

Severe Lactic Acidosis Associated with Burkitt's Lymphoma

Burkit Lenfomada Ciddi Laktik Asidoz

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Abstract

Lactic acidosis is a metabolic acidosis caused by either overproduction or underutilization of lactic acid. Overproduction of lactic acid, known as type A lactic acidosis, is frequent in critically ill patients with hypoperfusion states. Underutilization of lactic acid, known as type B lactic acidosis, is caused by many reasons, including hepatic and liver failure, thiamine deficiency, toxins, drugs, and certain malignancies such as lymphomas and leukemias. We report a patient with severe lactic acidosis and Burkitt's lymphoma without any signs of hypoperfusion that is relieved with chemotherapy. (*Yoğun Bakım Derg* 2015; 6: 57-9)

Keywords: Burkitt's lymphoma, lactic acidosis, metabolic acidosis

Received: 05.02.2015 **Accepted:** 27.05.2015

Özet

Laktik asidoz, laktik asidin aşırı üretimi veya yetersiz yıkılması sonucu oluşan bir tür metabolik asidozdur. Aşırı üretimi tip A laktik asidoz olarak isimlendirilir ve genellikle yoğun bakım hastalarında görülen hipoperfüzyon durumuna bağlı olarak gelişir. Tip B laktik asidoz laktik asidin yetersiz bir şekilde elimine edilmesinden kaynaklanır ve karaciğer yetmezliği, böbrek yetmezliği, tiamin eksikliği, toksinler, lösemi ve lenfoma gibi bazı maligniteler ve ilaç kullanımı gibi birçok nedeni vardır. Herhangi bir hipoperfüzyon bulgusu olmadan ciddi laktik asidozu olan ve kemoterapi ile düzelen Burkit Lenfomalı bir hastayı bildirdik. (*Yoğun Bakım Derg* 2015; 6: 57-9)

Anahtar sözcükler: Burkit lenfoma, laktik asidoz, metabolik asidoz

Geliş Tarihi: 05.02.2015 **Kabul Tarihi:** 27.05.2015

Introduction

Lactic acidosis is a common cause of metabolic acidosis in critically ill patients with diminished tissue perfusion. The most common reason for lactic acidosis is anaerobic metabolism secondary to low tissue perfusion and tissue hypoxia (Type A). However, lactic acidosis is also observed secondary to impaired oxidative phosphorylation without low tissue perfusion and tissue hypoxia (Type B). Type B lactic acidosis is associated with numerous clinical conditions, such as liver disease (decreased clearance of lactate), diabetes mellitus, thiamine deficiency, mitochondrial toxins (alcohol, salicylate, reverse transcriptase inhibitors, metformin, etc.), stroke, malignancies, and hereditary enzyme defects (1).

Furthermore, lactic acidosis is reported in patients with lymphoma. It is reported as a rare clinical condition with significant consequences (2). The mechanism of lactic acidosis in lymphoma is not exactly known, and management strategies are unclear. We report a case of lactic acidosis associated with lymphoma.

Case Presentation

A previously healthy 67-year-old man presented with a 2-month history of severe fatigue, generalized weakness, 7-kg weight loss, abdominal pain, and discomfort. He reported low-grade fever and night sweats. No change in bowel habits or urinary pattern was reported. On physical examination, he appeared cachectic with generalized muscle wasting. His temperature was 37.1°C (98.7°F), blood pressure was 117/72 mmHg, heart rate was 104 beats/min, and respiratory rate was 26 breaths/min. The patient had right lower quadrant tenderness and pain. A firm, tender, and fixed mass, measuring approximately 10 cm, was palpated in the right lower quadrant of the abdomen. Physical exam findings were otherwise normal.

Laboratory data revealed the following serum levels: sodium 133 mmol/L, potassium 4.7 mmol/L, chloride 100 mmol/L, blood urea nitrogen 26 mg/dL, creatinine 0.8 mg/dL, bicarbonate 5 meq/L, anion gap 28, glucose 93 mg/dL, lactate dehydrogenase 1706 U/L, aspartate transaminase 51 U/L, alanine transaminase 16 U/L, and uric acid 11.8 mg/dL. Complete

We presented this case at 11th Congress of The Turkish Society of Medical and Surgical Intensive Care Medicine (12-15 November, Antalya, Turkey).

Bu çalışma 11. Ulusal Dahili ve Cerrahi Bilimler Yoğun Bakım Kongresi'nde sunulmuştur (12-15 Kasım 2014, Antalya, Türkiye).

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DOI: 10.5152/dcbbyd.2015.759

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blood count revealed leukocyte 5.8×10^9 , hemoglobin 11.7 g/dL, and platelet 277×10^9 . Peripheral blood smear revealed no blast cells or abnormal leukocytes. Arterial blood gas revealed a pH of 7.29, PCO_2 10.3 mmHg, PO_2 88.2 mmHg, and lactate 11.3 mmol/L. Previously drawn blood cultures were negative. Other laboratory findings were within normal limits.

There was a big pelvic mass (12 x 12 cm), multiple small lymph nodes, and ascites were observed with computed tomography of the abdomen. Trucut biopsy obtained from the pelvic mass revealed the diagnosis of Burkitt's lymphoma.

The patient was transferred to the medical intensive care unit (ICU) upon developing respiratory distress and altered mental status. Metabolic acidosis was further increased to pH 7.17 with lactate levels of 13.8 mmol/L. The patient had to be intubated and ventilator support was initiated because of progressive respiratory distress. He was sedated with midazolam. He was hemodynamically stable with mean arterial pressure above 65 mmHg, and there were no any signs of low tissue perfusion. Urine output was above 1 ml/kg/h. Intravenous volume resuscitation and bicarbonate therapies were initiated. Despite aggressive volume resuscitation, lactate levels during the first 24 h were 12.7 mmol/L. Chemotherapy with vincristine, cyclophosphamide, and prednisolone was initiated the next day. Arterial lactate levels started to decline 12 h after the initiation of chemotherapy to 8.6 mmol/L. At 36 and 48 h, lactate levels were 2.7 mmol/L and 0.7 mmol/L, respectively, after chemotherapy.

Piperacillin-tazobactam was initiated on the 4th day of his admission because of fever above 38.3°C and serum procalcitonin level of 2.9 ng/mL after necessary samples were taken for tests. *Klebsiella pneumoniae* was observed when the sample from the endotracheal aspirate was cultured, and the antibiotic was changed to imipenem. He was successfully extubated on the 4th day of mechanical ventilation. He was transferred to the medical ward 2 days after extubation.

Discussion

Lactic acid is an end product of the anaerobic metabolism of glucose. Lactic acid is primarily metabolized to glucose by the liver, and a small percentage is metabolized by the kidneys. There are two different types of lactic acid. The first one is L-lactic acid produced by mammals, and the second one is D-lactic acid produced by bacteria. Type D-lactic acidosis is produced by intestinal bacteria because of the bacterial overgrowth in the ischemic bowel, short bowel syndrome, and intestinal obstruction (1). There are two types of lactic acidosis, either with overproduction or decreased clearance of lactic acid produced in mammalian cells. Type A lactic acidosis occurs with decreased tissue perfusion. There is no decreased tissue perfusion and tissue hypoxia in type B lactic acidosis. Type B lactic acidosis is associated with numerous clinical conditions, such as liver disease (decreased clearance of lactate), diabetes mellitus, thiamine deficiency, mitochondrial toxins (alcohol, salicylate, reverse transcriptase inhibitors, metformin, etc.), stroke, malignancies, and hereditary enzyme defects (3).

Lactic acidosis associated with leukemia and high-grade lymphomas were also reported. Lactic acidosis associated with hematological malignancies is very rare; however, it is associated with the high rate of mortality and morbidity (4). The mechanism of lactic acidosis in hematological malignancies is unclear, and there are many hypotheses trying to explain pathophysiology of lactic acidosis. It was claimed that diminished tissue perfusion and ischemia related to microembolus to tumor mass or pressure to vessels may cause lactic acidosis (5). Hepatic or renal failure secondary to tumor cell infiltration or ischemic injury may

also cause lactic acidosis; however, cancer patients with hepatic or renal failure do not develop lactic acidosis (2). Our patient did not have hepatic or renal failure.

Another hypothesis claims that some molecules that increase glycolysis in tumor cells are overexpressed. Type II hexokinase is a mitochondrial glycolytic enzyme, and it is overexpressed in tumor cells (6). Increased insulin-like growth factor binding protein that led to increased glycolysis was observed in cancer cells (4). Lactic acidosis and hypoglycemia demonstrated increased expression of both molecules (2, 7). We did not observe any hypoglycemic event in our patient during the ICU course.

Moreover, it was reported that tumor necrosis factor decreases pyruvate dehydrogenase enzyme activity by paracrine activity and leads to increase in lactate levels (8).

Thiamine is a cofactor for pyruvate dehydrogenase, and its decreased level causes lactic acidosis (9). We did not measure thiamine level; however, thiamine was intravenously administered to our patient.

Alcohol, salicylates, methotrexate, reverse transcriptase inhibitors (10), and metformin (11) cause lactic acidosis; however, our patient did not receive any of these medications.

Our patient was hemodynamically stable without any signs of low tissue perfusion; however, he had tachypnea and tachycardia that is consistent with the systemic inflammatory response syndrome. We considered that he had type B lactic acidosis with stable hemodynamics, normal central venous oxygen saturation, and absent low tissue perfusion signs.

Treatment for lactic acidosis that developed secondary to hematological malignancies is not known (4). Intravenous sodium bicarbonate and hemodialysis can be used until chemotherapy is initiated (12). Intravenous sodium bicarbonate can be administered for protection from respiratory failure and hemodynamic instability secondary to severe metabolic acidosis; however, this treatment can cause severe side effects, including hypervolemia and hypernatremia (13). In addition, lactic acid levels can be increased with sodium bicarbonate infusion (12). Renal replacement therapies (RRT) can decrease lactate levels and improve metabolic acidosis (14); however, we did not perform RRT because metabolic acidosis was controlled with volume resuscitation and sodium bicarbonate infusion, and lactate levels were abruptly decreased with the initiation of chemotherapy.

Primary treatment for malignancy-dependent lactic acidosis is chemotherapy. Chemotherapy should be initiated as soon as possible unless there is no contraindication. Lactic acid levels start to decrease with chemotherapy within hours, and it may take weeks to achieve normal levels (15). We initiated chemotherapy on the second day of ICU admission, lactate levels significantly decreased at the 12th hour, and normal levels were observed at the 48th hour after chemotherapy. Faster recovery compared with other cases reported can be secondary to aggressive volume resuscitation and high sensitivity of Burkitt's lymphoma to chemotherapy.

Conclusion

Type B lactic acidosis can be rarely observed in hematological malignancies and is a sign of poor prognosis. If there is an easily correctable reason such as thiamine deficiency and drugs causing lactic acidosis should be corrected. Otherwise, intravenous volume resuscitation and bicarbonate should be administered to control severe metabolic acidosis until chemotherapy is initiated.

Informed Consent: Due to the retrospective design of the study, written informed consent was not taken.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - R.C., H.M.; Design - R.C., H.M.; Supervision - K.G., R.C.; Resource - K.G., R.C.; Data Collection and/or Processing - G.E., I.B., K.G.; Analysis and/or Interpretation - H.M., K.G., R.C.; Literature Review - H.M., G.E., I.B.; Writer - H.M., R.C.; Critical Review - K.G., R.C.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Hasta Onamı: Çalışmanın retrospektif tasarımından dolayı yazılı hasta onamı bu çalışmaya katılan hastadan alınmamıştır.

Hakem değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - R.C., H.M.; Tasarım - R.C., H.M.; Denetleme - K.G., R.C.; Kaynaklar - K.G., R.C.; Veri toplanması ve/veya işlemesi - G.E., I.B., K.G.; Analiz ve/veya yorum - H.M., K.G., R.C.; Literatür taraması - H.M., G.E., I.B.; Yazıyı yazan - H.M., R.C.; Eleştirel İnceleme - K.G., R.C.

Çıkar Çatışması: Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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