CASE REPORT

NEONATAL DIABETES MELLITUS – IS TRISOMY 21 ASSOCIATED WITH REFRACTORY HYPERGLYCAEMIA?

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Background: Neonatal diabetes mellitus is a rare disorder characterized by refractory hyperglycaemia which is further divided into two types, transient (TNDM) and permanent neonatal diabetes (PNDM), which is associated with genetic aberrations at the human chromosome 6q24 accompanied with pancreatic structural abnormalities or β-cell dysfunction requiring insulin treatment. This case report analyzes a rare correlation between a case of permanent neonatal diabetes mellitus with Trisomy 21. **Methods:** An infant presented with intrauterine growth retardation and very low birth weight showing signs of persistent hyperglycaemia where genetic analysis suggested presence of permanent neonatal diabetes mellitus accompanied with Trisomy 21. Chest X-ray examination alongside an echocardiogram revealed significant pericardial tamponade. By the 6th week of life, pericardial effusion spontaneously resolved supported by normal follow-up echocardiograms without any treatment plan. The patient became euglycemic by 3rd week of life and discharged. **Conclusion:** Neonates with diabetes mellitus usually present with clinical features such as low-birth weight, ketoacidosis, consistent insulin-requiring hyperglycaemia and preterm. This case report shows a correlation between neonatal diabetes and genetic syndromes. Treatment plans can be improved by conducting genetic studies between these two variables and understanding the long-term outcomes.

Keywords: Hyperglycaemia; Intrauterine growth retardation; Trisomy 21; Pericardial tamponade

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INTRODUCTION

Neonatal diabetes mellitus (NDM), although a rare entity, generally occurs in the first week of life, with a maximum incidence of around 1 in 300,000.[1] It usually presents with persistent hyperglycaemia, showing little to no response to insulin, and normal serum insulin levels. This abnormality may be transient, which is usually 50% of NDM cases, and resolves spontaneously in most cases around 12 weeks after which body yields normal insulin response.[2] Here, we report a rare case of a neonate with intrauterine growth restriction showing persistent hyperglycaemia accompanied with pericardial effusion as well as Trisomy 21.

CASE REPORT

A baby boy was born via caesarean section at 36 weeks of gestation due to previous scar-and-breech presentation, to a G4 P3+0 mother who was diagnosed with gestational diabetes mellitus during pregnancy. The baby was born with a Very Low Birth Weight (VLBW) of 1380 grams. The heart sounds were normal as an echodiagram of the chest showed no abnormalities (Figure-1). Complete blood count and other biochemical parameters were within normal limits, except atypical lymphocytes on peripheral film. Chest X-ray was normal. On second day of NICU stay, hyperglycemia was observed and by third day, levels remained high above 400 mg/dL. However, on second-day, the patient developed hyperglycemia with glucose levels reaching 379 mg/dL. During 3rd week of stay, intermediate acting insulin was administered and the patient became euglycemic. The patient developed desaturation and enlarged cardiac shadow was observed on X-ray. After echocardiogram, pericardial effusion was observed which was causing cardiac tamponade (Figure-2). The family refused the procedure pericardiocentesis which was advised by a cardiologist. The CBC report showed progressively decreasing platelet counts and blast cells were observed on peripheral smear. Oncology was consulted and flow cytometry showed myeloid markers. Karyotyping and Fluorescence In-Situ Hybridization (FISH) for chromosome-21 was sent to lab for analysis which turned out to be positive. A septic workup excluded an infectious aetiology.

By 6-weeks of life, pericardial effusion completely resolved with conservative management. On a repeated CBC report, normal peripheral smears was observed leading to the conclusion of transient-myeloproliferative disorder as supported by diagnosis of Trisomy 21.[3] Patient was vitally stable and discharged. Ethical approval was obtained from the parents of the patient for use of details for research purposes.

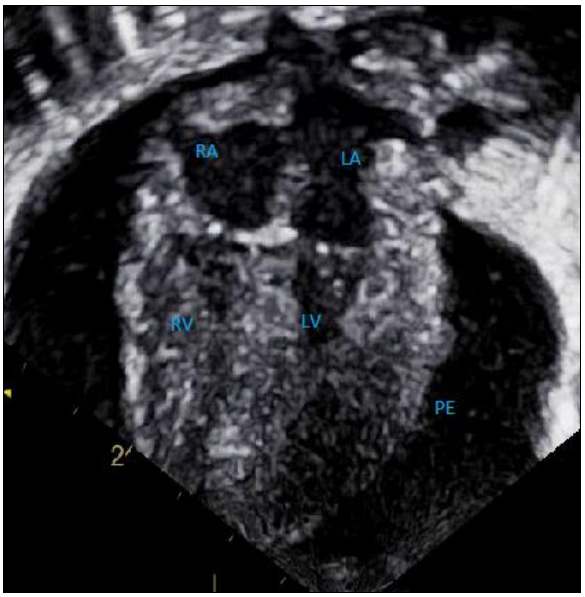

Figure-1: Initial echocardiogram at the time of diagnosis.

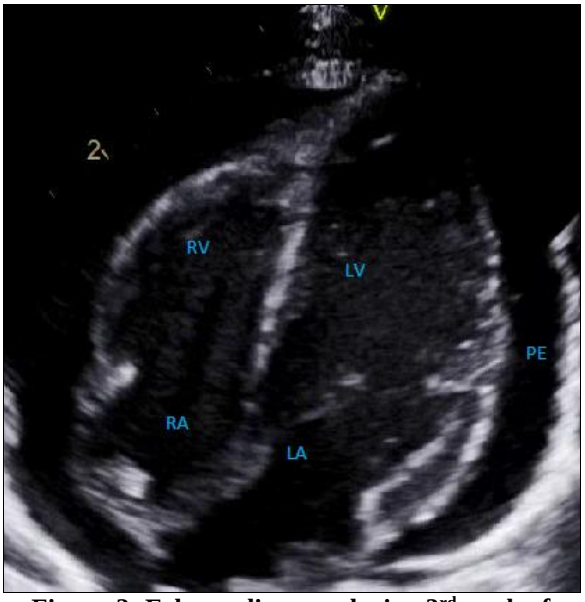

Figure-2: Echocardiogram during 3rd week of hospital admission

No molecular evidence was found for Transient Neonatal Diabetes Mellitus, which is sensitive to sulfonylureas after conducting a Methylation-Specific Multiplex Ligation-dependent Probe Amplification for TNDM chromosomes.

Neonatal diabetes mellitus is a rare condition. It is divided into transient and permanent neonatal diabetes mellitus which is characterized by low levels of insulin and persistent high levels of glucose. Overtime, metabolic disorders begin to develop.[4]

In a study by Abaci *et al*. an infant presented with diabetic ketoacidosis mimicking sepsis and pancreatic hypoplasia accompanied with Neonatal Diabetes Mellitus.[5] The presence of an infection or pancreatic hypoplasia does not always explain the hyperglycaemic levels as shown in our case. In a study by Barone *et al*. a VLBW-infant had high glucose levels even in the absence of these contributing factors.[4]

In a study by Johnson *et al*., upon analysis of the patients with Trisomy 21-PNDM, there was no mutation observed in the known genes seen in PNDM. As a result, the Trisomy21-PNDM patients had an overall low birth weight as compared to the non-Trisomy 21-PNDM patients suggestive of prenatal onset of β-cell dysfunction.[6] In our case, VLBW and PNDM can perhaps be explained due to the presence of Trisomy 21 in our patient.

Most studies recommend genetic-testing to be conducted before finalizing a treatment plan.[4] Some low-and-middle-income countries might not have access to such advanced genetic-testing facilities thereby misleading the patient diagnosis.

In conclusion, all new-borns should be carefully examined for signs such as dehydration, fever and weight loss. These signs could indicate the presence of diabetic ketoacidosis or pancreatic hypoplasia explaining the neonatal diabetes mellitus. However, the absence of these factors should point towards considering the presence of genetic syndromes. Our case highlights the importance of analysis at the genetic-level suggesting further investigation into the underlying mechanism between Trisomy 21 and Permanent Neonatal Diabetes Mellitus.

Ethical approval and consent to participate: Written informed consent was obtained from the parents of the patient for the case details to be used for any publication.

Consent to Publish: Written informed consent to publish was obtained from the parents of the patient for publication of this case report in a journal as well for other study purposes.

Availability of data and material: Case details are not publicly available because the data is patient medical records but are available from the corresponding author on reasonable request

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AUTHORS' CONTRIBUTIONS

All authors have read and approved the manuscript and its submission. We confirm that this work has not been published elsewhere and is not under consideration by another journal in whole or in part in any language.

Informed consent: Written informed consent was obtained from the parents of the patient for publication of this case report.

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