CASE REPORT

Persistent hyperlactacidaemia: about a clinical case

Ana Rita Saraiva Oliveira,¹ Rosalina Valente,² José Ramos,² Lurdes Ventura²¹Department of Pediatrics, Hospital São Teotónio-Centro Hospitalar Tondela Viseu, Viseu, Portugal²Department of Pediatric Intensive Care Unit, Hospital Dona Estefânia—Centro Hospitalar Lisboa Central, Lisboa, Portugal

Correspondence to

Ana Rita Saraiva Oliveira, ritas-oliveira@hotmail.com

SUMMARY

Lactate is the endogenous end product of the anaerobic glycolysis, whose production is favoured in situations of hypoperfusion or mitochondrial dysfunction. Leigh syndrome is a rare, progressive encephalomyopathy that represents a spectrum of mitochondrial genetic diseases phenotypically distinct, but with neuroradiological and pathological uniform presentation. We present the case of a 7-month-old infant, with a history of prematurity, psychomotor retardation and epilepsy, admitted to the paediatric intensive care unit (PICU) due to cardio-respiratory arrest because of respiratory infection. Hyperlactacidaemia was detected and was persistent. The study of redox potential was normal but MRI with spectroscopy identified bilateral and symmetrical lesions involving thalamic and basal ganglia, with small lactate peaks at T2 flair, findings that were suggestive of Leigh syndrome. Subsequent enzymatic study identified lack of pyruvate dehydrogenase. Persistent hyperlactacidaemia, in the appropriate clinical context, should lead to the screening of mitochondrial diseases.

BACKGROUND

Lactate is the endogenous end product of anaerobic glycolysis, formed in the final step of the metabolic process, by the action of lactate dehydrogenase on pyruvate.^{1 2} In normal aerobic conditions, lactate is constantly produced and consumed, and mostly is converted into pyruvate by oxidation in the mitochondria; the remainder is the precursor of the neoglucogenesis process.

The blood level of lactate is generally less than 2 mmol/l, and its production increases in situations of hypoperfusion and shock or mitochondrial dysfunction, including this case genetic (like mitochondrial diseases) or acquired conditions (such as systemic inflammatory response syndrome or liver toxicity, in most cases pharmacological).¹

The degree and duration of hyperlactacidaemia are actually considered important prognostic markers, with the monitoring of lactate blood levels being very important in critical patients, like those admitted to the intensive care units.

Metabolic diseases that are associated with defects of lipid and carbohydrate metabolism can also produce hyperlactacidaemia and the lactate levels are one of the key elements in the screening of this group of diseases.^{3 4}

CASE PRESENTATION

A nursing infant, male, 7 months old, with outcome of medically-assisted reproduction, with monochorionic trigemellar pregnancy and antecedents of prematurity (32 weeks of gestational age) was admitted to the neonatal intensive care immediately after

birth, where he remained for 52 days, requiring invasive mechanical ventilation until the 10th day of life.

After discharge, disruption of motor development and slight axial hypotonia persisted, which required referral to physiotherapy.

At 6 months, he was admitted to paediatric department with five episodes of generalised tonic-clonic seizures that appear with no fever, since then medicated with phenobarbital 5 mg/kg/day.

The patient was admitted to the paediatric intensive care unit (PICU) for cardio-respiratory arrest because of respiratory infection, probably of viral aetiology, with about 10 days of evolution, and for which he was observed in emergency department on the second day of the disease and has been medicated with symptomatic therapy (nasal decongestants, antipyretics) and nebulized bronchodilators.

On admission to the PICU, he presented a lactate level of 7.02 mmol/l. In subsequent evaluations, the lactate level was persistently elevated (>3 mmol/l).

INVESTIGATIONS

In the context of persistent hyperlactacidaemia after the acute phase and with the patient clinically stable, and also because of the psychomotor retardation and epilepsy, a study of redox potential was made, finding a lactate/pyruvate ratio of 8.

Imagiological evaluation by brain magnetic resonance (BMR) with spectroscopy study already made, identified bilateral and symmetrical lesions, involving thalamic and basal ganglia bilaterally with hyperintensity on T2 flair (figure 1), with small

Figure 1 Image of brain magnetic resonance with bilateral and symmetrical lesions, involving thalamic and basal ganglia bilaterally with hyperintensity on T2 flair.

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Figure 2 Spectroscopy study, with small peaks of lactate at this level, aspects of Leigh syndrome.

peaks of lactate at this level (figure 2), aspects that were suggestive of Leigh syndrome.

The dosage of pyruvate dehydrogenase was requested, finding a lack of its activity. The molecular study is in course.

The monozygotic twin was also evaluated, and a mild psychomotor retardation and also persistent hyperlactacidaemia were found; this resulted in the request for the same investigation to be done on his brother, and pyruvate dehydrogenase deficiency was diagnosed.

OUTCOME AND FOLLOW-UP

In the PICU, the children required ventilator support and maintenance; feeding difficulties were known to the mother, which resulted in tracheostomy and percutaneous gastrostomy.

During this period, he had some complications such as ventilator-associated pneumonia and sepsis associated with a central catheter; a rise in blood levels of lactate was noticed.

DISCUSSION

Leigh syndrome, described in 1951 by Denis Leigh, is rare genetic and progressive encephalomyopathy, with an estimated incidence of 1 : 40 000 stillborns.

It represents the most frequent expression of mitochondrial encephalopathy, corresponding to a spectrum of distinct genetic and phenotypical group of diseases which share the same neuroradiological and neuropathological characteristics, mainly symmetrical bilateral focal lesions found in areas of grey matter (base ganglia, thalamus, cerebellum, brain stem). The complementarity study with spectroscopy allows, through the determination of lactate peaks, greater diagnostic accuracy with a high predictive value.^{5 6}

Often associated with prematurity (not completely understood), the disease is manifested mostly by neurological

symptomatology (like development retardation, ataxia, seizures, dystonia, strabismus, feeding problems) but also non-neurological symptoms (like gastro-oesophageal reflux, gastro-intestinal dysfunction, cardiomyopathy, renal changes dimorphisms).

Generally the clinical signs appear during the first year of life, coinciding with a viral infection, as in the case presented, because the infectious complications are the main cause of decompensation.⁷

The disease has a progressive character, culminating in the death at the end of early childhood, generally because of heart and/or respiratory failure.^{3 8 9} Respiratory failure usually is multifactorial, and contributes to neurological changes, muscle weakness and the resulting metabolic acid enzymatic deficit. The patient in this study was aggravated by infectious complication, which was capable of generating greater respiratory muscle work, which culminated in cardio-respiratory arrest.

Learning points

- ▶ Persistent hyperlactacidaemia without hypoxia, and in appropriate clinical context, should imply the screening of metabolic diseases, especially mitochondrial disorders such as the pyruvate dehydrogenase deficits.
- ▶ The case described has a typical presentation; however it becomes particularly relevant by an emerging manifestation that led to hospitalisation in paediatric intensive care unit.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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