Case report

Case of acute hepatic injury and elevated ethanol levels in a non-alcoholic adult

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SUMMARY

Blood ethanol concentration is measured using different techniques. Gas chromatography/mass spectrometry is used in forensic laboratories to measure whole blood ethanol levels while enzyme immunoassay is often used in hospitals to measure serum or plasma ethanol levels. Lactic acidosis can theoretically cause false elevation of blood ethanol levels measured through enzymatic assay because this method measures the reduction of nicotinamide adenine dinucleotide (NAD⁺) to nicotinamide adenine dinucleotide-hydrogen (NADH) via the action of a dehydrogenase. Here, we present a rare incidence of ethanol level elevation in a non-alcoholic adult male secondary to lactic acidosis from a rare form of large B-cell lymphoma with infiltration of the liver.

BACKGROUND

Blood ethanol concentration is measured using different techniques. Gas chromatography/mass spectrometry (GC/MS) is the gold standard and is used in forensic laboratories to measure whole blood ethanol levels. Meanwhile, enzymatic ethanol assay to measure ethanol concentration in the serum or plasma is often used in hospital laboratories.^{1,2} However, elevated lactate and lactate dehydrogenase can theoretically cause false positive results of enzymatic ethanol assay and has been proven in post-mortem cases.³

There are multiple causes of lactic acidosis. These include hypoxemic such as hypoperfusion from shock, and non-hypoxemic as medication use such as biguanides and intravenous epinephrine, malignancy such as leukaemia and lymphoma, alcoholism and mitochondrial dysfunction, among others.

Lactic acidosis from malignancy is rare. Possible mechanism is anaerobic metabolism due to dense underperfused tumour cells or from neoplastic cells that shift to primarily anaerobic glycolysis.⁴

There is little literature on lactate and lactate dehydrogenase interference with enzyme ethanol assay in live patients. Here we present a rare case of falsely elevated blood ethanol concentration from lactic acidosis due to intravascular large B-cell lymphoma with liver infiltration.

CASE PRESENTATION

A 67-year-old Vietnamese man who was previously healthy presented to our institution for evaluation and management of acute hepatic injury. He initially presented to another hospital with a 2-week history

of upper respiratory tract symptoms and left upper quadrant pain. He had no fevers, weight loss and night sweats. He had no history of hepatic disease. He denied any illicit drug use, ethanol abuse or herbal supplement use. Recent medications include azithromycin and ceftriaxone for possible pneumonia. Physical examination revealed mild hepatosplenomegaly with right and left upper quadrant tenderness and no palpable lymphadenopathy. There was no jaundice, scleral icterus, caput medusa, palmar erythema or spider angiomas. On the second day of hospitalisation, he was found to have acute transaminitis, with aspartate aminotransferase (AST) to 1110 IU/L and alanine aminotransferase (ALT) to 419 IU/L from previously normal levels on presentation. His work-up was consistent with acute liver failure, with downtrending platelets, rising international normalized ratio (INR) and non-specific attenuation of the liver on CT scan. There was splenomegaly with possible infarct and no lymphadenopathy noted on the scan. Work-up for transaminitis revealed he did not have viral or autoimmune hepatitis. His ethanol level by enzymatic assay was elevated to 39.1 mg/dL and increased to 54.5 mg/dL without recent alcohol intake. He also had a lactic acid of 14.6 mmol/L, lactate dehydrogenase (LDH) of 17802 IU/L and uric acid of 15 mg/dL. He had no leukocytosis and had no growth on blood culture. Liver biopsy revealed that the liver was diffusely infiltrated with intrasinusoidal large lymphocytes, positive for CD20 and CD5, and negative for cyclin D1 and CD3. He was diagnosed with intravascular large B-cell lymphoma, complicated by tumour lysis syndrome. He also developed acute anaemia secondary to intra-abdominal haemorrhage after the biopsy. During his hospitalisation, his lactic acid peaked at 26.64 mmol/L leading to worsening acidosis with pH of 7.24, Pco₂ of less than 20 mm Hg eventually requiring intubation for respiratory support. He was started on rituximab with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) therapy. He also received rasburicase and hydration to manage early manifestations of tumour lysis syndrome. Of note, ethanol measurement via GC/MS was performed which showed ethanol level of less than 10 mg/dL. At the time of measurement, he had a lactic acid of 20.3 mmol/L, LDH of 16 534 IU/L and ethanol level by enzymatic assay of 49.3 mg/dL.

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OUTCOME AND FOLLOW-UP

He improved with the treatment and was discharged with close follow-up with his oncologist. He is currently in remission after completing six cycles of chemotherapy with the R-CHOP regimen and intrathecal methotrexate.

DISCUSSION

Most hospital laboratories use enzymatic ethanol assay to measure serum ethanol levels. A serum sample is mixed with alcohol dehydrogenase and nicotinamide adenine dinucleotide (NAD⁺), and ethanol level is measured indirectly through reduction of NAD⁺ to NADH using spectrophotometry.¹²

Theoretically, elevated lactate and lactate dehydrogenase can interfere with the aforementioned method and produce false positive elevation in ethanol levels. This is because lactate dehydrogenase catalyses the conversion of lactate to pyruvate with concurrent reduction of NAD⁺ to NADH, hence the false positive result. For this reason, forensic laboratories use GC/MS, the gold standard to measure whole blood ethanol levels. Postmortem elevation in lactate and lactate dehydrogenase was found to interfere with the enzymatic ethanol assay, such as in the study done by Badcock *et al* in infants who died from sudden infant death syndrome.³

The interference of lactate and lactate dehydrogenase from enzymatic ethanol assay measurement in the clinical setting has been studied before. Nacca *et al* measured the alcohol levels in trauma patients presenting in the emergency department via GC/MS after they were found to have elevated lactate (ranging from 2.4 to 24.2 mmol/L) and lactate dehydrogenase (ranging from 242 to 8838 IU/L) and elevated ethanol levels measured via enzymatic assay. All patients with a positive enzymatic ethanol result also had a positive GC/MS ethanol measurement.⁵ Another case report by Powers *et al* also found that elevated lactate and LDH had minimal interference with enzyme ethanol assays.²

In the case of our patient, he had intravascular large B-cell lymphoma, a rare extranodal type of diffuse large cell lymphoma characterised by the proliferation of lymphoma cells within the lumen of small blood vessels. The true incidence of this malignancy is unknown as most information come from case reports. Clinical presentations include constitutional B symptoms and organ dysfunction that may vary depending on which small vessels are occluded. The bone marrow, spleen and liver are more commonly affected, such as in our case.⁶ The high proliferative rate and large tumour burden of this hematologic malignancy as well as diffuse liver infiltration and injury led to elevated lactate and LDH levels. This elevation of lactate up to 20.3 mmol/L and LDH up to 16534 IU/L resulted in a false elevation of the enzymatic assay, confirmed by a negative ethanol level measured through GC/MS. Clinicians should be aware that elevated levels

of lactate and LDH can cause an elevation of ethanol level measured by enzymatic assay to a certain extent, especially in patients with liver failure and malignancy as it may affect clinical management.

We presented a rare incident of false elevation of ethanol levels measured by enzymatic assay secondary to lactate and lactate dehydrogenase interference in a live patient. In addition, this was due to a rare case of intravascular large B-cell lymphoma causing acute hepatic failure.

Learning points

- Blood ethanol level in the hospital is usually measured by enzyme assay which measures NADH.
- It is possible to have a false elevation in enzymatic ethanol assay in live patients with elevated lactic acid and lactate dehydrogenase because NADH⁺ is a by-product of lactic acid oxidation by lactate dehydrogenase.
- This is a unique case where there was false elevation in enzymatic ethanol assay in a live patient. The false elevation may be related to the degree of lactic acid and lactate dehydrogenase elevation.

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