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CASE REPORT | LIVER

Severe Pernicious Anemia Predisposing to Hypoxic Hepatitis

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ABSTRACT

Hypoxic hepatitis or ischemic hepatitis is most commonly encountered in critical care patients, most of whom have shock states secondary to cardiac or respiratory failure. We report a case of severe pernicious anemia predisposing to hypoxic hepatitis that had a good prognosis with simple treatment. Care should be taken in management of severe anemia, interpretation of serum vitamin B12 levels after blood transfusion, and the use of intravenous fluids.

INTRODUCTION

To our knowledge, there are no reported cases of severe pernicious anemia predisposing to hypoxic hepatitis (HH). We report a case of an uncommon pathology predisposing to an unusual complication that had a good prognosis with simple treatment.

CASE REPORT

A 59-year-old woman presented to the emergency department with complaints of fatigue and weakness for 2 months, associated with 2 weeks of dyspnea on exertion, orthopnea, and central chest pain exacerbated by lying down. Five days before presentation, she endorsed several episodes of nonbloody emesis, odynophagia, and anorexia, but no hematemesis, melena, or hematochezia. Previous medical history includes hypertension, vitamin B12 deficiency, and cerebrovascular accident 9 years ago. She had no history of obstructive sleep apnea, congestive heart failure, or chronic obstructive pulmonary disease. The patient was noncompliant with medications and clinic follow-ups. No other pertinent surgical, family, or social history was recorded.

Vital signs recorded at admission were blood pressure 102/55 mm Hg, heart rate 86 per minute, respiratory rate 20 per minute, and temperature 98.1°F. There was no hypotension in the early course of hospitalization. Physical examination revealed pale conjunctiva, bilateral fine crepitations up to the midchest, bilateral pitting edema, increased jugular vein distention, and no altered mental status. Laboratory workup revealed white blood cells 6.2 k/μL, hemoglobin 1.8 g/dL, platelets 63 k/μL, sodium 138 mEq/L, potassium 4.6 mEq/L, creatinine 1.0 mg/dL, aspartate aminotransferase (AST) 86 μ/L, alanine aminotransferase (ALT) 48 μ/L, lactate 20 mmol/L, vitamin B12 985 ng/mL, methylmalonic acid level 112,000 nmol/L, and positive intrinsic factor antibody (Table 1). Chest x-ray showed hazy opacities in bilateral perihilar regions and no cardiomegaly. Transthoracic echocardiography showed ejection fraction of 60–65% and no diastolic dysfunction. The peripheral smear showed schistocytes and multilobulated neutrophils.

In the emergency department, the patient received 2 L of normal saline fluid bolus, then was admitted to the intensive care unit where 2 units of packed red blood cells were transfused and vitamin B12 intravenous replacement was started. While vitamin B12 levels were obtained after transfusion, the methylmalonic acid level was markedly elevated and intrinsic factor antibodies were positive, consistent with the diagnosis of pernicious anemia. On the second day of admission, an increase in AST and ALT levels up to 10 times the upper limit of normal was noticed, whereas lactate improved to 2 mmol/L (Figure 1). AST and ALT levels gradually reduced back to normal over the next 4 days.

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Table 1. Laboratory values on admission

Test	Result	Normal values
White blood cells	6.2	4.4–10.6 k/μL
Hemoglobin	1.8	11.7–14.9 g/dl
Platelets	63	161–360 k/μL
Sodium	138	135–145
Potassium	4.6	3.5–5.0
Creatinine	1.0	0.6–1.4
Lactate dehydrogenase	3,372	85–210 μ/L
AST	86	0–40 u/L
ALT	48	5–35 u/L
Prothrombin time	17.8	11.5–13.9 s
PTT	23.0	24.7–35.1 s
INR	2.13	
Vitamin B12	985	190–900 ng/mL
Methylmalonic acid	112,000	87–318 nmol/L
Intrinsic factor antibody	Positive	
HBsAg	Negative	
HBsAb	Negative	
Hepatitis C virus	Nonreactive	
Hepatitis A IgM	Nonreactive	
ADAM TS13	Negative	

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; PTT, partial thromboplastin time.

DISCUSSION

HH, shock liver, and ischemic hepatitis have been the terms used to describe the clinical syndrome characterized by rapid increase in liver transaminases in the setting of ischemia, shock, or hypoxia.[1,2] Currently, diagnosis is based on 3 parameters: a state of reduced oxygen delivery to the liver, a significant and transient increase in serum transaminases, and last, the exclusion of other causes of liver injury like viral or medication or toxin induced hepatitis.[3]

Table 2. Laboratory values 3 weeks after hospitalization

Test	Result	Normal values
White blood cells	2.8	4.4–10.6 k/μL
Hemoglobin	11	11.7–14.9 g/dl
Platelets	222	161–360 k/μL
Lactate dehydrogenase	201	85–210 μ/L
AST	13	0–40 μ/L
ALT	10	5–35 μ/L
Vitamin B 12	675	190–900 ng/mL
Methylmalonic acid	152	87–318 nmol/L

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

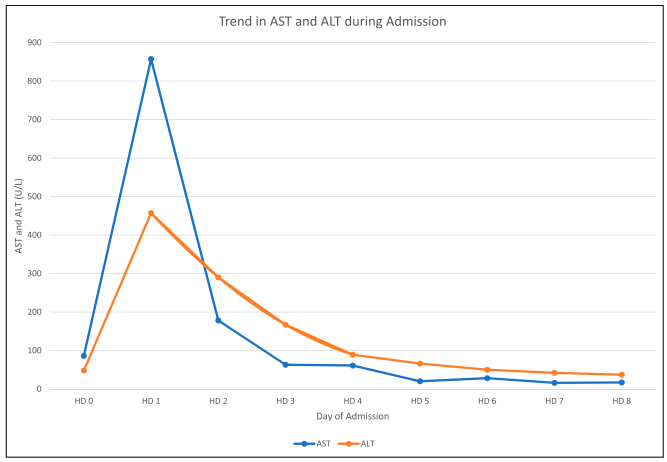

Figure 1. Trend in AST and ALT during Admission.

HH is most commonly encountered in critical care patients with an incidence between 2% and 2.5%, and most of these patients present in shock states secondary to cardiac or respiratory failure.[4–7] Our patient did not present with shock but with chronic severe anemia; indeed initial treatment with intravenous fluid might have been the precipitant of HH in our patient. A hemoglobin level of 1.8 g/dL could be compared with a shock state because there is an extremely low oxygen carrying capacity, and the infusion of 2 L of intravenous fluid before giving packed red blood cells might have worsened an already poor oxygen delivery state.

HH related to severe anemia was first described by Okras et al, which was followed by a study by Henrion suggesting that true shock is absent in up to half of the cases of HH.[5,8] Apart from ischemia, several studies have also proposed the effect of free radical injury from reperfusion as a contributing factor in HH. This might also have been a contributing factor in the development of HH in our patient because giving intravenous fluids was the likely precipitant of HH.[9,10] The typical pattern of AST and ALT elevation in HH is a peak within the first 24 hours, then levels drop down to half of the peak seen within 48 hours,

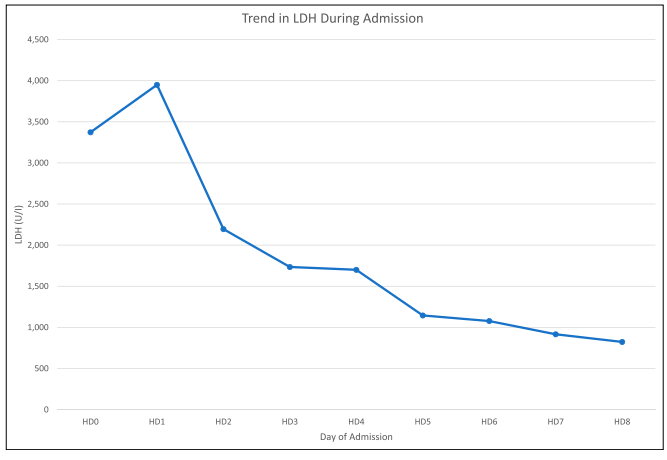

Figure 2. Trend in lactate dehydrogenase during admission.

then slowly return to baseline over the next 10–15 days. Lactate dehydrogenase (LDH) also elevates to a significantly higher level than that seen in viral hepatitis.[1,5,11] The deranged liver function tests in the present case were consistent with this pattern and supports the diagnosis of HH. One feature worth mentioning is that the peak in LDH seen in this case can be attributed to 2 factors: the hemolysis caused by the B12 deficiency and the hypoxemia of the liver, both known to increase LDH levels. Given that the LDH levels were so drastically elevated, both factors likely contributed to this.

Prognosis of patients with HH is very poor. Mortality in hospitalized patients has been reported to be as high as 56%, the cause of death is not directly due to HH but is related to the underlying disease.[1,2] Although there is no reported mortality of HH secondary to vitamin B12 deficiency anemia considering the rarity of this clinical entity, we postulate it maybe comparative considering the similarity in pathophysiology and the severity of the anemia that could very well be compared with any severely decompensated chronic condition or shock state.

The patient was transferred to the general medicine floors where she stayed for 6 additional days until her hemoglobin levels improved. Liver enzyme trend was consistent with the typical pattern of HH (Figure 2). She was discharged and seen in the clinic 3 weeks later, and her laboratory results showed methylmalonic acid level 152 nmol/L and vitamin B12 level was 675 pg/mL (Table 2).

DISCLOSURES

Author contributions: C. Mbachi, P. Palacios Agueta, Y. Wang, and B. Mba wrote and edited the manuscript. C. Mbachi is the article guarantor.

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Informed consent was obtained for this case report.

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