Case Report / Olgu Sunumu

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Type B Lactic Acidosis in A Child with Relapsed non-Hodgkin Lymphoma

Nüks non-Hodgkin Lenfomalı Bir Çocukta Tip-B Laktik Asidoz

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Abstract

Lactic acidosis is a major cause of metabolic acidosis in critically ill patients. Herein we report a child with relapsed non-Hodgkin's lymphoma admitted to the pediatric intensive care unit (PICU) with profound lactic acidosis. On admission, he was treated with fluid replacement and a vasopressor, followed by continuous veno-venous hemodiafiltration to correct acidosis. As lactic acid levels remained high despite all treatments, thiamine was added to the therapy, which did not influence metabolic status either. Lactic acidosis could only be corrected by aggressive chemotherapy during his stay in the PICU. The patient died on the 68th day of PICU admission due to underlying progressive disease. Clinicians should start aggressive chemotherapy as soon as possible in patients with a recurrence or advanced cancer who have type-B lactic acidosis.

Keywords: Non-Hodgkin lymphoma, lactic acidosis, metabolic acidosis

Öz

Laktik asidoz, kritik hastalarda metabolik asidozun başlıca nedenlerindendir. Bu olgu sunumunda, derin laktik asidoz ile çocuk yoğun bakım ünitesine yatırılan, relaps non-Hodgkin lenfomalı bir çocuğu sunuyoruz. Yatışı takiben hastaya sıvı replasmanı ve vazopresör verildi, ardından asidozun düzeltilmesi için sürekli veno-venöz hemodiyafiltrasyon uygulandı. Tüm tedavilere rağmen laktik asit seviyeleri yüksek kaldığından, tedaviye tiamin eklendi ancak asidoza yanıt alınamadı. Laktik asidoz, yoğun bakım ünitesinde kaldığı süre boyunca ancak agresif kemoterapi ile düzeltilebildi. Hasta çocuk yoğun bakım ünitesine kabulünün 68. gününde altta yatan progresif hastalık nedeniyle kaybedildi. Klinisyenler, tip-B laktik asidozlu nüks veya ilerlemiş kanserli hastalarda mümkün olan en kısa sürede agresif kemoterapiye başlamalıdır.

Anahtar Kelimeler: Non-Hodgkin lenfoma, laktik asidoz, metabolik asidoz

Introduction

One of the most common causes of metabolic acidosis in critically ill patients is lactic acidosis (LA).[1] LA is predominantly derived from impaired tissue oxygenation, which is later called type-A LA. Drugs, toxins, hereditary metabolic diseases, vitamin deficiency, and malignancy are among the causes of type-B LA, in which the lactic acid is related to cellular metabolism.[2] Herein we report a patient with lymphoma admitted to the pediatric intensive care unit (PICU) with profound type B LA, which only resolved with chemotherapy.

Case Report

A 10-year-old boy had a non-Hodgkin's lymphoma diagnosis five months ago. He had completed the BFM 2012 protocol 15 days ago. The disease relapsed as the bone marrow aspiration and biopsy revealed mature B-cell leukemia infiltration. He was admitted to the PICU due to profound LA. On admission, he had tachycardia with a heart rate of 135/minute. Arterial blood pressure was 123/79 mmHg with normal peripheral pulses and capillary refill time. Invasive mechanical ventilation was started on admission due to hyperpnea and tachypnea. Preliminary laboratory studies showed increased anion gap

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metabolic acidosis (pH: 7.04, pCO_2: 36.2 mmHg, HCO_3: 9.5 mmol/L, lactate: 9.9 mmol/L), leukocytosis, anemia, and thrombocytopenia with a white blood cell count of 25.1x10^3 cells/µL, hemoglobin of 6.3 g/dL, and platelet count of 42x10^3 cells/µL. Peripheral blood smear revealed L3 type blasts, compatible with bone marrow biopsy results. Renal function tests were normal. Aspartate aminotransferase was increased to 303 U/L, alanine aminotransferase was 42 U/L, and the glucose level was 65 mg/dL. Lactate dehydrogenase levels were extremely high at 20777 U/L. The chest X-ray was normal. Echocardiography showed normal systolic function with a 68% ejection fraction. The computer tomography scan of the chest and abdomen revealed new mediastinal and mesenteric lymphadenopathies.

Cytoreductive prophase therapy, a regimen consisting of corticosteroids (dexamethasone 10 mg/m^2 daily for 5 days) and low-dose cyclophosphamide (200 mg/m^2 daily for 2 days) was started. Noradrenaline infusion was started after adequate intravenous fluid replacement for the underlying shock, although he had no signs of impaired tissue perfusion. Red blood cell transfusion was administered to maintain the hemoglobin level above 7 g/dL. Meropenem and teicoplanin were added empirically since sepsis could not be ruled out as he had a fever of 38 °C and a mildly increased C-reactive protein of 9.2 mg/L. As lactic acid remained high (reaching a level of 15 mmol/L despite fluid replacement and vasopressors), continuous veno-venous hemodiafiltration therapy was started. It was discontinued 9 days later since it had no effect on metabolic acidosis. Type-A LA was ruled out. Thiamine 200 mg/day was administered intravenously for 5 days, which was later continued per oral with biotin 10 mg/day. Lactic acid levels did not diminish with vitamin replacement either.

On the 7th day of PICU admission, ICE chemotherapy was added to rituximab. The ICE protocol included ifosfamide (1500 mg/m^2 daily for 3 days), carboplatin (450 mg/m^2 daily for 1 day) and etoposide (100 mg/m^2 daily for 3 days). The lactate level decreased to normal throughout the 3-day ICE protocol while his white blood cell count was declining to zero (Figure 1). The patient's lactic acid remained low until the white blood cell count-mostly consisting of blasts- started rising on the 25th day of PICU admission. He received the second course of ICE therapy and regained metabolic stability immediately. During this episode, LA responded only to ICE chemotherapy (Figure 1). The patient died on the 68th day of PICU admission due to underlying progressive disease.

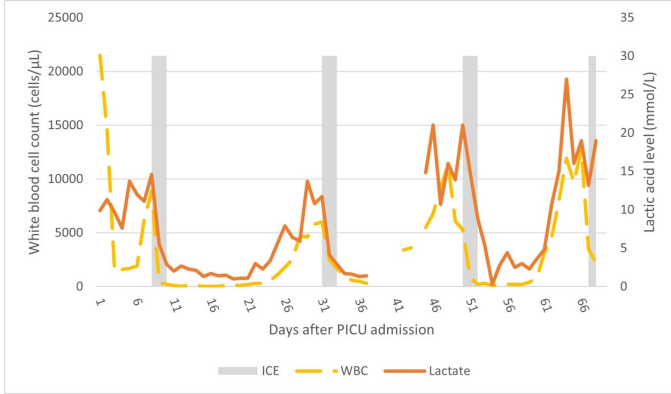

Figure 1. White blood cell count and lactate levels throughout chemotherapy
PICU: Pediatric intensive care unit, WBC: White blood cell

Discussion

LA is caused by the accumulation of lactate and protons in the body's fluids and is frequently associated with unfavorable clinical outcomes.[3] The higher lactate reflects the worse outcome.[1] Frequently, hyperlactatemia is associated with tissue hypoxia in critically ill children.[2] When our patient was admitted to the PICU, we tried conventional therapies targeted at restoring tissue perfusion and oxygenation. We started invasive ventilation, administered adequate intravenous fluid, started a vasopressor infusion, and broad-spectrum antibiotics. LA persisted despite hemodynamic stabilization.

Thiamine deficiency due to insufficient intake and replacement leads to profound LA and encephalopathy, which responds immediately to thiamin administration.[4] Due to underlying malnutrition, our patient could have developed thiamin deficiency. We tried thiamin administration, which had no influence on the lactic acid level.

We administered bicarbonate infusion on the first day of admission, then continuous veno-venous hemodiafiltration for 9 days to correct metabolic acidosis. None of these measures influenced his lactate level.

Type-B LA is thought to be a rare complication of malignancy. Lymphomas, leukemia, and less commonly, solid tumors cause LA via increased glycolytic activity of malignant cells and tumor tissue hypoxia.[2,5] Type B LA is a rare complication that has a poor prognosis in leukemia and lymphoma patients.[6] After other interventions, our patient's LA only responded to chemotherapy targeting the underlying malignancy. In conclusion, although most patients with LA have hemodynamic compromise, it may develop in the absence of impaired tissue oxygenation. Clinicians should consider the early administration of aggressive chemotherapy to cancer patients with recurrent or advanced disease who develop type B LA. Parents of the patient gave informed consent prior to this report.

Ethics

Informed Consent: Parents of the patient gave informed consent prior to this report.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: T.B., E.Ç., G.E., Design: T.B., G.Ö., G.A., Data Collection or Processing: T.B., G.E., G.A., Literature Search: T.B., E.Ç., M.D., Writing: T.B., G.A., E.Ç., M.D.

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