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Neonatal Diabetes Mellitus: A Case Report and Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author BGM designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors ASB and OJA managed the analyses of the study. Author DNN managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Aims: To report a case of a neonatal diabetes mellitus observed in the Nouveau Village de Pédiatrie, Democratic Republic of Congo, between June 2014 and June 2018.
Cases Presentation: Neonate diabetes is a rare disease. It occurs to 1 newborn over 300000. Two forms are described: the transient and the definitive neonatal diabetes mellitus. We report a case of a male and term newborn, hospitalised for a neonatal infection, who had hyperglycemia. Therapeutic implications are discussed in the light of literature findings.
Conclusion: Neonatal diabetes is a rare phenomenon but alert signs must be known. Screening of blood glycemia disorders should be systematic in sick newborn for early detection and successful treatment.

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1. INTRODUCTION

Diabetes occurring under 6months of age is termed “neonatal” or “congenital” diabetes [1]. It is a rare disease, occurring for 1 child out of 300 000 live births [2]. It has two forms: a transient or definitive form. Clinical signs in the transient form occur in the first weeks of life with hyperglycaemia, impaired intra-uterine growth, severe dehydration, macroglossia, umbilical hernia, muscular hypotony, congenital abnormalities on the nervous system, heart and kidneys. There may also occur a growth delay [3,4]. At the end pf the first trimester of life, there is a remission, followed by a recidivism as a definitive diabetes mellitus for 50% of cases. This happens most often at the adolescence. The change of the pancreatic function in this affection exists all along life but worsens at this periods of increased metabolic demand (puberty) [2]. It is an increased expression of a gene located on the chromosome 6q24 submitted to a mechanism of parental history [2-4].

In the definitive neonatal diabetes (DNND), the secretion of insulin becomes insufficient soon after the birth. Many diseases are associated with DNND, and the molecular mechanisms of some among them have now been decrypted, but do not concern genetics. The discovery of mutations of the genes coding for potassic channels of the beta cells has an important therapeutic consequence. Indeed, ligands of potassic channels like sulfonylureas have been used successfully, allowing wean from insulin treatment that one believed definitive for affected children [2-4]. Recent studies have implied that the deficit in insulin output in TNDM can arise from a delayed maturation of the pancreatic islets and B-cells, as a consequence of altered expression of genes on chromosome 6 [5]. It was first associated with paternal uniparental disomy of chromosome 6 (UPD6) in 1995, suggesting it was disorder of imprinting. Another novel but rare genetic cause of TNDM involves mutations in the *HNF-1B* (hepatocyte nuclear factor-1B gene) [6,7] which was previously known to be responsible for maturity-onset diabetes of the young 5 (MODY5).

To date, permanent NDM is known to be caused by approximately a dozen genes involved in pancreatic development, B-cell apoptosis, or dysfunction. Mutations in the *KCNJ11* or *ABCC8* genes, encoding the K_{ATP} channel subunits KIR6.2 (ATP-sensitive inward rectifier potassium channel) and SUR (sulfonylurea receptor)1, respectively, account for the majority of PNDM cases [8]. Mutations of the *KCNJ11* gene compromises the sensitivity of inhibitory ATP by the KIR6.2 subunit, causing permanent opening of the potassium channel and preventing cell depolarisation and insulin secretion [9]. A number of other syndromes have been associated with PNDM, reflecting that the roles played by the genes extend beyond pancreatic B-cell dysfunction. Maternally inherited diabetes associated with early-onset bilateral sensorineural deafness is one such example of mitochondriopathy secondary to a messenger deoxyribonucleic acid (mDNA) A3243G point mutation. A suspicion of mitochondrial diabetes is provided by a strong familial clustering of diabetes [10].

2. PRESENTATION OF THE CASE

It was a male newborn, aged of 1 day, with 3000g of birthweight who was received in the Nouveau Village de Pédiatrie, in Kisangani town, Democratic Republic of Congo. He was referred from a first level hospital where he was born.

He was the first born of a young mother of 22 years. The gestational age was 38 weeks. There was neither history of maternal fever prior to parturition nor premature rupture of the membranes. There was no history of diabetes in the family. During the pregnancy, no screening for gestational diabetes was realised. The newborn had fever noticed 3 hours after the birth, respiratory distress and continuous crying. He was agitated and his fontanelle was deeply depressed. The cutaneous fold was permanent. Axillary temperature was 39.1°C. Fasting plasma glucose (Contour®, Bayer) was 279 mg/dl. White blood count was 9000 per mm^3, with 40% of granulocytes. Cerebrospinal fluid analyses were negative. he was treated with Rocéphine® (2x150 mg/day), amikacine (45 mg/day). He received rapid acting insulin n (ACTRAPID®): first a bolus of 3UI intravenously followed by 0,1 U every hour. In the evolution, the blood glucose did not lower (381 mg/dl 12 hours later) and the respiratory distress worsened. He died 36 hours after his admission.

3. DISCUSSION

Clinical signs observed on this newborn were reported by many authors: hyperglycemia,

severe dehydration without an evident loss of water by digestive disorders [4,11]. About birthweight, many studies report, in the majority of the cases, a hypotrophy [2,11]. Nevertheless, cases of eutrophic newborn, like in this presentation, have been reported [12].

Note that the newborn begun treatment in a first level hospital where only sepsis was addressed at. Earlier diagnosis by systematic screening could lead to prompt genetic diagnosis and targeted treatment, thereby avoiding the most severe sequelae of hyperglycaemia in neonates [13].

As there are accuracy issues with the simple convenient bedside POCT devices, many workers have tried to compare these with the gold standard laboratory estimation. When analysing the performance of glucometers in the hypoglycemic range, glucometers are required to perform to the standards of the US National Committee for Clinical Laboratory Standards (NCCLS) or the American Diabetic Association (ADA).In 1994, the ADA recommended that a glucometer should achieve a total error (system + user) of less than 10% for the plasma glucose concentration range 1.6–22.2 mmol/L (30–400 mg/dL) [14,15].

The insulin treatment proved to be satisfactory for some cases [16], but recent policies are dominated by the antidiabetic sulfonamides [17-21]. A long time in the past, this form of diabetes has been treated like type 1. But neonatal diabetes has been revolutionised by the discovery of its genetic basis. The identification of a chromosomal mutation carrying on the KCNJ11 genes or the ABCC8 led to a radically different and more efficient approach. Sulfonylureas proved superiority to insulin, regarding metabolic control, economic accessibility for the parents and a bigger stability of the glycated haemoglobin [18-22].

4. CONCLUSION

Neonatal diabetes is a rare phenomenon but alert signs must be known. Screening of blood glycemia disorders should be systematic in sick newborn for early detection and successful treatment.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study had the agreement of research Authorities of the faculty of medicine and Pharmacy of the University of Kisangani.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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