SPECIAL FEATURE

Case Report/Focused Review
Fred A. Lopez, MD • Feature Editor

Lactic Acidosis: A Rare Oncological Emergency in Solid Tumors at Presentation

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ABSTRACT

Lactic acidosis is a potentially life-threatening complication characterized by accumulation of blood lactate resulting in low arterial pH. The majority of lactic acidosis in malignancies are reported in association with hematologic malignancies. It may result from an imbalance between lactate production and hepatic lactate utilization, but the exact pathophysiology is far more complex than what we can fathom from current micromolecular studies. We report a case of a 71-year-old male with metastatic lung cancer presenting with fatal lactic acidosis in the absence of liver involvement. Review of the literature reveals only 27 reported cases of solid tumors presenting with lactic acidosis, of which nearly all of them had extensive liver metastasis. Patients were treated with aggressive fluid resuscitation, bicarbonate administration and hemodialysis, but the only effective treatment modality was early aggressive chemotherapy initiation.

Key Indexing Terms: Lactic acidosis; Solid tumors; Chemotherapy; Liver; Tumor burden. **[Am J Med Sci 2016;▮(▮):▮▮▮–▮▮▮.]**

BACKGROUND

Our understanding of lactic acidosis and its association with malignancies has been evolving since it was first described by Field et al.[1] Luft et al[2] defined lactic acidosis with the criteria of pH $\leq$ 7.35 and serum lactate $\geq$ 5 mEq/L. Approximately more than 80 cases of malignancies with lactic acidosis at presentation have been documented in literature; most are associated with hematologic malignancies.[3-7] However, an exhaustive review of the literature reveals only 27 reported cases of solid tumors presenting with lactic acidosis. These patients, all but 4 of whom had extensive liver metastasis, were treated with aggressive fluid resuscitation, bicarbonate administration and hemodialysis, but the only effective treatment modality was early aggressive chemotherapy initiation. Chemotherapy works by cytoreducing the tumor and the hepatic involvement, but the exact pathophysiology is far more complex than what we can fathom from current micromolecular studies. We report a case of solid tumor presenting with fatal lactic acidosis in the absence of liver involvement.

CASE

A 71 year-old white male presented with a 1-week history of chest discomfort, shortness of breath and unintentional weight loss. During the work-up, which included a computed tomography chest scan, he was found to have a right upper lobe lung mass (Figure 1). He subsequently underwent biopsy of the mass. His routine blood work at that time showed hemoglobin 10.5 g/dL, white blood cell count 6,700/μL and normal renal and liver function tests. On the day following the biopsy, the patient sustained a fall from generalized weakness, further suffering subarachnoid and subdural hemorrhage. He was admitted to the neurosurgery intensive care unit. Work-up on the day of hospitalization showed the patient in severe metabolic acidosis with high anion gap (AG) and elevated creatinine (Cr). His significant medical comorbidities included a remote history of myocardial infarction with percutaneous intervention, systolic dysfunction with an ejection fraction of 45%, peripheral vascular disease, hypertension, dyslipidemia and hypothyroidism. He had a remote history of tobacco abuse of 40 pack-years. At presentation, the patient was alert and oriented with stable vital signs and normal physical examination.

A complete blood count showed a hemoglobin 10.2 g/dL, a white blood cell count 6,300/mm^3 and a stable thrombocytopenia at 133,000/μL. His significant laboratory abnormalities included Cr 2.1 mg/dL, potassium 5.9 mEq/L, AG 22 and lactate 15 mmol/L, which worsened to Cr 3.1 mg/dL, potassium 6.5 mEq/L, AG 38 and lactate $>$25 mmol/L on day 2. The patient's liver enzymes were within normal limits; bicarbonate level was 11 mEq/L and arterial blood gas showed a pH of 7.11. He had no signs of sepsis, shock or ischemia and multiple blood cultures drawn were negative. A computed tomography scan of abdomen and pelvis showed normal liver with no abnormal intra-abdominal findings. The patient was initially treated with sodium bicarbonate and further started on emergent hemodialysis.

On day 2, a transient improvement in the metabolic acidosis was noted, despite lactate levels trending up (Figure 2). During days 6-9, metabolic acidosis started to deteriorate, by which time the lung biopsy result showed high-grade neuroendocrine tumor with mixed large-cell and small-cell features. Immune histochemical stain was positive for the markers CD56, CAM 5.2, AE1/AE3 and

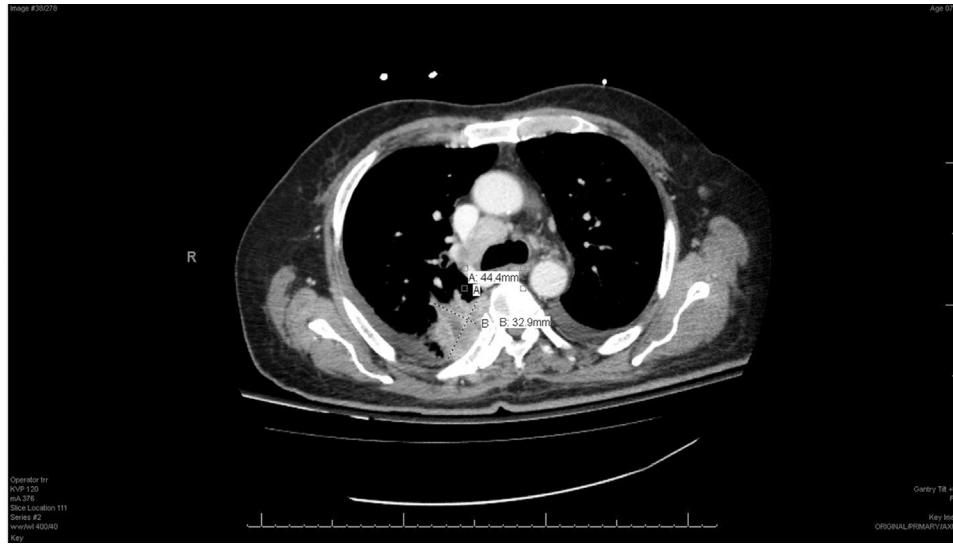

FIGURE 1. Computed tomography scan of the chest with contrast showing the lung mass.

ck7 and negative for p63, ck5/6, TTF1, ck20 and CD3 with Ki-67 staining showing more than 50% positivity. These findings confirmed the diagnosis of neuroendocrine carcinoma. Owing to the presence of nucleated red blood cells, myelocytes and thrombocytopenia, a bone marrow biopsy was performed, which showed extensive infiltration with immunohistochemical evidence of neuroendocrine differentiation.

The patient was started on chemotherapy from day 8 of hospitalization with dose-adjusted cisplatin, etoposide, concomitant dexamethasone and Neupogen. With initiation of chemotherapy, lactate started to trend down. On day 11, he developed febrile neutropenia and was started on broad-spectrum antibiotics; however, the next day he went into severe respiratory failure and required mechanical ventilation. The patient continued to deteriorate, was placed on comfort care on day 18, and died soon after extubation.

DISSCUSSION

Lactic acidosis is often described as a rare and an ominous complication of hematologic malignancies with significant tumor burden or extensive liver involvement. There are only a few cases reported for solid tumors presenting with lactic acidosis, nearly all of which had extensive hepatic involvement. Conversely, our patient had a poorly differentiated lung carcinoma and lactic

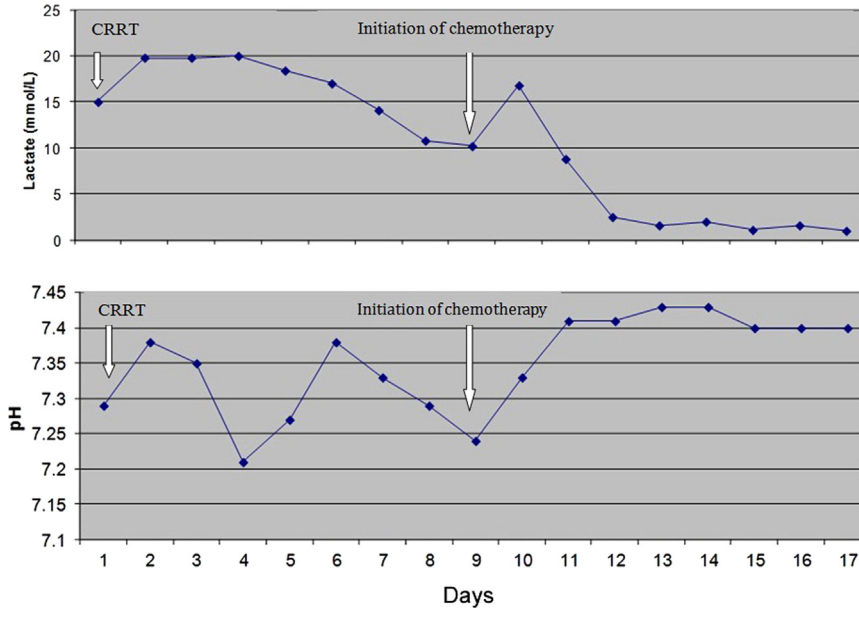

FIGURE 2. Trend of lactate levels following chemotherapy.