HYPOGLYCAEMIA IN AN INFANT OF A MOTHER WITH FASTING HYPERGLYCAEMIA - A CASE REPORT

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SUMMARY
We report a case of perinatal death from hypoglycaemia in an infant of a mother who had fasting hyperglycaemia diagnosed at 31 weeks of gestation and managed with diet alone. Blood glucose values were not conclusive of gestational impaired glucose tolerance by WHO and American Diabetes Association standards, yet autopsy histological findings in the pancreas were similar to that described in neonates of a diabetic mother. We therefore emphasize that all pregnant women with inconclusive glucose values for diagnosis of full blown gestational diabetes mellitus should be fully investigated and closely monitored during antenatal care. The infants of such mothers may be at a higher risk of hypoglycemia in the immediate post natal period and would require similar monitoring and aggressive management.

Keywords: Gestational impaired glucose tolerance, infant hypoglycemia

INTRODUCTION
Gestational impaired glucose tolerance (GIGT) is carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. Factors such as age, obesity and family history are important in the clinical presentation of the disorder and its severity.

The pathogenesis of GIGT is not clear. It is believed that condition reflects the predisposition of a woman to type 2 diabetes mellitus or just an extreme manifestation of metabolic changes during the pregnancy [1, 2].

The incidence of impaired glucose tolerance in pregnancy is 3-10% and about 80% represent cases of gestational diabetes[3, 4].

Studies done in Nigeria show that incidence of diabetes mellitus (DM) among pregnant women was 1.7%. Pre-gestational diabetes accounted for 39% while gestational diabetes was responsible for 61% of cases. The perinatal mortality was 12.5% and higher than in controls (3.5%)[5]. Perinatal mortality associated with poor control of diabetes was as high as 42.9%[6].

American National Maternal and Infant Health Survey in 1988 reported that 4% of pregnancies resulted in live birth associated with DM. Most of these (88%) represent cases of gestational diabetes mellitus (GDM), 8% non-insulin-dependent diabetes (Type 2 DM), and 4% insulin-dependent diabetes mellitus (Type 1 DM)[7].

Modified criteria for diagnosis of impaired glucose tolerance recommended by WHO are: fasting plasma glucose more than 5.5 but less than 7.0 mmol/l and 2 hr postprandial glucose value equal or more than 7.8 but less than 11.1 mmol/l after 75g oral glucose load. Accordingly to WHO recommendations the same criteria are used for diagnosis of impaired glucose tolerance in pregnant women[8].

American Diabetes Association (ADA) recommends performing 50gm oral glucose challenge test (OGCT) for all pregnant women at 24-28 weeks of gestation. A value of more than 7.2 mmol/l for the 1 hour postprandial glucose are selected for full investigation including oral glucose tolerance test (OGTT). The ADA recommends the 100 gm OGTT as more sensitive for diagnosis of GIGT[9].

Some reports from developing countries suggest that the values ought to be lower (6.6 mmol/l for 2 hr postprandial glucose value after 75 gm oral glucose load) and point out that the WHO values may not pick up GIGT in some cases due to subregional and ethnic variations[10,11].

Except for macrosomia, the major factors contributing to increased risk of morbidity and mortality in the neonates of diabetic mothers (respiratory

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distress, growth restriction, polycythaemia, hypoglycaemia, congenital malformations, hypocalcaemia and hypomagnesaemia) are not described in neonates of mothers with GIGT[12]. The literature on the effects of GIGT on neonates is however very scanty.

The most common pancreatic pathology found in 85% of neonates of mothers with gestational diabetes are islet hypertrophy, increase islet cell volume, pleomorphism of B-cell nuclei, eosinophilic insulitis of large islets, peri- and intrainsular fibrosis[13]. Some features appear more constantly in reported cases then others. Occasionally the same features have been described in pancreas of the neonates of prediabetic and "normal" mothers, which probably represent cases of non-established impaired glucose tolerance. To our knowledge, there is no study done on gestational diabetes in Ghana.

The purpose of this report therefore is to document clinical and autopsy findings in a neonate of a mother who had fasting hyperglycaemia, but did not show typical glucose values for GIGT or GDM after 75 gm oral glucose load and to call attention to the increased risk of hypoglycemia in such infants.

Case Report

A male neonate was admitted after delivery at the Neonatal Intensive Care Unit Korle-Bu Teaching Hospital on account of blue asphyxia. He was delivered by caesarian section due to transverse lie and previous caesarian section. The mother was G2P1+1; a regular attendant at the antenatal clinic who complained of unexplained weakness and had fasting hyperglycaemia, however did not show other abnormalities after 75 oral glucose load at 31 weeks (5.6 mmol/l fasting blood glucose and 7.5mmol/l 2-h postprandial glucose after 75 gm loading dose). She was diagnosed as GIGT though the values did not meet the WHO criteria and managed on diet[9] only. Two subsequent fasting glucose levels before delivery were within normal limits. No repeat of 2-hour postprandial glucose was done.

On examination he was a mature infant, weight 3300gm, dull, pale with blue extremities, in respiratory distress (respiratory rate-148 per min) but adequate air entry bilaterally, and no transmitted sounds or crepitations. He had tachycardia with regular pulse, heart rate 140 beats per min, with normal heart sounds and no murmur. Other systems were normal.

Initial diagnoses were: 1. Severe respiratory distress; 2. Mild birth asphyxia; 3. Anemia ?cause.

He was put under radiant heater for warmth and oxygen was given by mask. Random blood glucose was checked and it was 2.2mmol/l and 2.6mmol/l later. IVF 157 ml 10% Dextrose/24 hrs, IV Ampicillin 157 mg/12 hrs and IV Gentamicin 12.6 mg/24 hrs were started. However, after 22 hours of admission the child ceased breathing and no cardio-pulmonary activity was noted. Resuscitation measures were not successful.

On postmortem, external examination showed a male mature neonate. His weight was 3200gm, head circumference - 36 cm, chest- 32 cm and crown-heel 48 cm. The skin and mucosal membranes were pale and there was peripheral cyanosis. The umbilical stump was intact. The main gross pathological findings were solid, rubbery and reddish lungs, which sunk in water, congested internal organs, shock kidneys and cerebral oedema with cyanosed grey matter and markedly congested white matter. The pancreas was not enlarged, but it was firm in consistency. Its weight was normal (27gm) and no ectopic pancreatic tissue was found. Whole pancreas, representative samples of lungs and kidneys were taken for further histological examination.

Histological examination of the lungs revealed patchy atelectasis, vascular congestion with intra alveolar fibrin deposition and micro haemorrhages. Focally some of alveolar walls were lined by waxy hyaline membranes (Figure 1).

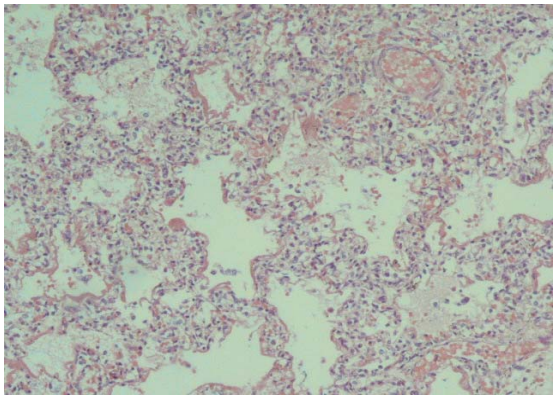

Figure 1 Lung with hyaline membranes and congestion of septae. H &E,X 400

Section of kidneys showed severe acute tubular necrosis predominantly along the proximal tubule

segment with hyaline and granular pigmented cast formation. Focal necrosis was seen in the distal tubules (Figure 2). The pancreas showed interstitial primary islets present only focally, but giant islets or islet hypertrophy were not noted. There was infiltration of the pancreatic mesenchyme by lymphocytes and occasional eosinophils not associated with the largest islets. The intestitial fibrous septae were thickened (Figure 3).

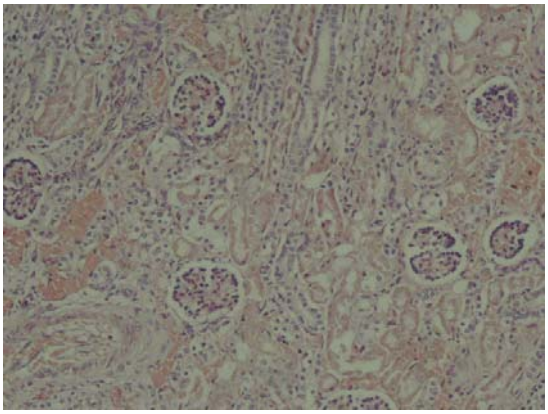

Figure 2 Kidney with tubular necrosis. H&E, X400.

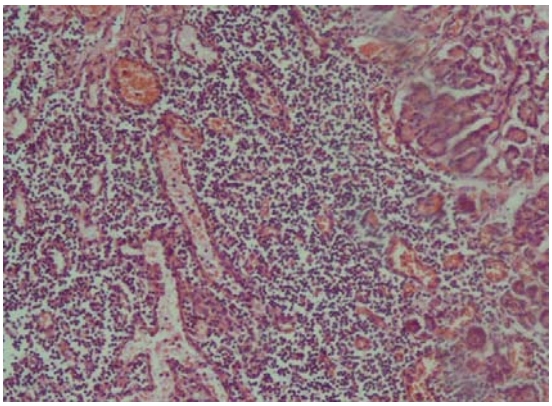

Figure 3 Pancreas with interstitial lymphocytic infiltrate. H&E, X400.

Histological diagnoses of acute respiratory distress syndrome and ischemic type of acute tubular necrosis were made. The cause of death was certified as cerebral hypoglycaemia.

DISCUSSION

In the presented case the neonate was born to a mother who had impaired fasting hyperglycaemia, not well established GDM, based on 5.6 mmol/L for fasting blood glucose and 7.5 mmol/L for 2-h postprandial glucose values.

Studies done in Nigeria[14,15] show that mean fasting plasma glucose +2 standard deviations (SD) of all pregnant women was 5.3 mmol/l and 2 h postprandial glucose level (75 g oral glucose tolerance test) at 2-SD and 4-SD above the mean were 6.5 mmol/l for impaired glucose tolerance and 8.0 mmol/l for gestational diabetes. Although these figures would allow the labeling as impaired glucose tolerance, they are much lower than the WHO and ADA values for the diagnosis of the condition and by the standards of both the mother only had impaired fasting glycaemia [8, 9]. The blood glucose data was inadequate to confirm impaired glucose tolerance and because the OGTT was not repeated, total exclusion of gestational diabetes is impossible as well.

Gross evidence of shock was present in this case (shock lungs, shock kidneys, cerebral oedema) and histological features can be explained by hypoglycaemia or possible hypocalcaemia or combination of both.

The main differential diagnosis in this case is respiratory distress syndrome in newborn, which presents similarly grossly, but histologicaly characterized by poor development of alveoli with massive atelectasis of alveoli and presence of hyaline membrane.

The features of ischemic acute tubular necrosis (ATN) in kidneys are consistent with changes due to inadequate blood flow due to marked hypotension and shock. However, in ischemic ATN necrotic areas are patchy, affecting in most cases proximal tubules and ascending limbs of Henle's loop. In this case the necrotic areas were found in both proximal and distal tubules that suggest presence of toxic type of ATN that could explained by administration of antibiotics such as Gentamicin.

We did not see islet hypertrophy or increased islet cell volume, but observed the presence of large septal primary islets, that is different from features of normal full term pancreas with endocrine tissue lying centrally within developing lobules.

The eosinipholic peri-insulitis, which has been reported in 50% of pancreas of neonates from pregnancies complicated by GDM, was absent in this case, but lymphocytes infiltration and interstitial septal fibrosis were present. The significance of lymphocytic infiltration of the pancreas is still controversial. Though it described by some authors in pancreas of newborn from GDM pregnancies, others suggest that it is an independent find-

ing probably involved in the degeneration of primary islets [13]. The similarity of the autopsy findings in the pancreas to that of a neonate of a diabetic mother and the fact that the oral glucose tolerance test was not repeated, would make exclusion of full blown gestational diabetes in the mother impossible.

CONCLUSION

We conclude that this is a case of perinatal death from hypoglycaemia in an infant of a mother who had fasting hyperglycaemia diagnosed at 31 weeks of gestation. It was not certain that the mother in this case did not have gestational diabetes mellitus since the tests were not repeated and the histological features of the pancreas were similar to that described in the neonate of a diabetic mother.

We therefore emphasize that all pregnant women with inconclusive glucose values for diagnosis of full blown gestational diabetes mellitus during an oral glucose tolerance test should have the tests repeated[8,9] (preferably with a 100gm loading dose) and closely monitored during antenatal care. Infants of such mothers may be at a higher risk of hypoglycemia in the immediate post-natal period.

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