

# Seizure as a Presentation of Permanent Neonatal Diabetes Mellitus due to Mutation in KCNJ11 Gene: A Case Report

Sibabratta Patnaik, Bandy Sahoo, Mukesh Kumar Jain, Reshmi Mishra and Jyotiranjana Behera

Department of Paediatrics, Kalinga Institute of Medical Sciences, Bhubaneswar, India

**Correspondence:**

Sibabratta Patnaik  
Department of Paediatrics  
Kalinga Institute of Medical Sciences,  
Bhubaneswar, India  
Email: drsbpatnaik45@gmail.com

DOI: 10.3126/jnps.v40i1.28611

Submitted on: 2019-04-25

Accepted on: 2020-05-13

**Acknowledgements:** None

**Funding:** Nil

**Conflict of Interest:** None declared

**Permission from IRB:** Yes

**To cite this article:** Patnaik S, Sahoo B, Jain MK, Mishra R, Behera J. Seizure as a presentation of permanent neonatal diabetes mellitus due to mutation in KCNJ11 gene: A case report. J Nepal Paediatr Soc. 2020;40(1):56-9

**ABSTRACT**

Diabetes Mellitus in first six months of life is usually monogenic and is referred to as neonatal diabetes mellitus. The incidence of neonatal diabetes is extremely rare and varies from 1:89000 to 1:400000 live births. We report a two months old baby presenting with repeated seizures; on evaluation found to have diabetic ketoacidosis and initially managed with IV insulin infusion. Genetic study revealed heterozygous mutation, p. Valin 252 Leu in KCNJ 11 gene. This mutation suggests responsiveness to oral glibenclamide. The baby has responded to therapy. Seizure as a presenting feature for hyperglycemia is a rare entity.

**Key words:** glibenclamide; K<sup>+</sup> ATP Channel; KCNJ 11 gene; Neonatal Diabetes Mellitus



This work is licensed under creative common attribution 3.0 license



## INTRODUCTION

Diabetes Mellitus in first six months of life is usually monogenic and is referred to as neonatal diabetes. The incidence of neonatal diabetes varies from 1:89000 to 1:400000 live births. Neonatal diabetes can be divided into two clinical subtypes: permanent neonatal diabetes mellitus (PNDM) that requires continuous treatment since diagnosis and transient neonatal diabetes mellitus (TNDM) that typically resolves after a few weeks to months. Oral sulfonylurea for the treatment of neonatal diabetes is supported by researchers and clinicians; still insulin treatment is acutely required in most infants with newly diagnosed diabetes mellitus to treat ketoacidosis.<sup>1</sup> We report a case of NDM who presented with repeated seizures and found to have diabetic ketoacidosis.

## CASE REPORT

Eight weeks old female baby, with no significant antenatal history, born by Caesarian section at term, with birth weight of 2.9 kg was referred to our centre for repeated seizures. Family history was non contributory. She was hemodynamically stable, drowsy and was responding to sound and touch. Clinical examination did not reveal any abnormality. However random blood glucose (RBS) estimation showed 'high' reading with laboratory value of 684 mg/dl. Her complete blood count, renal function tests and electrolytes were all within normal limits. Urine reports showed ketone bodies. Arterial blood gas revealed metabolic acidosis with pH 7.06, PCO<sub>2</sub> 15 mm Hg, PO<sub>2</sub> 79 mm Hg, bicarbonate 8 and BE -15. Further investigations showed glycosylated haemoglobin (HbA1C) level 10.7% (normally less than 5.6) and C-peptide level less than 0.30 ng/ml (0.81-3.85). MRI Brain revealed diffusion restriction in left cerebellar hemisphere, bilateral globus pallidus, posterior limb of bilateral internal capsule, right corona radiata and right centrum hemiovale, suggestive of acute infarct. CSF examination and EEG were within normal limits. Her thyroid function test was normal. Ultrasonogram of the abdomen was also normal.

She was diagnosed as a case of neonatal diabetes mellitus (NDM) and managed with soluble insulin infusion. Her glucose level came under control

slowly and seizures were also well controlled with phenytoin and levetiracetam. Subsequently, insulin was changed to subcutaneous insulin. Blood sample was sent for the mutation analysis and the reports came as heterozygous mutation p. Valin 252 Leu in KCNJ 11 gene. Both the parents did not have this mutation and this is suggestive of de-novo mutation. Oral glibenclamide was started and insulin was gradually tapered off. Presently the baby is on our regular follow up and doing well.

## DISCUSSION

Neonatal diabetes mellitus (NDM) is defined as persistent hyperglycemia occurring in first six months of life. It is a monogenic form of diabetes, where insulin depletion occurs due to abnormal pancreatic islet development, decreased beta cell mass, or beta cell dysfunction. It can either be transient or permanent. Transient neonatal diabetes mellitus (TNDM), accounting for 50 to 60% of total NDM cases, is characterised by spontaneous resolution of diabetes within 12 weeks to few months of age, only to relapse years later. Permanent NDM (PNDM) has no period of remission and must be treated lifelong.<sup>1</sup>

PNDM is known to be caused by more than a dozen genes involved in pancreatic development, beta cell apoptosis or dysfunction. Mutation in genes ABCC8 and KCNJ-11 for ATP-sensitive potassium (K<sup>+</sup> ATP) channel of beta cells of pancreas are the commonest cause of permanent NDM. These mutations impair the ability of the channel to close, in response to metabolically generated ATP, thereby preventing glucose-induced insulin secretion from beta cells of pancreas. Sulfonylurea drugs directly close the K<sup>+</sup> ATP channels and facilitate insulin release in response to food. Oral glibenclamide, a non-selective sulfonylurea, is effective in closing K<sup>+</sup> ATP channels in beta cells, nerves, muscles and in brain. So glibenclamide not only controls blood glucose level, it improves neurologic function also. So screening for ABCC8 and KCNJ-11 genes is essential in all PNDM cases, so that switching from insulin to sulfonylurea can be made at the earliest.<sup>2</sup>

Our patient had a heterozygous mutation in P. Val 252 Leu in KCNJ-11 gene. Parents did not have the

same mutation, so it was thought to be de-novo in origin.

Few case report series of permanent neonatal diabetes have been reported from India.<sup>2-10</sup> In a study from AIIMS, New Delhi, in the period from Jan-2009 to Dec-2015, 11 babies were detected to have NDM, out of which nine were PNDM.<sup>3</sup> Similarly from South India, a study from Institute of Child Health and Hospital for children, Chennai, over a period of 12.5 years from 1999 to 2012, 28 babies were found to have diabetes before six months of age.<sup>4</sup> In another study from Chennai, Childs Trust Hospital, from Jan-2004 to Dec-2014 over 11 years, nine cases of PNDM were detected.<sup>5</sup> Only one case was reported from eastern India (Kolkata)<sup>7</sup> and this is the first case of neonatal diabetes reported from eastern state Odisha.

Seizure in early infancy can be due to hypoglycaemia, but very rarely it can happen due to hyperglycemia. Whenever a child comes to hospital with status epilepticus, blood sugar level is one of the first things to be done thinking of hypoglycemia. But very rarely we can get high sugar value in a seizing child. High blood sugar in

baby is a thrombogenic state and can lead to cerebral thrombosis and present with seizures due to cerebral infarction. DEND syndrome is a very rare, generally severe form of NDM characterised by a triad of developmental delay, epilepsy, and neonatal diabetes.<sup>6</sup>

## CONCLUSIONS

Hyperglycemia can rarely be a cause of refractory seizure. K<sup>+</sup> ATP channel mutations are the most frequent causes of NDM, especially in PNDM. Molecular analysis is a must in all NDM cases and transition to sulfonylurea treatment is usually successful in these patients.

## REFERENCES

1. Kataria A, Gopi RP, Mally P, Shah B. Neonatal diabetes mellitus: current perspective. *Research and Reports in Neonatology*. 2014;4:55–64. DOI:10.2147/RRN.S38206.
2. Radha V, Ramya B, Gopi S, Kavitha B, Preetika S, Thai K, et al. Successful transition to sulphonylurea therapy from insulin in a child with permanent neonatal diabetes due to a KCNJ11 gene mutation. *J Diabetol*. 2018;9:65-7. DOI:10.4103/jod.jod\_37\_17.
3. Jain V, Satapathy A, Yadav J, Sharma R, Radha V, Mohan V, et al. Clinical and Molecular Characterisation of Children with Neonatal Diabetes Mellitus at a Tertiary Care Center in Northern India. *Indian Pediatr*. 2017;54:467-71. DOI:10.1007/s13312-017-1049-7.
4. Poovazhagi V, Thangavelu S, Senthil S, Jahnvi S, Venketasan R, Mohan V. Clinical profile and outcome of infantile onset diabetes mellitus in southern India. *Indian Pediatr*. 2013;50:759-63. DOI:10.1007/s13312-013-0219-5.
5. Saikh ST, Jadhav SS, Shivane VK, Lila AR, Bandgar TR, Shah NS. Childhood onset of sulfonylurea responsive neonatal diabetes due to a novel homozygous autosomal recessive mutation in the ABCC8 gene which was presumed to be type 1b diabetes before genetic analysis. *AACE Clinical Case Rep*. 2016;2:117-21. DOI: 10.4158/EP15773.CR.
6. Sriram P, Priyambada L, Mondal N, Suresh R, Prakash V. Neonatal diabetes mellitus. A case report. *Curr Pediatr Res*. 2010;14(1):55-57.
7. Abraham N, Ahamad A, Unnikrishnan AG, Kumar H, Ellard S. Permanent neonatal diabetes mellitus due to an ABCC8 mutation: a case report. *JOP. J Pancreas*. 2014;15(2):198-200. DOI:10.6092/1590-8577/1947.
8. Ganesh R, Suresh N, Vasanthi T, Ravikumar KG. Neonatal diabetes: A case series. *Indian Pediatr*. 2017;54:33-6. DOI:10.1007/s13312-017-0993-6.

9. Naaraayan SA, Varadharajan P, Dhakshayani RV, Chandramohan R. Neonatal Diabetes-From Insulin to Oral Hypoglycemic Agent: Case Report. *Diabetes Case Rep.* 2:121. DOI:10.4172/2572-5629.1000121.
10. Wali P.P, Parakh H, Reddy K.B, Jain S, Reddy P. A Rare Case Report of Familial Neonatal Diabetes Mellitus. *Int J Pediatr Res.* 2018;5(6):336-338. DOI:10.17511/ijpr.2018.6.06.