


A Rare Case of Severe Lactic Acidosis in a Patient With Mantle Cell Lymphoma

Journal of Investigative Medicine High
Impact Case Reports
Volume 9: 1–3
© 2021 American Federation for
Medical Research
DOI: 10.1177/23247096211034040
journals.sagepub.com/home/hic


Kok Hoe Chan, MD¹ , Laxminarayan Prabhakar, MD¹,
Omar Al-Radideh, MD¹, Byron Okwesili, MD¹,
Gowthami Are, MD¹, and Hamid Shaaban, MD¹

Abstract

Lactic acidosis is an extremely rare paraneoplastic manifestation of hematological malignancies, and often carries an extremely poor prognosis. Mantle cell lymphoma is an aggressive and rare form of non-Hodgkin lymphoma. To the best of our knowledge, it is extremely rare to have severe lactic acidosis in patients with mantle cell lymphoma. In this article, we are reporting a rare case of mantle cell lymphoma diagnosed with typical cluster differentiation (CD markers) in bone marrow examination with persistent lactic acidosis refractory to intravenous hydration that responded well to chemotherapy. Malignant lactic acidosis is a medical emergency that needs rapid evaluation and identification that shows improved prognosis after the introduction of chemotherapy.

Keywords

lactic acidosis, mantle cell lymphoma, non-Hodgkin lymphoma

Introduction

Mantle cell lymphoma (MCL) accounts for approximately 7% of adult non-Hodgkin lymphoma in the United States and Europe.¹ The prevalence of MCL increases with age, with 68 years being the median age of diagnosis. MCL is theorized to have 2 separate cellular origins,^{2,3} giving rise to different clinical presentations. The classical pathway involves lymph nodes and extra nodal sites such as the gastrointestinal tract. Classical MCL also comprises B-cells that express SOX 11 that block the differentiation of B-cells. The leukemic MCL, on the other hand, involves peripheral blood, bone marrow, and occasionally the spleen but usually spares the lymph nodes.^{2,3} MCL is an aggressive and rare form of non-Hodgkin lymphoma. To our knowledge, it is extremely rare to have severe lactic acidosis in patients with MCL. Lactic acidosis has been reported frequently in diffuse large B-cell lymphoma but not with MCL. Herein, we present a case of a 59-year-old gentleman with severe lactic acidosis and newly diagnosed MCL.

Case Report

A 59-year-old man presented to the emergency room complaining of abdominal pain and distention for 2 months duration. He also complained of 35 lbs unintentional weight loss, loss of appetite, shortness of breath, dizziness, and generalized weakness. He otherwise denied fever, chills, and night

sweats. Initial vital signs were stable and physical examination was only notable for a soft, distended abdomen with tenderness over the left upper quadrant. Complete blood count showed pancytopenia, with white blood cell count of 2.4/ μ L ($4.4-11 \times 10^3/\mu$ L), hemoglobin 8.2 g/dL (13.5-17.5 g/dL), and platelets 60/ μ L (150-400/ μ L). Initial complete metabolic panel showed bicarbonate 15 mmol/L (22-28 mmol/L), alkaline phosphatase 118 U/L (40-115 U/L), and lactic acid 10.1 mmol/L (0-2 mmol/L). Computed tomography abdomen pelvis with oral and IV (intravenous) contrast showed massive splenomegaly measuring about $26 \times 17 \times 9$ cm, with a minimum volume of 2 L along with retroperitoneal and mediastinal lymph nodes. The patient then underwent a bone marrow biopsy, which showed a hypercellular bone marrow and florid population of B-cell lymphocytes positive for CD5, CD20, CD22, CD43, CD79a, cyclin D1, and BCL-2 with rare CD10 positive B-cell lymphocytes, and negative CD23 (Figure 1a-e). Scattered background T-cell lymphocytes were highlighted with CD3. Rare hematopoietic cells

¹Saint Michael's Medical Center, New York Medical College, Newark, NJ, USA

Received June 2, 2021. Revised June 26, 2021. Accepted July 1, 2021.

Corresponding Author:

Kok Hoe Chan, MD, Department of Internal Medicine, Saint Michael's Medical Center, 111, Central Avenue, Newark, NJ 07101, USA.
Email: kchan2@primehealthcare.com



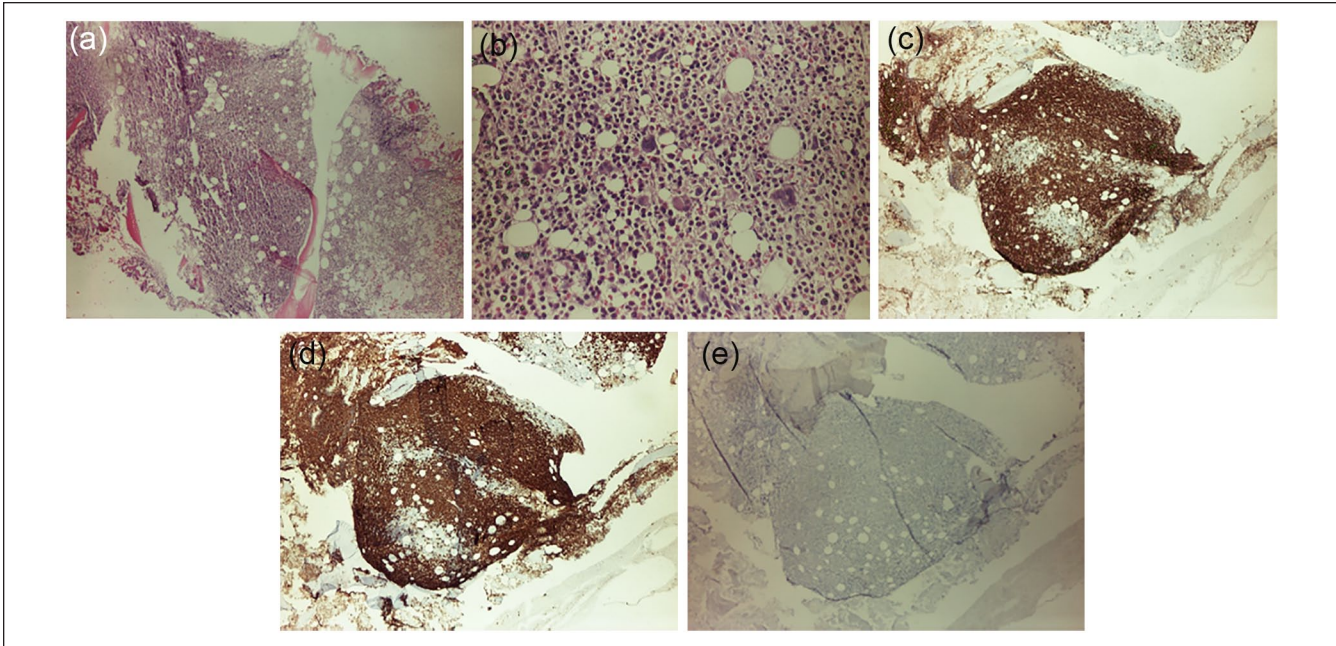


Figure 1. (a) Bone marrow biopsy which showed a hypercellular bone marrow and florid population of B-cell lymphocytes on hematoxylin and eosin stain at 40× magnification. (b) Bone marrow biopsy which showed a hypercellular bone marrow and florid population of B-cell lymphocytes on hematoxylin and eosin stain at 40x magnification. (c) Bone marrow biopsy which showed a hypercellular bone marrow and florid population of B-cell lymphocytes that stained positive for CD5. (d) Bone marrow biopsy which showed a hypercellular bone marrow and florid population of B-cell lymphocytes that stained positive for CD20. (e) Bone marrow biopsy which showed a hypercellular bone marrow and florid population of B-cell lymphocytes that stained positive for CD23.

including dysmorphic megakaryocyte were noted. The patient was diagnosed with MCL.

Management and Outcome

Throughout his stay in the hospital, he had persistently elevated type B lactic acidosis that was non-responsive to fluids. Only on starting therapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) as an outpatient did an improvement in lactic acidosis become evident. A computed tomography scan of the abdomen pelvis with IV contrast, midway through the R-CHOP cycles, showed massive splenomegaly with several unchanged prominent retroperitoneal lymph nodes, but an improvement in lactic acidosis was seen. The patient was subsequently referred for evaluation for hematopoietic stem cell transplant.

Discussion

Lactic acidosis is defined as serum lactic acid of more than 5 mmol/L with serum pH of <7.35 and further classified based on the underlying physiology.⁴ Lactic acid is generated by fermentation of glucose molecules and consists of L-lactate found in humans and D-lactate that is seen in bacterial species. Lactate is further subdivided into B, A, and D according to the main mechanism leading to it.⁵ Type B lactic acidosis in malignancy has a unique mechanism that can be accounted for by the preference of malignant cells for the glycolytic

pathway even in normoxic conditions favoring proliferation, commonly known as the Warburg effect. In most cases the liver can utilize the Cori cycle to counteract lactic acidosis.⁶ The development of persistent lactic acidosis may indicate neoplastic liver infiltration^{7,8}; however, in patients with intact liver function with no evidence of metastases there is still much to explore about what predisposes these patients to lactic acidosis. Also the presence of high levels of lactate may reflect the poor prognostic outcome of the malignancy.⁸ It has been suggested that vitamin or enzyme deficiencies affect the metabolic pathways leading to high levels of lactic acid. Of these vitamins, thiamine deficiency or riboflavin might have an essential role in development of type B lactic acidosis.^{4,9} This observation is strengthened by improvement in type B lactic acidosis via the supplementation of intravenous thiamine.¹⁰

Hematological malignancy associated with lactic acidosis was commonly reported in aggressive lymphoid tumors but other malignancies such as multiple myeloma have also been reported.¹¹ Of the published studies on type B lactic acidosis in hematological malignancy, non-Hodgkin lymphoma accounted for about 52% of the cases. Lactic acidosis has also been frequently reported in patients with diffuse large B-cell lymphoma. This association not only indicated a poor prognosis but also carries a very high risk of mortality.⁸ To the best of our knowledge, MCL with severe type B lactic acidosis was rarely reported. Ohtsubo and colleagues¹² have reported one case of blastoid variant of MCL that showed

complete normalization of lactic acid after successful treatment with chemotherapy and rituximab maintenance therapy. The exact mechanism and pathogenesis of lactic acidosis in MCL is still poorly understood. Based on the theories of the Warburg effect, the extensive proliferation of the malignant cells in MCL, which favor the glycolytic pathway, may lead to severe lactic acidosis. However, further study is still needed to explore this complex relationship of MCL and lactic acidosis.

Management and treatment for MCL is complex and choosing the appropriate strategy and systemic treatment depends on many factors including but not limited to age, physical fitness, presence of normal lactate dehydrogenase deficiency and B symptoms.¹³ Until the chemotherapy can control the tumor and suppress the production of the lactic acid, several treatment approaches such as bicarbonate infusion and renal replacement therapy may be adopted to control the lactic acid, as to prevent the devastating sequelae of its accumulation including hemodynamic instability and respiratory muscle failure.^{5,14} All in all, the management of severe lactic acidosis in patients with malignancy should be centered on the treatment of the cancer, which in most cases will improve the lactic acidosis.

Conclusion

Lactic acidosis is an extremely rare paraneoplastic manifestation of hematologic malignancies and often carries an extremely poor prognosis. Improvement is seen in a limited number of cases following initiation of chemotherapy. Lactic acidosis has been reported frequently in patients with diffuse large B-cell lymphoma. To our knowledge, this is one of the few cases to report such a severe lactic acidosis in a patient with MCL. Further studies are necessary to explore the complex relationship of MCL and lactic acidosis.

Acknowledgments

We would like to express our gratitude to Dr Eliezer Segueria for the pathology images.

Author Contributions

KHC contributed to the conception and design, acquisition, analysis, and interpretation of data, as well as participate in drafting and revision of the manuscript. LP, OA, and BO actively participated in analysis of data, drafting, and revision of manuscript. GA and HS contributed to idea design, data analysis, and critically revised the manuscript and approved the final submission of manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iD

Kok Hoe Chan  <https://orcid.org/0000-0002-2550-1122>

References

1. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of haematological malignancy by sub-type: a report from the Haematological Malignancy Research Network. *Br J Cancer*. 2011;105:1684-1692.
2. Jares P, Colomer D, Campo E. Molecular pathogenesis of mantle cell lymphoma. *J Clin Invest*. 2012;122:3416-3423.
3. Vegliante MC, Palomero J, Pérez-Galán P, et al. SOX11 regulates PAX5 expression and blocks terminal B-cell differentiation in aggressive mantle cell lymphoma. *Blood*. 2013;121:2175-2185.
4. Luft D, Deichsel G, Schmülling RM, Stein W, Eggstein M. Definition of clinically relevant lactic acidosis in patients with internal diseases. *Am J Clin Pathol*. 1983;80:484-489.
5. Fall PJ, Szerlip HM. Lactic acidosis: from sour milk to septic shock. *J Intensive Care Med*. 2005;20:255-271.
6. Ruiz JP, Singh AK, Hart P. Type B lactic acidosis secondary to malignancy: case report, review of published cases, insights into pathogenesis, and prospects for therapy. *ScientificWorldJournal*. 2011;11:1316-1324.
7. Sayyed AH, Aleem A, Al-Katari MS, et al. Acute lymphoblastic leukemia presenting with liver infiltration and severe lactic acidosis. *Am J Case Rep*. 2018;19:453-457.
8. Sillos EM, Shenep JL, Burghen GA, Pui CH, Behm FG, Sandlund JT. Lactic acidosis: a metabolic complication of hematologic malignancies: case report and review of the literature. *Cancer*. 2001;92:2237-2246.
9. Friedenber AS, Brandoff DE, Schiffman FJ. Type B lactic acidosis as a severe metabolic complication in lymphoma and leukemia: a case series from a single institution and literature review. *Medicine (Baltimore)*. 2007;86:225-232.
10. Masood U, Sharma A, Nijjar S, Sitaraman K. B-cell lymphoma, thiamine deficiency, and lactic acidosis. *Proc (Bayl Univ Med Cent)*. 2017;30:69-70.
11. Sia P, Plumb TJ, Fillaus JA. Type B lactic acidosis associated with multiple myeloma. *Am J Kidney Dis*. 2013;62:633-637.
12. Ohtsubo K, Imamura R, Seki R, et al. Blastoid variant of mantle cell lymphoma with lactic acidosis: a case report. *Int J Hematol*. 2004;80:428-431.
13. Jain P, Wang M. Mantle cell lymphoma: 2019 update on the diagnosis, pathogenesis, prognostication, and management. *Am J Hematol*. 2019;94:710-725.
14. Prikis M, Bhasin V, Young MP, Gennari FJ, Rimmer JM. Sustained low-efficiency dialysis as a treatment modality in a patient with lymphoma-associated lactic acidosis. *Nephrol Dial Transplant*. 2007;22:2383-2385.