is one of the treatable causes. Neonatal hypocalcemia (NHC) due to congenital hypoparathyroidism, either permanent or transient, is extremely rare. Its biochemical abnormalities include hypocalcemia, hyperphosphatemia and low levels of intact parathyroid hormone (PTH). Isolated congenital hypoparathyroidism in which deficiency of PTH has no association with maternal, syndromic or endocrine defects is a very rare entity. We are reporting a case of a newborn who presented with seizures on the 5th day of life and later on investigations revealed hypocalcaemia due to isolated congenital hypoparathyroidism.

KEY WORDS: Neonate, Seizure, Hypocalcaemia, Hypoparathyroidism, Hyperphosphatemia.

doi: http://dx.doi.org/10.12669/pjms.315.7807

How to cite this:
Hussain S, Sabir M, Ali M, Shah SA. Neonatal idiopathic primary hypoparathyroidism: A rare cause of neonatal seizures . Pak J Med Sci 2015;31(5):1277-1279. doi: http://dx.doi.org/ 10.12669/pjms.315.7807

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION
Seizures in the neonatal period have diverse etiology and hypocalcemia is one of the treatable metabolic causes.1,2 Neonatal hypocalcemia may be transient or permanent, early or late onset and primary or secondary. Hypoparathyroidism is one of the rare causes of late onset neonatal hypocalcemia. Isolated congenital (idiopathic) primary hypoparathyroidism is a rare congenital entity which is usually sporadic but familial cases have also been reported.3,4 Hypoparathyroidism can also occur as a part of maternal, autoimmune disorders, polyendocrinopathy, with dysmorphic syndromes like CATCH 22, DiGeorge, velo-cardiofacial defect, post thyroidectomy complications and basal ganglia calcification.5,4,6 True incidence of hypoparathyroidism is not known but from Japan it is reported as 7.2/million people.

CASE REPORT
A male neonate presented on 18th day of life with history of recurrent seizures for the last 14 days. Seizures were focal and characterized by twitching of eyes, jerky movements of limbs, multiple episodes per day, brief in duration, about 1-2 minutes and seized spontaneously. The baby remained well between the seizures. There were no associated features like fever or reluctance to feed. He was born as spontaneous vertex delivery in a hospital to consanguineous parents as twin pregnancy. The other twin remained healthy and seizure free. He had one elder female sibling who was alive and healthy. No history of maternal illness or drug intake during pregnancy and antenatal records were unremarkable.

1. Shabbir Hussain, MBBS, FCPS, Clinical fellowship in neonatology (UK), Consultant Paediatrician/Neonatologist, Combined Military Hospital, Mardan, Pakistan.
2. Moin-ud-Din Sabir, MBBS, Combined Military Hospital, Mardan, Pakistan.
3. Mubaral Ali, MBBS, 
4. Syed Awais-ul-Hassan Shah, MBBS, 
1,3,4: Combined Military Hospital, Peshawar, Pakistan.

Correspondence:
Dr. Shabbir Hussain, 
Consultant Paediatrician/ Neonatologist 
Paediatrics Department, 
Combined Military Hospital, 
Peshawar, Pakistan. 
E-mail: shabbirmoeez@yahoo.com

* Received for Publication: March 28, 2015
* Revision Received: April 13, 2015
* Accepted for Publication: June 19, 2015
On examination he was irritable. Vital signs were within normal limits, anthropometric data at 50th centile, systemic examination unremarkable and no dysmorphic features. Focal seizures were observed characterized by twitching of eyes, jerky movements of limbs and were controlled with I/V Midazolam. Baseline investigations were sent along with a partial septic screening. Broad spectrum antibiotics were started along with supportive paraphernalia.

Results of investigations revealed normal blood counts, Renal function tests, blood glucose, electrolytes and C reactive protein but hypocalcemia was noted. Intravenous calcium replacement was done and seizure stopped. He remained well for 24 hours and again started having seizures. Again metabolic screening (blood glucose, calcium, magnesium, electrolytes) Inborn error of metabolism screening (ABGs, lactate and ammonia) and Ultrasonography brain were done. Again it revealed hypocalcemia. To find out the cause of persistent hypocalcemia, further laboratory workup (phosphate, alkaline phosphatase, vit D and PTH levels) was done. It was suggestive of hypoparathyroidism. X-Ray chest and Echocardiography were done to rule out DieGorge syndrome. ECG revealed prolonged Q-T interval. Maternal bone profile and PTH level were within normal limits. A final diagnosis of congenital primary hypoparathyroidism was made and patient managed with I/V calcium and oral cholecalciferol. Seizures ceased completely and on 7th day of hospitalization patient was discharged on oral medication (calcium and cholecalciferol) with follow up advice. At 6 month follow up he is thriving well with no evidence of nephrocalcinosis or any other complication and metabolic profile is within normal range.

**DISCUSSION**

Hypocalcaemia is a common metabolic problem of neonatal period. Neonatal hypocalcemia is defined as total serum calcium of less than 7 mg/dL (1.75 mmol/L) or ionized calcium less than 4 mg/dL (1 mmol/L) in preterm neonates and less than 8 mg/dL (2 mmol/L; total) or <1.2 mmol/L (ionic fraction) in term neonates. It is divided into early and late onset depending upon age of neonate. Late onset hypocalcemia usually occurs at the end of first week of life and hypoparathyroidism is a rare cause of late onset hypocalcemia.

Hypoparathyroidism can occur in isolation or in combination with other autoimmune/genetic defects. Sanjad and Sakati have described such associations of hypoparathyroidism with facial dysmorphism, growth failure and mental retardation. DiGeorge syndrome has also association with hypocalcemia. Isolated cong hypoparathyroidism can occur as a sporadic or familial disorder with inheritance by autosomal dominant, recessive or X linked modes of transmission. Defects in the prepro PTH gene located at 11p15 gene locus and mutations in calcium sensing receptor gene (3q21-24) have been associated in cases of isolated PTH deficiency.

One of the differential diagnosis is hypomagnesemia. It can lead to decreased levels of calcium, Vit D and PTH. But if we correct hypomagnesemia with parenteral magnesium then calcium, vit D and PTH levels are automatically corrected.

**Investigation Summary**

| Serial | Investigation       | Result                  | Values                  |
|--------|---------------------|-------------------------|-------------------------|
| 1:     | CBC                 | Normal                  |                         |
| 2:     | CRP                 | < 6mg/dl (Normal)       |                         |
| 3:     | GLUCOSE             | 60 mg/dl                |                         |
| 4:     | AMMONIA             | 40 umol/l               | 12-60umol/l             |
| 5:     | LACTATE             | 0.8mmol/l               | 0.5-2.2 m mol /l        |
| 6:     | ABGs                | Normal                  |                         |
| 7:     | USG BRAIN           | Normal study            |                         |
| 8:     | XRC                 | Normal                  |                         |
| 9:     | ECHOCARDIOGRAPHY    | Normal                  |                         |
| 10:    | ECG                 | QT c-prolonged          |                         |
| 11:    | MAGNESIUM           | 0.9mmol/l               | 0.7-1.1mmol/l           |
| 12:    | CALCIUM             | 1.5mmol/l               | 2.1-2.6mmol/l           |
| 13:    | PHOSPHATE           | 6.5mg/dl                | 2.5-4.5mg/dl            |
| 14:    | VIT D               | 15ng/ml                 | 20-150ng/ml             |
| 15:    | PTH                 | 9pg/ml                  | 14-67pg/ml              |
In our case patient presented on the 5th day of life with seizures and had hypocalcemia, raised phosphate, normal magnesium and low PTH levels in comparison with two cases presented by Atika2 of isolated congenital hypoparathyroidism. Patient was treated with calcium supplementation and remained symptom free till 6th month of life, after that the follow up was lost. Similarly Rocha et al presented a case with hypocalcaemia and low PTH levels but in contrast to ours their patient had hypomagnesaemia.11

Aim of reporting this case is to emphasize that at times, presentation of extremely rare disorders may mimic with very common illnesses but a high index of suspicion should be kept in mind to diagnose rare disorders like neonatal congenital primary hypoparathyroidism.

Declaration of interest: None

REFERENCES

1. Kossoff EH, Silivia MT, Maret A, Carakushansky M, Vining EP. Neonatal hypocalcaemic seizures: case report and literature review. J Child Neurol. 2002;17:236-239. doi: 10.1177/088307380201700319
2. Atika Z, Yaqoob M, Waseem R, Abbas A. Isolated congenital hypoparathyroidism: Follow up of two sisters. Pak Pediatr J. 2013;37:188-190.
3. Drake TG, Albight F, Bauer W. Chronic idiopathic hypoparathyroidism: report of 6 cases with autopsy findings in one. Ann Intern Med. 1954;12:1751. doi: 10.7326/0003-4819-12-11-1751
4. Akçaküç M, Güneş T, Kurotoðlu S, Çetin N, Özkul Y, Narin N, et al. Asymmetric crying facies associated with congenital hypoparathyroidism and 22q11 deletion. Turk J Peds. 2004;46:191-193.
5. Ramen CB. A case report of basal ganglia calcification- a rare finding of hypoparathyroidism. Oman Med J. 2009;24:84-86. doi: 10.5001/omj.2009.44
6. Patil MB, Patil SM. Facio-Auriculo-Vertebral sequence in association with congenital hypoparathyroidism. Ind Peds. 2012;49:670-671.
7. Jain A,agarwal R, Sankar MJ, Deorari A, Paul VK. Neonatal hypocalcaemia in the Newborn. Indian J Pediatr. 2010;77:1123-1128. doi: 10. 1007/s12098-010-0176-0
8. Sanjad SA, Sakati NA, Abu-Osba YK, Kaddoura R, Milger RDG. A new syndrome of congenital hypoparathyroidism, severe growth failure and dysmorphic features. Arch Dis Child. 1991;66:193-196.
9. Brown EM, Gamba G, Riccardi D, Lombardi M, Butters R, Kifor O, et al. Cloning and characterization of an extracellular calcium sensing receptor from bovine parathyroid. Nature. 1993;366:575-580. doi: 10.1038/366575a0
10. Finegold DN, Armitage MM, Galliani M, Matise TC, Pandian MR, Perry YM, et al. Preliminary localization of a gene for autosomal dominant hypoparathyroidism to chromosome 3q13. Pediatr Res. 1994; 36:414-417. doi: 10.1203/00006450-199409000-00024
11. Rocha C, Gonfinetti N, Pelluci L, Rocha MS. Hypocalcaemia and neonatal seizures: a rare case of congenital hypoparathyroidism. Arq Neurosiquitr. 2002;60:138-141. doi: 10.1590/s0004-282X2002000100025

Authors’ Contribution

Shabbir Hussain: Conceived, designed, data collection, preparation of the manuscript.
Moin-ud-Din Sabir and Mubarak Ali: Data collection, statistical analysis, review and final approval of manuscript.
Syed Awaiz-ul-Hassan Shah: Review and editing of manuscript, data analysis and final approval.
Shabbir Hussain: Takes the responsibility and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.