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# Case of Fatal Type B Lactic Acidosis in Primary Undifferentiated Ovarian Cancer

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**Abstract**

Lactic acidosis, characterized by an imbalance between lactic acid production and clearance, presents a significant challenge in the management of critically ill patients. Although commonly attributed to tissue hypo perfusion or hypoxemia (Type A), recent years have witnessed increasing reports of Type B lactic acidosis associated with malignancies, posing diagnostic and therapeutic dilemmas as well as the question of its true prevalence in solid malignancies. We present the first reported case of Type B lactic acidosis with extensive undifferentiated ovarian carcinoma in a 46-year-old female, highlighting the complexities in its diagnosis and management. Despite surgical intervention and supportive care, the patient experienced persistent lactic acidosis, hypoglycemia, and multiorgan dysfunction. Diagnostic considerations included tissue ischemia, sepsis, and the Warburg phenomenon. Management challenges included sepsis with no signs of infection and early chemotherapy initiation amidst critical illness. Ultimately, the patient's deteriorating condition led to a transition to comfort care measures, reflecting the grave prognosis associated with malignancy complicated by Type B lactic acidosis. This case underscores the need for heightened awareness of Type B lactic acidosis in the oncologic setting, emphasizing the importance of early recognition and tailored interventions to optimize patient outcomes.

**Keywords:** Lactic Acidosis; Warburg Phenomenon; Solid Tumor Malignancy; Undifferentiated Ovarian Carcinoma; Chemotherapy; Case Report.

**Teaching Points:** Understanding Type B lactic acidosis and its relationship to the Warburg phenomenon; Clinical presentation and complications; Management strategies; Research and future directions

## Introduction

Lactic acidosis is defined as an imbalance between lactic acid production and clearance and poses a challenge in the care of critically ill patients [1]. Lactate is predominantly metabolized by the liver (80-90%) via gluconeogenesis, and less so, in the kidneys, and lactate accumulation is a primary cause of anion gap metabolic acidosis in critically ill patients. The diagnostic criteria include a plasma lactate level above 5 mmol/L and a plasma pH below 7.35 [2]. While lactic acidosis encompasses multiple subtypes, Type A and Type B classifications are the most discussed. Type A lactic acidosis commonly arises from tissue hypoperfusion or acute hypoxemia. Conversely, Type B lactic acidosis presents a broader spectrum of etiologies, including toxin-induced cellular metabolic impairment.

Conditions such as sepsis, liver disorders, diabetes, thiamine deficiency, and malignancy contribute to this pathophysiological cascade. Historically associated primarily with hematological malignancies such as leukemia and lymphomas, recent decades have witnessed an increasing incidence of Type B lactic acidosis in solid tumors in the absence of tissue hypoperfusion or

hypoxemia [2,3]. This shift underscores the evolving landscape of lactic acidosis etiology, prompting a deeper exploration into its mechanisms and clinical implications [2].

Otto Warburg proposed that the connection between lactic acidosis and malignancy is based on the ability of tumor cells to metabolize glucose into lactate under anaerobic conditions at a much greater rate than in normal cells [3]. This concept suggests a deviation from the typical understanding of differentiated cells that rely on mitochondrial oxidative phosphorylation for cellular energy production. Interestingly, hypotheses suggest that tumor cells favour aerobic glycolysis to fuel their metabolic needs, despite the less efficient ATP yield compared to oxidative phosphorylation. Various hypotheses have explored this metabolic shift in tumor cells, suggesting that specific cancer-associated mutations enable rapid proliferation at the expense of efficient ATP generation. Nonetheless, the lack of definitive evidence underscores the need for a deeper understanding of the mechanisms governing cell proliferation and cancer to shape future treatment strategies [4].

## Case Presentation

A 46-year-old female with a medical history of hypertension, hyperlipidemia, and uterine fibroids presented with abdominal pain, abdominal distention, and clinical deterioration for more than a few months. MRI revealed a large (17 cm) pelvic mass with extensive involvement of the rectosigmoid colon, which was subsequently removed 9 days after imaging via abdominal hysterectomy and bilateral salpingo-oophorectomy. The pelvic tumor was fixed to the mesentery of the rectosigmoid colon extending from the promontory with extensive serosal involvement of the rectosigmoid. During the procedure, one liter of free fluid was removed, consistent with ascites and omental disease. Extensive carcinomatosis was visualized within the mesentery, small bowel, cecum and appendix. Invasion of the mesenteric vein and artery was also detected via inspection. Surgical complications included intraoperative bladder perforation due to fixation of the bladder wall to the tumor. The bladder was repaired intraoperatively, and no leakage was evident after the bladder was filled with methylene blue. A bubble test of the distal colon was negative for leaks. There was no evidence of disease in the jejunum and no obstruction of the small or large bowel. The surgery resulted in suboptimal debulking due to the extension of the disease. The patient received 2 units of packed red blood cells and 750 ml of colloid during the procedure. There was approximately 1,500 ml of blood loss.

Pathology revealed undifferentiated carcinoma of the right and left ovaries and tubes with stage IIIC disease. The patient's postoperative admission was prolonged due to slow return to bowel function and ambulatory status. She was discharged on hospital day 5 after tolerating a regular diet, regular bowel movements and no nausea or vomiting. Her Foley catheter was inserted at discharge. Her pain was well controlled with oral tramadol. The only postoperative concern was a slight decrease in her sodium concentration, and she was discharged with sodium tablets. She had a significantly elevated white blood cell count prior to surgery, which persisted postoperatively but began to trend downward at discharge. Cultures were drawn postoperatively and remained negative. During this time, the patient remained afebrile and normotensive without tachycardia.

The patient was readmitted on postoperative day 8 with severe gastric pain, nausea, and vomiting. On physical examination, the patient presented with 4+ pitting edema of the bilateral upper and lower extremities. Labs upon admission were considered significant for hypoglycemia (69 mg/dl), hyponatremia (129 mmol/L), a high anion gap (21 mmol/L), lactic acidosis (7.6 mmol/L), hypercalcemia (10.8 mg/dl), elevated AST (40 units/L), normal ALT (23 units/L), high alkaline phosphatase (287 units/L), low protein (4.6 g/dl), and low albumin (1.4 g/dl). Hematology was significant for elevated white blood cell count (56.62x10^9/L), low red blood cell count (2.88x10^6/mcl), anemia (Hgb 8.8 g/dl), and thrombocytopenia (>1 millionx10^9/L). Her vital signs included tachycardia (107-130) and tachypnea (17-32), but she remained afebrile (36.2 C). At this time, she was diagnosed with a UTI and severe sepsis, and she was given fluid resuscitation and cefepime. Lactic acidosis was attributed to the septic state, although CT and cultures were unremarkable for any evidence of infection. Hematologic abnormalities were attributed to the bone marrow response to malignancy. Her Foley urinary catheter was removed, and she was voiding on her own. On postoperative day 9, Flagyl was added to her regimen for broader coverage of anaerobes because CT revealed possible evidence of bladder leakage and no clinical improvement in response to the current antibiotic regimen.

On postoperative day 11, her hemoglobin concentration decreased from 8.8 g/dl to 7.1 g/dl, and she was given 1 unit of packed red blood cells. Due to a lack of clinical improvement, she underwent an exploratory laparotomy in which a bladder leak was visualized and repaired. No active bleeding was visualized in the pelvis. Intraoperative washout was completed with the placement of a 15-round drain in the pelvis. There was no abscess visualization, bowel perforation, or ischemia contributing to her septic state. Post operation, she continued to be tachycardic (up to 147), tachypneic (up to 54), and afebrile. Cefepime and FLF were continued, and the Foley catheter was maintained in place. CT- and US-guided placement of a 12 French left lower quadrant drain was performed, the Foley urinary catheter remained in place, and enteral feeding began. Lactic acidosis was still attributed to sepsis, although there was no obvious cause, as microbiology and imaging results were all negative for signs of infection.

On postoperative day 12, large-volume ascites were noted on CT imaging, and it was determined that she developed abdominal compartment syndrome, which was decompressed via exploratory

laparotomy. Radiology also revealed markedly fatty liver on CT. She was semi electively intubated due to persistent tachypnea and lactic acidosis. Vascular access was obtained via the CVC and arterial line.

Her laboratory results revealed continuing lactic acidosis (15.8 mmol/L), leukocytosis (89.39x10^9/L), thrombocytopenia (601x10^9/L), and anemia (Hgb 7.1 g/dl). Antimicrobial therapy was switched to vancomycin, meropenem and micafungin. High-dose thiamine was continued to help metabolize lactate, and vasopressin was started. Her urine output improved. Lactic acidosis was still attributed to the septic state and was unlikely to be due to the Warburg phenomenon. Psychosocial support was given to the family, as prognosis was very guarded due to the high risk of worsening shock and multiorgan dysfunction.

On postoperative day 13, the patient was evaluated for hemophagocytic lymphohistiocytosis, but her ferritin level was normal, and this differential diagnosis was not made. Lactic acidosis continued, and the Warburg phenomenon was considered further. Based on the literature, a referral was requested to begin immediate chemotherapy. She became non-oliguric with acute kidney injury. An echocardiogram was performed, which ruled out Takotsubo cardiomyopathy, and Lasix diuresis began to decrease water overload.

On postoperative day 14, she was titrated off pressors and became febrile (39°C). Chest X- ray revealed small bilateral effusions and opacities in the right upper lobe. She returned to the operating room for second abdominal compartment syndrome washout, placement of 2 more JP drains, mesh placement, and wound VAC but continued to have open fascia. Blood cultures continued to remain negative. It was decided that the Warburg phenomenon was more likely, and if the source of infection was still not evident over the next 24-48 hours, chemotherapy would begin.

On postoperative day 15, she began carboplatin chemotherapy. Precedex was discontinued to see if she returned to afebrile. Fluconazole and Zosyn were added for antifungal coverage. One day after beginning carboplatin, she was noted to have multiple episodes of bloody urine and remained febrile. She experienced significant pain when sedation was reduced. At this time, the family decided to continue comfort measures only and stopped all active treatment. The patient subsequently died within hours.

## Discussion

The literature has reported 32 cases of intractable lactic acidosis in the setting of malignancy. To our knowledge, this is the second gynecologic case and the first reported case of ovarian carcinoma with associated Type B lactic acidosis. Although rare, the outcomes of undifferentiated solid tumor gynecologic cancers can be devastating. Our aim in this case is to discuss the challenges and significance of early diagnosis and treatment.

In this case, report, the patient's most significant metabolic derangement was consistent lactic acidosis. Type A lactic acidosis is the most common type of lactic acidosis. The etiology of Type A is tissue hypoperfusion, and hypoxia [4]. Common causes of tissue ischemia include hypovolemia, sepsis or cardiac and pulmonary failure [4]. In this case, the cause of her hyperlactatemia was originally interpreted to be urinary sepsis due to her recent bladder trauma and her presence of an indwelling Foley catheter. However, this was never justified, as her cultures remained negative, and she remained clinically unstable despite antibiotic treatment. It was then assumed that the patient had tissue ischemia from abdominal compartment syndrome after her bladder pressure was found to be 30. However, her repeated surgical decompression did not significantly reduce her lactic acid levels. Therefore, with sepsis and tissue ischemia ruled out as causes of lactic acidosis, the source of lactic acidosis remained unknown, and other factors were considered.

Type B lactic acidosis is another cause of lactic acidosis but is much more uncommon. Type B lactic acidosis is caused by impaired metabolism and is more commonly caused by diabetes, alcoholism and malignancies [5-7]. Several hematologic cases of lactic acidosis have been reported in the literature [1,3,6,8,9,10], but there are a few cases of solid cancers with lactic acidosis [5,7,11,12-15]. Lactic acidosis in these large solid tumors has been hypothesized to be due to the Warburg effect [11]. This theory hypothesizes that elevated lactate is a result of anaerobic glycolysis, which is the primary metabolic mechanism by which malignant cells proliferate [4]. In this case report, it is assumed that the patient's lactic acidosis was due to this phenomenon. Although the patient underwent primary surgical removal, the tumor was extensive, and a large portion of the tumor remained postoperative. Therefore, rapid tumor progression likely led to her lactic acidotic state. This case report emphasizes the importance of considering all causes of lactic acidosis in complex patients.

Additionally, it should be noted that radiologically acknowledged fatty liver on CT imaging. Other similar cases reported these findings. It remains unknown whether this was a factor in her lactic acidosis, but this seems unlikely due to her normal liver function and normal liver enzymes.

Despite adequate nutrition, this patient also suffered from hypoglycemia. According to prior case reports in the setting of malignancy, hypoglycemia can contribute to excess consumption of glucose from malignant cell proliferation [8,9,12]. In this case, it is theorized that the patient's high tumor burden and ongoing lactic acidosis played a major role in her consistent hypoglycemia.

The current literature on the treatment of solid tumor malignancies with unexplained severe lactic acidosis is limited. Thiamine administration is a staple treatment for lactic acidosis because it reduces anaerobic metabolism and shunts pyruvate toward the

synthesis of acetyl-CoA for aerobic metabolism [16]. Despite thiamine infusion, the patient did not respond well. The current literature suggests that early-onset chemotherapy is most effective [3,10,16]. However, it is important to note that early-onset chemotherapy is difficult to administer in critically ill patients given the notion that it could further increase clinical deterioration. In patients with similar solid tumor malignancies, patients and families choose to provide comfortable care due to the severity of the illness [5,11,13-5]. To our knowledge, there has only been one report of early initiation of chemotherapy prolonging survival [17]. Therefore, more research is needed to establish standards of care for these patients.

## Conclusion

This is a rare case of refractory Type B lactic acidosis secondary to undifferentiated ovarian cancer. This case highlights the importance of early recognition of Type B lactic acidosis in the setting of malignancy. Early detection of the underlying cause of Type B lactic acidosis may alter the course of this metabolic oncologic emergency. It is also critical to establish treatment strategies for patients who face these metabolic derangements so that prognosis can be improved.

## References

1. Sanivarapu R, Upadrista PK, Otero-Colon J, Shah K, Cadet B, et al. (2022) An Oncological Emergency: Severe Type B Lactic Acidosis From Warburg Effect in Diffuse Large B-cell Lymphoma. Cureus. 14:e26557.
2. de Groot R, Sprenger RA, Imholz AL, Gerding MN. (2011) Type B lactic acidosis in solid malignancies. Neth J Med. 69:120-123.
3. Liu QS, Harji F, Jones A, Tarnower AC. (2020) Type B lactic acidosis: a rare oncological emergency. BMJ Case Rep. 13:e233068.
4. Vander Heiden MG, Cantley LC, Thompson CB. (2009) Understanding the Warburg effect: the metabolic requirements of cell proliferation. Science. 324:1029-1033.
5. Viteri-Noel A, Cobo-Reinoso ME, de Felipe-Noguerales B, Manzano L. (2021) Lactic Acidosis as an Unusual Finding in Undifferentiated Carcinoma. Case Rep Oncol. 14:1237-1241.
6. Schuh AM, Leger KJ, Summers C, Uspal NG. (2018) Lactic Acidosis in a Critically Ill Patient: Not Always Sepsis. Pediatr Emerg Care. 34:e165-e167.
7. de Groot R, Sprenger RA, Imholz AL, Gerding MN. (2011) Type B lactic acidosis in solid malignancies. Neth J Med. 69:120-123.
8. Claudino WM, Dias A, Tse W, Sharma VR (2015) Type B lactic acidosis: a rare but life threatening hematologic emergency. A case illustration and brief review. Am J Blood Res. 5:25-9.
9. Sillos, E.M, Shenep, J.L, Burghen, G.A, Pui, C, Behm, F, et al (2001) Lactic acidosis: a metabolic complication of hematologic malignancies. Case report and review of the literature. Cancer 92: 2237–2246.
10. Farn Huei C, Daniel C, Laurel JL (2009) “Severe Lactic Acidosis in a Patient with B-Cell Lymphoma: A Case Report and Review of the Literature”, Case Reports in Medicine.
11. Hausken J, Haave EM, Haugaa H, Løberg EM, Kongsgaard UE. (2018) A patient with solid gynecologic cancer causing lactic acidosis, severe hypercalcemia, and hypoglycemia. Clin Case Rep. 7:64-70.
12. Muntz HG, Brown E. (1992) Lactic acidosis and hypoglycemia: a metabolic complication of advanced gynecologic malignancy. Int J Gynecol Cancer. 2:163-167.
13. Krimmel JD, Packer CD. (2015) Type B Lactic Acidosis in a Patient with Gastric Adenocarcinoma and Extensive Hepatic Metastases. Med Princ Pract. 24:391-393.
14. Gharia B, Seegobin K, Mahida H, Shaikh M, Matthews Hew T, et al (2018) Fatal Type B Lactic Acidosis Associated With Metastatic Colorectal Cancer: A Case Report With Review of Literature, Pathogenesis, and Treatment. J Investig Med High Impact Case Rep. 6:2324709618788101.
15. Munoz J. (2011) Severe lactic acidosis in a patient with metastatic prostate cancer. J Cancer Res Ther. 7:201–2.
16. Ruiz JP, Singh AK, Hart P. (2011) Type B lactic acidosis secondary to malignancy: case report, review of published cases, insights into pathogenesis, and prospects for therapy. ScientificWorldJournal. 11:1316-1324.
17. Rice K, Schwartz SH. (1985) Lactic acidosis with small cell carcinoma. Rapid response to chemotherapy. Am J Med. 79:501-503.