



An Unusual Case of Lactic Acidosis in Colon Cancer: A Case Report and Review of the Literature

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Abstract

Most patients with lactic acidosis are often first evaluated for sources of infection and tissue hypoxia. However in the absence of tissue hypoxia, type B lactic acidosis should be considered as a possible differential. Type B lactic acidosis or lactic acidosis secondary to medications, metabolism, or malignancy, is a rare paraneoplastic syndrome associated with hematological malignancies, and with increasing frequency, solid tumors that are correlated with poor overall prognosis. We present a case of a 61-year old female with stage IV colon cancer who presented to the ER with constant dull achy right upper quadrant pain for 2 days. She was found to have lactic acidosis and hyperprolactinemia in the absence of tissue hypoxia or infection. We believe that our case report can add to the limited data regarding this rare syndrome in solid tumors.

Keywords: Lactic acidosis Type B; Hematological malignancies; Hyperprolactinemia

Introduction

Most clinicians are familiar with lactic acidosis. However few are able to delineate the types of lactic acidosis and their clinical presentations, especially type B. Type B lactic acidosis as a diagnosis is not as well recognized with established hematological malignancies. Our case provides evidence to growing literature of this paraneoplastic syndrome in solid tumors.

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Case Presentation

The patient is a 61-year-old Hispanic woman with a history of stage IV colon cancer, who presented to the ER department with two days of constant dull, achy, right upper quadrant pain. On physical exam, the patient was tachycardic and hypertensive. She had marked abdominal distention and tenderness in right upper quadrant. Her laboratory workup on admission revealed a white blood cell count of $23.93 \times 10^3/\text{UL}$, hemoglobin of 9.0 g/dL, hematocrit of 29.7%, sodium of 133 mmol/L, potassium of 4.3 mmol/L, chloride of 97 mmol/L, bicarbonate of 20 mmol/L, anion gap of 16 mmol/L, calcium of 8.7 mg/dL, lactic acid of 6.4 mmol/L, blood urea nitrogen of 6 mg/dL, creatinine of 0.62 mg/dL, albumin of 2.1 g/dL, serum protein of 6.2 g/dL, total bilirubin of 1.6 mg/dL, aspartate aminotransferase of 151 IU/L, alanine aminotransferase of 31 IU/L, alkaline phosphatase of 455 U/L, lipase of 139 IU/L. Urinalysis revealed yellow urine with specific gravity greater than 1.035 and trace bacteria. Blood cultures were negative for growth at 42 h.

CT of the abdomen and pelvis with contrast revealed significant interval progression of hepatic metastasis with resultant hepatomegaly. There was moderate abdominal ascites and bilateral pleural effusions. Interval progression of the aortocaval lymphadenopathy and interval enlargement of the visualized pulmonary metastatic nodules was observed.

The patient was admitted to the medical floor and managed with IV saline 200 cc/hr, Zosyn 4.5 g IVPB every 8 h, vancomycin 1000 mg every 12 h. Her initial anion gap readings were 16 and improved from 16 to 13 over 4 h. Her lactic acid reading was 6.4 mmol/L and worsened from 6.4 mmol/L to 8.1 mmol/L over the same time span.

The patient clinically looked well and did not demonstrate systemic signs of hyperlactatemia. No interventions were performed for her lactic acidosis and hyperlactatemia. Her pain was well controlled and she decided she would no longer like any treatment with chemotherapy and opted for hospice care. On hospital day 3, the patient was discharged to hospice for end of life care.

Discussion

Epidemiology

Type B lactic acidosis is typically due to an accumulation of lactate from secondary sources, including malignancy, metabolic diseases and medications. Lactic acidosis is more typically seen in patients with hematologic malignancy. However there has been an increase in the numbers of cases regarding lactic acidosis in the setting of solid malignancy, such as gastric carcinoma, metastatic breast cancer and colon cancer [1-3].

Pathophysiology

Rapid growth and expansion of solid tumors, results in a tumor that outgrows its own blood supply. This leads to a hypoxic environment and anaerobic glycolysis, which produces lactic acid. While this mechanism of lactic acid production is well understood, other factors are known to contribute to tumor cell lactic acid production.

The Warburg effect describes the property of cancer cells to undergo excessive glycolysis, which contributes both to cell production of ATP and rapid growth and proliferation [4]. This increased rate of glycolysis, which occurs in anaerobic conditions, results in hyperlactenemia, which has been found to promote tumor progression [5]. The up regulation of glycolysis has been attributed to Hypoxia-Inducible Factor (HIF), which leads to the over expression of glycolytic enzymes such as hexokinase [6]. This increased production of lactic acid by cancer cells rarely presents with systemic effects [7].

In regards to our patient, while her lab results were indicative of sepsis, the patient was clinically stable and all investigations to find a source of her infection were negative. The patient had no evidence of tissue hypoxia but had an anion gap of 16 mmol/L and bicarbonate level of 20 mmol/L, classifying her as having Type B lactic acidosis. There are several proposed mechanisms that can explain why a patient with advanced malignancy may present with hyperlactatemia. However the etiology is thought to be multifactorial. Our patient was previously diagnosed with colon cancer that presented as an obstructing tumor in the hepatic flexure of the ascending colon. At that time, the cancer was staged as moderately differentiated stage 2 adenocarcinoma enteric type, with K RAS mutation on exon 12. She had resection of the tumor followed by adjuvant chemotherapy with 8 rounds of Oxiplatin and 10 rounds of Fluorouracil. Unfortunately, the tumor reoccurred several months later with metastasis to the liver and lungs, despite maintenance with Avastin.

There are not many reported cases of lactic acidosis related to solid tumors, and even fewer reports of colon cancer-related lactic acidosis. In many but not all of these cases, extensive liver metastasis was found [8]. This contributes to the hypothesis that liver dysfunction in the setting of metastasis results in decreased lactate clearance [3]. However, not all of the reported cases involved liver metastasis in the setting of other liver disease, such as cirrhosis and hepatic failure, therefore lactic acidosis remains uncommon [2].

There is also a comparable case report of patient with stage IV small cell lung cancer who presented with lactic acidosis associated with thiamine deficiency. This presentation further suggests that the source

of lactate is associated with solid tumor. Thiamine supplementation resolved the lactic acidosis [9]. However, thiamine deficiency presents with signs and symptoms that were not observed in our patient. Other studies showed increased thiamine accumulation in cancer cells and a constant level of thiamine pyrophosphate in cancer cells, leading to decreased thiamine in patients with malignancy [10]. Thus, checking thiamine levels in patients with hyperlactatemia and using thiamine to correct the acidosis have been proposed.

The treatment of hyperlactatemia and type B lactic acidosis secondary to malignancy has yet to be established. The most commonly reported successful treatment was treatment of the malignancy itself. Attempts of correcting the lactic acidosis with bicarbonate infusions and thiamine, even when a patient is not deficient, have proven to be unsuccessful [11]. Hyperlactatemia and type B lactic acidosis in patients with malignancy seems to be a poor prognostic factor. Studies are lacking to prove this; however, one study assessing the prognostic value of lactic acid in patients with metastatic lung cancer found that the overall survival rate in patients with elevated lactic acid was shorter [12].

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