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CASE REPORT

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Transient neonatal diabetes or neonatal hyperglycaemia: A case report

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Abstract Transient neonatal diabetes and neonatal hyperglycaemia both present in the neonatal period with features of hyperglycaemia, dehydration and weight loss. Differentiating these conditions clinically is difficult. We describe the case of a 13 day old female whom we managed recently who could have had either condition. Hyperglycaemia is not as commonly documented as would be expected for the frequency of neonatal disease and when it does occur, it will worsen neonatal morbidity and mortality. Blood glucose levels in babies on dextrose infusion should be monitored regularly in order to help individualise glucose requirements.

Introduction

Neonatal hyperglcaemia has been defined by various authors, with slightly different blood glucose levels. Digiacomo[1] et al defines neonatal hyperglycaemia as a blood sugar greater than 8.3mmol/L in preterm babies, and blood sugar greater than 6.9mmol/L in term babies. Kallapur[2] et al defines neonatal hyperglycaemia as a blood sugar level above 6.9mmol/L following a 4 hour fast in neonates. Hyperglycaemia may coexist with a number of clinical conditions in the neonatal period though, more commonly, hypoglycaemia is likely to exist.

Two clinical entities, somewhat similar in presentation and treatment but differing in aetiology and prognosis, present with hyperglycaemia in the newborn period; neonatal diabetes and transient neonatal hyperglycaemia. Both conditions present with hyperglycaemia with severe dehydration, glycosuria, and absent ketonuria[2,3] usually on a background of a septicaemia.[4] The conditions are differentiated with serum insulin studies, levels being normal in the baby with transient neonatal hyperglycaemia.

The case below highlights an encounter with a neonate who could have had either of both conditions. Unfortunately, our inability to perform a serum insulin assay, and the continued deterioration until eventual demise of this infant, left us without a definite diagnosis. This case is highlighted so that we may realise the contributory effect that hyperglycaemia, when present, has to neonatal mortality.

Case report

Baby ST was a 13 day old female delivered at a gestational age of 38 weeks, birth weight 2.5kg. She presented with a 12 hour history of refusal of feeds and seizures, which were noted at presentation. There was no history of fever, diarrhoea or vomiting and she was being exclusively breast fed; frequency and adequacy of feeds were apparently appropriate. Seizure was generalized tonic and was aborted with paraldehyde. The baby was delivered at the Teaching Hospital after 8 hours of labour, and there was no history suggestive of perinatal asphyxia. The mother is a 22 year old primiparous who attended ANC at the Teaching Hospital. Duration of pregnancy was not adversely eventful.

On examination, she was acutely ill looking with a wizened facie, she was severely dehydrated, febrile (38.8^0C), with poor peripheral perfusion and with features of a chest infection. Weight at admission was 1.4kg (56% of birth weight), OFC 35cm, and length 48cm. Investigations revealed a random blood sugar of 20.1mmol/L (glucometer), 18.7mmol/L (glucose oxidase); PCV 55%, Platelets $180x10^{12/L}$, WBC $14.8x10^{9/L}$ with polymorphs 46%, lymphocytes 42%; Serum electrolytes Na 133mmol/L, K 3.1mmol/L; BUN Urea 18.9mmol/L, Creatinine 224mmol/L. Urine showed + glucose but no ketones. The assessment made at this time was that of a 13 day old term female with Primary Failure to Thrive, with Sepsis and an Acute Renal Injury complicating dehydration. At that time she was too ill to have a lumbar puncture done. She received two boluses of normal saline at 20ml/kg/dose over the first two hours. At the end of the second bolus she made 2ml of

urine and, her random blood glucose (RBS with the glucometer) was now 19.7mmol/L.
She continued on normal saline at 15% deficit minus anti-shock. A repeat RBS an hour later showed 17.3mmol/L. At this point she was commenced on soluble insulin at 0.05IU/kg/hr[3] as hourly boluses. Intravenous Ceftazidime was commenced and 2hourly RBS estimations continued. Nine hours after admission RBS dropped to 12.6mmol/L; at this time intravenous fluids were changed to 4.3% dextrose in 0.18 saline. Two hours later, blood glucose dropped to 9.8mmol/L and remained between 7.8 and 10.4mmol/L over the next 8 hours. Insulin studies were not done as facilities for this are unavailable in this environment.

At 38hr on admission, her clinical condition was found to have deteriorated, with temperature instability, diminished peripheral pulses, and worsening peripheral perfusion in spite of adequate hydration. Blood sugar fluctuated between 11.0 and 15.9mmol/L. At this point we assumed that Systemic Inflammatory Response Syndrome had set in and started her on dopamine at 5µg/kg/min. The two-hourly blood glucose estimation and intravenous insulin continued. From about the 47 hour on admission, blood glucose was noted to have begun to decline, falling to 8.0mmol/L; at that time the insulin dose was skipped. She died at the 63 hour on admission and it was noted that the final two readings before her demise were within normal limits (3.6mmol/L and 2.8mmol/L).

A post-mortem lumbar puncture revealed bloody CSF on macroscopic appearance. Microscopically, RBC were numerous, 30 WBC/cmm^3 with 20% lymphocytes and 80% PMN, no growth on culture. Her parents unfortunately declined a post mortem.

Discussion

Hyperglycaemia is thought to be associated with a number of primary pathologic conditions [infection, asphyxia, hyperosmolality (following hyperosmolar feeds or hypernatraemic dehydration), seizures, respiratory distress][2,5] and drugs [steroids, β^2 agonists, phenytoin, theophylline, intravenous glucose infusion][5] used in the neonatal period. It is also more common in the preterm and intrauterine growth restricted (IUGR) infant, as they appear to have a reduced capacity for insulin secretion.[6] In clinical practice, hyperglycaemia mostly occurs following the introduction of glucose containing intravenous fluids, and responds appropriately to a reduction in the glucose concentration of the infusion. The evidence for hyperglycaemia occurring with or as a complication of other clinical entities are few; Nalini et al[5] working with 1171 neonates found a prevalence of 0.94% (prevalence in very low birth weight babies was 2.9%), in this environment documentation of the occurrence of hyperglycaemia occurring with/complicating primary morbidities is nonexistent. Give the frequency of neonatal illness, it is either this problem does not occur, or is poorly documented when it does occur.

Neonatal diabetes can also cause neonatal hyperglycaemia. It is defined as persistent hyperglycaemia occurring in the first months of life, lasting for more than 2 weeks and requiring insulin for management.[7] It is considered distinct from autoimmune type 1 DM, which manifests after the first 3 to 6 months of life.[8] It is a rare disorder, occurring in only 1:500,000 live births,[7] and may be permanent or transient with/without recurrences.[9] The condition was first described in the infant son of a physician who presented with polydypsia, polyphagia, polyuria, dry skin after birth.[3] It is characterised by hyperglycaemia, glycosuria, hypoinsulinnaemia and absent or minimal ketonuria. Babies are usually full term, small for gestational age, and described as having an aged appearance and alert facies.[10] Babies with the transient form respond to insulin with normalization of growth and weight gain, and remission is usually apparent by about the 3rd month of life.[11] In majority of cases, the child relapses at about the age of puberty (median age 14 years) with type 2 (nonautoimmune) diabetes.[11] Growth and development however remain normal. In the permanent form (about half of babies presenting with neonatal diabetes), insulin therapy is needed for life.[12]

In the case of the neonate highlighted, she presented with clear features of failure to thrive, with sepsis and dehydration. In majority of instances, in our clinical experience, the result of a random blood sugar done at admission would usually require for hypoglycaemia to be corrected. The finding of hyperglycaemia in the diabetic range is indeed a rare occurrence, and for that reason insulin is not one of the usual drugs in the NICU emergency arsenal.

Treatment of the underlying cause is usually sufficient to correct hyperglycaemia in neonates with transient neonatal hyperglycaemia. Unfortunately in this case, we lost the opportunity to arrive at a definitive diagnosis/ arrive at a definite cause of the hyperglycaemia as the baby gave in early into the primary pathology, and we lacked the capacity to run serum insulin assay. Reversion of her blood glucose to near normal levels terminally was more likely due to a terminal hepatic insufficiency.

Conclusion

Hyperglycaemia, though not a primary diagnosis on its own, is capable of worsening morbidity and mortality. It therefore needs to be handled as a separate entity with insulin therapy. In the case highlighted, while not giving total credence to the hyperglycaemia, it is certain that it contributed to poor outcome. As has been previously stated, it is more common for hypoglycaemia to be the co-morbid finding at admission of most sick neonates. The finding of hyperglycaemia, demonstrated here, further buttresses the need for random blood sugar estimation to become part of routine admission work-up.

Taking into cognisance that hyperglycaemia is more likely to occur in babies on intravenous glucose infusion, it may become necessary, as a matter of principle, to check blood glucose levels in babies in dextrose infusion; this would help us individualise glucose requirements.

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