Diabetic ketoacidosis in an uncommon setting: management and neuromonitoring in a neonate

Cetoacidosis diabética en un escenario infrecuente. Manejo y neuromonitorización en un neonato

Dear Editor:

Neonatal diabetes mellitus (NDM) manifests with persistent hyperglycaemia in the first 6 months of life. It is an infrequent diagnosis (incidence, 1:90 000–1:160 000 live births[1,2]). The presentation at onset varies, ranging from asymptomatic to diabetic ketoacidosis (DKA).[1,2] The main complication of DKA is cerebral oedema, although poorly controlled hyperglycaemia has also been associated with neurologic and cognitive deficits.

We present the case of a male neonate with adequate weight (3815 g; z score, 0.92), with no history of interest, admitted at 24 h post birth due to respiratory distress, pallor and lethargy. The vital signs were normal. Respiratory support was initiated with nasal continuous positive airway pressure, in addition to antibiotherapy. The patient required volume expansion with isotonic saline solution. The initial laboratory tests evinced hyperglycaemia (>685 mg/dL), metabolic acidosis (pH, 7.10; bicarbonate, 3.8 mmol/L) and ketonaemia (serum ketones, 6.1 mmol/L). The initial workup included blood tests, microbiological tests, lumbar puncture and toxicology testing.

Due to the suspicion of DKA, having ruled out other possible causes of hyperglycaemia, we initiated intravenous insulin therapy at a dose of 0.025 IU/kg/hour. The suspicion was confirmed by the following results: beta-hydroxybutyrate level, 8 nmol/L (<1 nmol/L); plasma insulin below 0.2 μIU/mL (2.6–24.9 μIU/mL); C-peptide, 0.10 ng/mL (1.10–4.40 ng/mL); free fatty acids, 1.88 mmol/L (0.10—0.60 mmol/L).

In relation to fluid therapy, the patient developed osmotic diuresis, yet did not have clinically significant dehydration. He lost 6.5% of his birth weight, which was within the range of physiological weight loss in the first hours of life. Therefore, we calculated the fluid replacement rate to compensate for the diuresis past 2 mL/kg/h. After 6 h of infusion of isotonic saline solution, glucose was added to maintain blood glucose levels in the normal range (150—200 mg/dL). The patient did not develop any electrolyte imbalances, and required 1.5 mEq/kg/day of potassium acetate.

We remained watchful for the development of clinical signs of cerebral oedema. We monitored the regional cerebral oxygen saturation by means of near-infrared spectroscopy (NIRS) and repeated head ultrasounds. The cerebral oxygen saturation values obtained by NIRS were of approximately 80%, without significant changes during the care episode.

The transcranial doppler ultrasound scan evinced increased peak systolic and end-diastolic velocities of 48.3 and 20.8 cm/s, respectively (normal values, ∼39.5 cm/s and ∼11.4 cm/s) with a decreased resistance index of 0.57 (0.6—0.8).

The ketoacidosis resolved after 20 h of intravenous insulin therapy (maximum, 0.08 IU/kg/h). At 12 days, the patient started treatment with continuous subcutaneous insulin infusion. The illness had resolved completely by age 6 months, and turned out to be a transient form of NDM. He did not develop any complications and his neurodevelopment was normal.

The diagnostic evaluation included an echocardiogram and an abdominal ultrasound examination, both of which were normal. Genetic testing did not detect pathogenic variants associated with NDM.

Neonatal diabetes is infrequent, and its diagnosis requires a high level of suspicion.[1,2] In our patient, the presence of hyperglycaemia, ketonaemia and metabolic acidosis suggested the onset of diabetes, which responded well to insulin therapy.[1,2]

The main complication of DKA is cerebral oedema. It is clinically significant in 0.3%–1% of patients, in which case it is associated with a high mortality (20%–30%), and it is more likely the more severe the DKA.[3]

Initial hypotheses on its aetiology proposed that cerebral oedema was secondary to the abrupt change in serum osmolality on treatment initiation; later, the Pediatric Emergency Care Applied Research Network (PECARN) group demonstrated that the fluid administration rate was not associated with the rate of brain injury.[4] Furthermore, there is evidence that in many cases, brain injury is already present at the time of treatment initiation.[3,5] Therefore, cerebral oedema would not be the cause but the consequence of brain injury.

New hypotheses regarding cerebral oedema in the context of DKA suggest that oedema would develop through a complex pathophysiological mechanism involving cytotoxic, ischaemia-reperfusion and inflammatory processes, resulting in impaired cerebrovascular autoregulation and a decreased brain oxygen consumption.[3]

This would be consistent with the high values obtained by NIRS. Glaser et al. used NIRS to monitor patients with DKA. Eighty-seven percent of patients had regional cerebral oxygen saturation values greater than 80%, independent of the fluid administration rate. In addition, these high values persisted for hours after DKA had been resolved.[6] This is also what we observed in our patient.

In our patient, another Doppler ultrasound finding was consistent with the impairment of cerebrovascular autoregulation. The increases in the peak systolic and end-diastolic velocities, in addition to the decreased resistance, were evidence of cerebral hyperaemia. This supports the hypothesis of ischaemia-reperfusion being involved in the development of brain injury, as the features were the same as those found in infants with cerebral reperfusion injury.

In conclusion, we present the case of a patient with a clinical presentation that is rare in the neonatal period, with evidence of impaired cerebrovascular autoregulation during the follow-up, in spite of which the patient did not develop clinically relevant brain injury or any associated sequelae.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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