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Case Report

Consequence of Diabetic Environment and Significance of Glycemic Control in Early Pregnancy: A Case Report

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Abstract

Microcephaly describes a structural defect of the fetal head circumference; causes being extensive, and heterogeneous including both known and undetermined etiologies. No conventional treatment/s is currently available to minimize the risk of anomaly. Maternal hyperglycemia is often associated with adverse perinatal outcomes upsetting embryonic development. A tight glycemic control possibly restructures interwined teratogenically capable pathways balancing the reactive oxidative species metabolism. However, only few studies have highlighted on changes in response to diet and metabolic conditions for increased risk for anomalies in diabetic and obese pregnancies. Management strategies often miss recommended preconception counseling in unplanned pregnancies. In this report, a patient of early pregnancy with bad obstetric history successfully responded to an optimized glycemic control to avoid a major congenital defect like microcephaly.

Keywords: Gestational Diabetes Mellitus; Glycemic Control; Insulin; Microcephaly

Key Messages

- Optimum glycemic control in early pregnancy is necessary to avoid congenital anomalies like microcephaly.
- Insulin management in later stages of pregnancy may help the management protocol.
- Control of hyperglycemia may ameliorate the early fetal organogenesis.

Introduction

Microcephaly can be diagnosed either prenatally or postnatally. The condition is usually defined by the measurement of occipito-frontal circumference (head circumference), more than 2 standard deviations (SDs) below the mean for age and sex or less than 3rd percentile for age and sex [1]. The prevalence of pre-gestational and gestational diabetes (GDM) is increasing globally [2]; incidence in India ranging from 3.8% to 41% [3]. Maternal hyperglycemia is often associated with adverse pregnancy outcomes perturbing fetal development and organogenesis [4] resulting macrosomia, sacral agenesis, microcephaly to name a few [5]. Majority of women with predisposition for pre-diabetics and/or GDM may not achieve optimum glycemic control and require specific pharmacotherapy. Diet management, weight control, insulin sensitizers or oral hypoglycaemic agent are commonly used measures for optimization of glycemic control. A bulk of patienthood not overtly hyperglycemic but with undiagnosed hyperinsulinemia has a predisposition to hyperglycemia. The present case required a

tight glycemic control in both early and later stages of pregnancy with dietary invention/s and insulin management respectively. Since fasting glucose is considered as a reflection of metabolic abnormality, control of the same might help to avoid the adverse consequences that did already happen in this patient.

Here we present a case with previous recurrent bad obstetric performance. The clinical and biochemical features are discussed in detail. Institutional Review Board Approval (IRM/HEC-05/PC/02/2020) was obtained for reporting the case. The work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Case Report

A 35-year-old woman, reported to our clinic in April'2019 with history of one spontaneous miscarriage and consecutive deliveries of two microcephaly babies on July 2016 and September 2018 weighing 1.79 kg (Figure 1A) and 2.21 kg (Figure 1B) with head circumference (HC) of 30.7 cms and 29.8 cms respectively. Both babies died around 7th month. Pre-conception investigation/s like Hb, TORCH profile, anticardiolipin and anti-Lupus antibody were found within normal limits on both occasions. However, levels of blood sugar and insulin and/or HbA1C were not measured.

During current pregnancy, her body mass index was 26.3 and blood pressure was 118/82 mmHg. She had no history of consanguineous marriage. There was a strong family history (F/H) of type 2 diabetes as both of her parents were diabetic. The patient had no history of hypertension, thyroid or connective tissue disorders or symptoms suggesting diabetes. Both husband and wife were karyotypically normal. The F/H was unremarkable for congenital abnormalities or genetic disorders. The patient never travelled outside the country. In addition to routine examination/s, we performed insulin (fasting (F)/post-prandial (PP)), sugar (F/PP), homocysteine, uric acid, TSH, fT4, and urine R/E. Reports came normal excepting insulin (F: 43 U/l; PP: 126 U/l) with a high normal fasting glucose (118 mg/dl). Necessary dietary intervention/s with weight control and administration of insulin sensitizers (combination of metformin 500 mg twice daily with myo-inositol 4 g once daily) was advised for 3 month/s. Insulin and glucose levels became normal after treatment. She conceived spontaneously. Last menstrual period (LMP) and expected date of delivery (EDD) were 11/11/19 and 18/8/2020 respectively. At 6th week of pregnancy, routine antenatal examination/s was within normal limits. Anomaly scan report was normal. Antenatal period was uneventful; excepting in the latter half of pregnancy. Her average fasting and two hour plasma glucose values were 86 mg/dl and 128 mg/dl which increased to 112 mg/dl and 151 mg/dl respectively. HbA1C after 7 months was 6.1%. With the rise of PP glucose level to 151 mg/dl, insulin (actrapid) was administered twice daily in the dose of three units before breakfast and two units before dinner. Blood glucose was monitored regularly before administration of insulin with glucometer and the dose was adjusted accordingly as per values. Her fasting and two hour plasma glucose levels were maintained as 86 mg/dl and 118 mg/dl, respectively. At 38 completed weeks, elective caesarean section was performed. A live and healthy male baby was delivered weighing 2.91 kg (Figure 1C) with HC of 32.97cms at birth. After delivery, neonatal examinations revealed no structural or functional abnormality. USG pictures of the previous babies with microcephaly and normal baby is documented (Figure 1 D-F).

Figure 1: Photograph of the babies with and without microcephaly along with comparative head circumference before and after glycemic control.

Legend: Head circumference (HC) of baby 1 is 25.51 cms instead of (31.45 ± 2.5) cms at birth (Figure 1A). HC at 33weeks 2days is 23.97 cms instead of (29.87 ± 1.98) cms (Figure 1D). HC of baby 2 (Fig 1B) is 26.12 cms instead of (32.03 ± 2.1) cms at birth. HC at 34 weeks 5 days is 25.1 cms instead of (30.48 ± 2.03) cms (Figure 1E). Both HC is less than 2 SD. As per the CDC-infant head circumference for age (11), both babies are diagnosed as microcephaly. Figure 1C represents a live and healthy baby weighing 2.91 kg with a HC of 32.97cms (32.3 ± 1.7) cms at birth. HC at 35weeks 6 days is 31.89 cms instead of (30.9 ± 2.54) cms (Figure 1F).

Discussion and Conclusion

Causes of microcephaly are heterogeneous. Common causes include metabolic and/or genetic disorders, intrauterine infection, teratogen exposure (including in utero drug or toxin exposure and infectious agents). This case signifies the importance of optimizing glycemic control in all pregnancies with or without the stigma of pre-conceptional hyperglycemia. Pregnancy itself is a hyperglycemic disorder.

Hence, proper correction of pre-existing or predisposition to diabetes is an absolute necessity. Although American Diabetes Association recommends preconception counseling about glycemic control to all women desiring pregnancy, studies seldom focus precisely on maternal blood insulin and glucose level prior to pregnancy. Numerous pregnancies not only in India but globally are unplanned. Therefore, intervention strategies do not correctly correspond in the period of important phase of organogenesis i.e. the initial few weeks of first trimester of pregnancy. This may be the reason to overlook glucose and/or insulin levels in the specific phase of initial three pregnancies of the patient.

In this case, the patient was diagnosed as hyperinsulinemic with a tendency of possible hyperglycemia. Pre-gestational diabetes alters growth and structure of the human yolk sac [6], compromising embryonic development [7]. Hyperglycemia, stress mediator induces possible organ malformation and could cause damage an oxidative to the developing yolk sac, via membrane changes, mitochondrial dysfunction to name a few [8]. Microcephaly and oxidative stress possess some common template with regard to changes in DNA damage response which is pivotal during neural development [9]. This may be the possible mechanism of structural abnormality like microcephaly in the case presented in this communication.

Initial impairment of glucose tolerance leading to diabetes is characterized by both hyperinsulinemia and subsequent hyperglycemia. We favor insulin during pregnancy because it is effective and easily adjusted based on glucose levels, as well as lack of data regarding long-term outcomes in offspring exposed to oral antihyperglycemic drugs excepting metformin in utero [10]. To this end, amelioration of a minor defect like glycemic control during early fetal organogenesis may prove effective to avoid a major congenital defect like microcephaly.

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Author Contributions

Conceived and designed the paper: SK BNC HK PC. Performed the experiments: SK NG. Analyzed the data: NG HK. Wrote the paper: BNC PC.

Conflict of Interest

None declared.

Bibliography

1. "Division of Birth Defects and Developmental Disabilities N, Centers for Disease Control and Prevention". Facts about microcephaly; (2016).
2. McCance D., *et al*. "A practical manual of diabetes in pregnancy". John Wiley and Sons, (2017).
3. Padhi S., *et al*. "Type II diabetes mellitus: a review on recent drug based therapeutics". *Biomed Pharmacotherapy* 131 (2020): 110708.
4. Eriksson U J and Wentzel P. "The status of diabetic embryopathy". *Upsala Journal of Medical Sciences* 121 (2016): 96-112.
5. Najmi A., *et al*. "Early onset gestational diabetes mellitus: A case report and importance of early screening". *Journal of Family Medicine and Primary Care* 8 (2019): 1772-1774.
6. Cosmi E., *et al*. "Structural-tridimensional study of yolk sac in pregnancies complicated by diabetes". *Journal of Perinatal Medicine* 33 (2005): 132-136.
7. Dong D., *et al*. "New development of the yolk sac theory in diabetic embryopathy: molecular mechanism and link to structural birth defects". *American Journal of Obstetrics and Gynecology* 214 (2016): 192-202.
8. WHO. "Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications. Part I:Diagnosis and Classification of Diabetes Mellitus WHO/MCD/MCS/99". 2nd ed. Geneva: WHO; (1999): 1-59.

9. Vana DR. "The molecular crosstalk: oxidative stress, genomic instability and neurodegenerative disorders". *Biomedical Research* 28 (2017): 14.

10. Hyer S., *et al*. "Metformin in Pregnancy: Mechanisms and Clinical Applications". *International Journal of Molecular Sciences* 19 (2018): 1954.

11. Data Table of Infant Head Circumference-for-age Charts, National Center for Health Statistics at CDC.gov/growthcharts/html_charts/hcageinf.htm dated 7/19/2021.