A Case of Acute Lymphoblastic Leukemia Accompanied with Lactic Acidosis and Kidney Enlargement

Han Su Cho, M.D., Seung Oh Choi, M.D., Dong Chun Seol, M.D.,
Hyun Sung Yoon, M.D., Young-Il Jo, M.D. and Hong Ghi Lee, M.D., Ph.D.

Department of Internal Medicine, Konkuk University School of Medicine, Seoul, Korea

There have been several reported cases of acute lymphoblastic leukemia with severe lactic acidosis in adults. In these cases, kidney and liver enlargement that was caused by leukemic infiltration frequently accompanied the acute lymphoblastic leukemia and severe lactic acidosis. Chemotherapy is the only treatment that can rapidly correct the lactic acidosis and normalize the liver and kidney enlargement. We report here on a case of acute lymphoblastic leukemia that was accompanied with severe lactic acidosis and kidney enlargement. ***(Korean J Hematol 2008;43:170-173.)***

Key Words: Acute lymphoblastic leukemia, Lactic acidosis, Leukemic infiltration, Kidney enlargement, Liver enlargement

INTRODUCTION

It has been rarely reported that acute lymphoblastic leukemia is accompanied with severe lactic acidosis in adults. In that case, kidneys and liver enlargement resulting from leukemic infiltration are frequently accompanied.[1,2] According to the references, chemotherapy is the only way to ameliorate the lactic acidosis associated with hematological malignancies, which prognosis is very poor.[2,3,4]

We reports a case of acute lymphoblastic leukemia accompanied with severe lactic acidosis and kidney enlargement. Following systemic chemotherapy and an allogeneic stem cell transplantation, the patient remained in free of leukemia for 15 months after a leukemia diagnosis.

CASE REPORT

An 18 year-old male was presented with upper abdominal discomfort with indigestion for 3 weeks and weight loss of 12kg over a month. He denied smoking or alcohol intake. There was no remarkable past medical history or family medical history.

On physical examination, his blood pressure was 125/82mmHg; pulse rate 101/minute; respiration rate 26/minute; body temperature 36.2°C. He appeared moderately ill and distressed and mildly dehydrated; otherwise, there was no significant abnormal finding.

On the day of admission, WBC count was 4,440/μL, Hb 8.9g/dL, platelet count 56,000/μL, ESR 8mm/hr., CRP 3.4mg/dL, BUN 30.7mg/dL,

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교신저자 : 이홍기, 서울시 광진구 화양동 4-12
㉾ 143-729, 건국대학교 의과대학 내과학교실
Tel: 02-2030-7521, Fax: 02-2030-7748
E-mail: mlee@kuh.ac.kr

Correspondence to : Hong Ghi Lee, M.D., Ph.D.
Department of Internal Medicine, Konkuk University School of Medicine
4-12, Hwayang-dong, Gwangjin-gu, Seoul 143-729, Korea
Tel: +82-2-2030-7521, Fax: +82-2-2030-7748
E-mail: mlee@kuh.ac.kr

creatinine 1.1mg/dL, Ca 9.7mg/dL, AST 38IU/L, ALT 25IU/L, lactic acid 12mmol/L, glucose 85 mg/dL, LDH 1,875IU/L. An initial arterial blood gas study on room air showed pH 7.29, PCO_2 21.4 mmHg, PO_2 152.8mmHg, HCO_3 10.3mmol/L, O_2 saturation 99.2%. A bone marrow biopsy and aspiration demonstrated lymphoid blasts of 85%, a cellularity of 90%, which was diagnostic of T cell type acute lymphoblastic leukemia. Leukemic markers were positive for CD2++, CD4+++, CD5++, CD7++, CD8+++, CD34+, and HLA-DR+. A chromosomal study showed 46, XY, t (9; 13), t (9; 14) [3]/46, XY [7]. A p16 deletion was detected in 12% of tested cells for ALL FISH.

A computed tomography (CT) of abdomen showed diffuse enlargement of both kidneys, measuring 13.1cm and 13.4cm, respectively (Fig. 1).

On the hospital day 5, he began to undergo a daily hemodialysis. Although the arterial pH was corrected with repeated hemodialysis and urine alkalinization, the blood lactic acid concentrations and arterial HCO_3 were not improved at all. On the hospital day 8, an induction chemotherapy, DVPAps regimen (daunorubicin, vincristine, prednisolone, asparaginase) started for the treatment of acute lymphoblastic leukemia. The blood lactic acid concentration decreased to 2.5mmol/L and HCO_3 increased to 32.5mmol/L within 2 days following chemotherapy (Fig. 2). On the hospital day 39, a bone marrow biopsy and aspirate showed pathological complete remission and a abdominal CT revealed marked decrease in the size of both kidneys, 9.9cm and 11.4cm, respectively (Fig. 3).

About 6 months after the diagnosis of acute leukemia, he underwent an allogeneic peripheral blood stem cell transplantation from a HLA-matched unrelated donor following 3 cycles of consolidation chemotherapy. He has been doing well in persistent complete remission for 9 months after the transplantation.

DISCUSSION

Lactic acidosis is a condition in which exces-

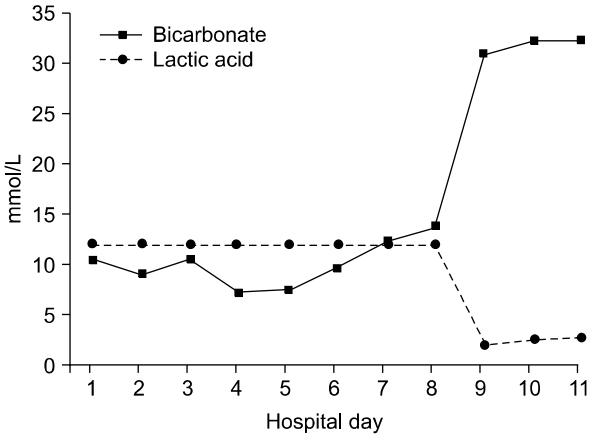

Fig. 2. Changes of bicarbonate and lactic acid. Graph reveals changes of lactic acid & bicarbonate level after hemodialysis (HD #5) & chemotherapy (HD #8).

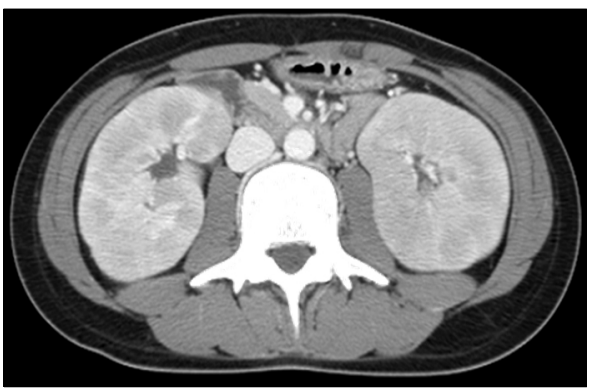

Fig. 1. Initial abdominal CT. Abdominal CT reveals diffuse parenchymal swelling of both kidneys.

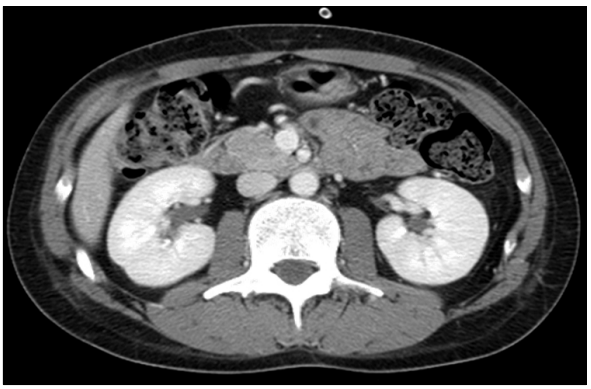

Fig. 3. Abdominal CT after chemotherapy. Abdominal CT after chemotherapy reveals normalization in the size of both kidneys.

sive lactic acid results from the imbalance between production of lactic acid from the tissues that perform glycolysis and consumption of it from the tissues that use lactic acid. Lactic acid, which is the end product of anaerobic glycolysis, is produced when the oxygenation is inadequate, and is metabolized into glucose again in the liver and kidney.[1-3] Lactic acidosis is classified into type A lactic acidosis, induced by extensively low diffusion and hypoxia as the result of circulatory failure such as shock, sepsis and hypoxia, and type B lactic acidosis induced by hematological malignancies.[1,3,6] The pathophysiology of type B lactic acidosis in patients with hematological malignancy has been still uncertain, but it is considered to be multifactorial.[1-5]

Firstly, lactic acid is converted to pyruvate and then to glucose in the liver and kidney.[1-3] In patients with hematologic malignancy there occurs dysfunction in the liver and kidney owing to the tumor infiltration and ischemic damage, thus decreasing lactate clearance and finally accumulating lactate.[1,3,5,7]

The other mechanism is concerned with overexpression or aberrant expression of glycolytic enzymes such as hexokinase and insulin like growth factor-1. Tumor cells overexpress hexokinase or insulin like growth factor-1 and increase glycolysis, which raises the glucose level, and consequently, proliferates tumor cells again. Since tumor cells use anaerobic metabolism despite the existence of oxygen, a lot of glucose turns to lactic acid.[1-3,5]

TNF-alpha also is known as one of significant factors in developing type B lactic acidosis. TNF-alpha deactivate of pyruvate dehydrogenase and change of hepatic glucose metabolism which result in increased levels of lactate. Thiamine deficiency is another factor when considering the development of type B lactic acidosis.[1,2] Thiamine is an important contactor of pyruvate dehydrogenase complex, so without thiamine, this enzyme fails to convert pyruvate to actetyl coenzyme A and instead anaerobic metabolismt occurs by conversion into lactate.[1,4]

In this patient, the cause of type B lactic acidosis is considered to be multiple. But based on the fact that the patient's initial WBC count was not high, main cause of lactic acidosis is considered to be decrease of the lactate clearance by kidney infiltration of leukemic cell. Since the patient could not have the liver and kidney biopsy because of several conditions including the decrease of platelet, it was impossible to prove histologically if there was the leukemic infiltration or not. Reviewing previous case report, liver and kidney biopsy was done in only a few of cases. In many cases, existence of leukemic infiltration of liver and kidney was examined through CT findings only. It needs to consider, through further research, the necessity of the liver and kidney biopsy proving the existence of leukemic cell infiltration before chemotherapy.

Hemodialysis and alkalization is an effective treatment in the case of type A lactic acidosis, but type B lactic acidosis which is associated with hematological malignancies does not respond to hemodialysis or alkalization, and is only resolved by chemotherapy.[2,3,5] Hemodialysis and alkalization was performed on our patient in order to eliminate the lactic acid, resulting in no change of the blood lactic acid level and HCO_3 concentration. However, after starting chemotherapy, the patient had improvement in symptoms and the blood lactic acid level and HCO_3 concentration showed improvement (Fig. 2). Abdominal CT after the chemotherapy also showed resolution of both kidney enlargements.

The marker study is thought to be in need of further research as few studies have mentioned it.[1]

As seen in this case, patients with acute lymphoblastic leukemia accompanied by lactic acidosis have liver and/or kidney infiltrations, and chemotherapy is the only treatment that can rapidly correct lactic acidosis and normalize liver and kidney infiltrations. Hematological malignancy must be considered as the underlying dis-

ease in patients with lactic acidosis with an unknown reason. We report our experience and successful treatment of a patient with acute lymphoblastic leukemia associated with severe lactic acidosis and kidney enlargement.

요 약

성인에서 급성림프구성벽혈병과 동반된 심한 젖산증은 드물게 보고되고 있으며 젖산증이 발현되는 경우 신장이나 간의 침윤으로 인한 비대가 흔하게 동반된다. 문헌에 의하면 혈액학적 악성종양과 연관된 젖산증은 오직 항암치료에 의해서만 해소가 되는 것으로 보고되고 있다. 저자들은 급성림프구성백혈병과 심한 젖산증, 신장 침범이 동반된 환자를 경험하였기에 보고하는 바이다.

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