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LETTER TO THE EDITOR

Fatal type B lactic acidosis in a patient with end-stage liver disease related to homozygous sickle cell disease

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Hepatic involvement by sickle cell disease (SCD) can result in a variety of symptoms ranging from mild to life-threatening. Acute intrahepatic cholestasis is a rare but often fatal condition, with multi-organ failure as a terminal event. The following observation is suggesting that extreme hyperbilirubinemia may be associated with energetic failure.

A 16-year-old girl was admitted to the intensive care unit (ICU) for seizures. She had a complicated medical past history in relation to homozygous SCD. At the age of 3 months, she received a liver transplantation for a fulminant hepatic failure due to neonatal hemochromatosis. At the age of 15, she developed a chronic renal failure with a corticoresistant nephrotic syndrome due to a membranoproliferative glomerulonephritis and focal segmental glomerulosclerosis connected with sickle cell nephropathy. A few months later, she developed a progressive liver disease with jaundice. Liver biopsy could rule out rejection and was in favor of sickle cell–related sinusoidal and centrilobular damage. She had a progressive worsening of liver function, with a predominant cholestatic pattern, and of her chronic renal failure. She was treated by blood exchange transfusions to lower hemoglobin S levels. The recent hospital admission was justified by the worsening of kidney injury leading to intermittent hemodialysis. Additionally, she presented coagulation disorders in relationship with hepatic and renal failure, but also with a thrombocytopenia from both central and peripheral origin. A catheter-related infection due to *Staphylococcus epidermidis* caused bacteremia. She complained of headache and a brain computed tomography revealed a limited subarachnoid hemorrhage at the convexity of the right frontal lobe, without evidence of intracranial hypertension. She then presented four episodes of generalized tonic-clonic seizures and was transferred to the ICU after having received a total of 16 mg midazolam and a loading dose of 750 mg intravenous levetiracetam. She was put on mechanical ventilation, continuous venovenous hemofiltration (CVVH), and continuous electroencephalogram (EEG) monitoring. Admission laboratory investigations revealed total bilirubin 59.9 mg/dL, ALAT 120 IU/L, INR 1.9, creatinine 5.39 mg/dL, platelet count 26,000/μL, hemoglobin S 0.7%, and arterial lactate 7.6 mmol/L. Hemodynamic conditions were stable without vasopressors. The continuous EEG monitoring confirmed the control of epileptic activity and levetiracetam therapy (750 mg b.i.d) was maintained; the patient became progressively responsive to pain and voice. By contrast, lactic acidosis continued to progress despite bicarbonate administration and CVVH, and the patient died 24 h after ICU admission. There was no direct evidence for cardiogenic, hypovolemic, or septic shock. Just before death, blood was drawn for lactate/pyruvate determination and a very high lactate/pyruvate ratio was found (lactate 30.73 mmol/l, pyruvate 0.35 mmol/l, L/P = 87.8); additionally, hypoglycemia was noted with a ratio of blood 3-hydroxybutyric acid/acetoacetate of 6.03. Mitochondrial toxicity was suspected as hyperlactatemia due to dysoxia seemed unlikely. The only medication that was introduced recently was levetiracetam. Among the other medications simultaneously prescribed, none was considered a potential inducer of type B

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lactic acidosis. Among epileptic drugs, levetiracetam is not known to induce lactic acidosis and is safely used in patients with epilepsy related to mitochondrial diseases [1]. Lactic acidosis following convulsions is usually less severe and self-limiting with short-lasting seizures [2]. The last hypothesis could be that this type B lactic acidosis was the terminal manifestation of sickle cell hepatopathy (SCH), perhaps precipitated by recent infection, seizures, or drugs. Acute liver failure may be the primary cause of death for 8–10.7% of patients with SCD [3, 4]. Extreme hyperbilirubinemia appears as a key indicator for severe SCH [5]. Energetic failure due to mitochondrial breakdown may be one of the possible presentations of this end-stage liver disease.

Compliance with ethical standards

Consent An informed consent was obtained from the relatives.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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