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Pernicious Anaemia as a Cause of Ischemic Hepatopathy

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Abstract: ***Pernicious anemia, a condition characterized by the deficiency of vitamin B_{12}, can lead to significant systemic complications due to its impact on red blood cell production and neurological functions. One of the less commonly discussed but severe complications of pernicious anemia is ischemic hepatopathy, also known as shock liver. Ischemic hepatopathy occurs due to the sudden decrease in blood flow to the liver, often precipitated by cardiovascular instability. This condition can manifest in patients with pernicious anemia due to the increased risk of cardiovascular events and circulatory insufficiency associated with severe anemia. This abstract explores the pathophysiological mechanisms linking pernicious anemia to ischemic hepatopathy, including the roles of hypoxemia, microvascular dysfunction, and cardiac output reduction. Early diagnosis and management of pernicious anemia are critical in preventing the progression to ischemic hepatopathy. Clinical awareness of this potential complication is essential for timely intervention and improving patient outcomes.***

Keywords: Pernicious Anemia, Ischemic Hepatopathy, Vitamin B_{12} deficiency, Disseminated intravascular coagulation

1. Introduction

Severe anaemia is proportionally related to low oxygen delivery to vital organs, which can cause ischemia and subsequently end organ damage [1]. Most commonly affected organs are the heart, brain and kidneys. Only rare cases of ischemic hepatitis have been reported so far associated with profound anaemia in the absence of a shock like state. Hypoxic hepatitis or ischemic hepatopathy 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 pernicious anaemia predisposing to Ischemic Hepatopathy**.** Ischemic hepatopathy is diagnosed on the basis of a rapid increase and subsequent rapid decrease in transaminase values in the absence of other causes of liver disease [1].

Pernicious anemia is defined as severe lack of Intrinsic factor [IF] due to gastric atrophy. It is more common in northern European but occurs in all countries. Disease occurs more common in close relatives and other autoimmune disease, for example, thyroid disease, vitiligo, hypoparathyroidism, type 1 diabetes mellitus and Addison disease. It is also associated with premature greying of hairs, blue eyes and hypogammaglobulinemia. It is also associated HLA-3. Type 1 antibody sometimes also associated thyrotoxicosis, myxoedema, Hashimoto's thyroiditis or Diabetes mellitus. Parietal cell antibody is detected in 90% of patient with PA but it is also associated with other subjects [3].

1) Type 1 antibody block the binding of vitamin B12 to intrinsic factor. They are found in both plasma and gastric juice.
2) Type 2 antibody – prevent binding of the intrinsic factor-vitamin B12 complex to its ileal receptor.
3) Type 3 antibody – recognise the alpha and beta subunits of gastric proton pump of parietal cell [4].

Biopsy findings of pernicious anemia:[3]

- Shows loss of gastric and fundal glandular elements but with preserved antral glandular cells. The infiltrate of plasma cells and lymphocyte contains excess of CD4 cells. They directed against H+/K+ ATPase pump.
- Also, H. pylori is associated in early atrophic gastritis with later replaced with autoimmune process.

2. Case History

A 17-year-old male brought to Emergency Room with complaints yellowish discoloration of sclera, Haematuria, Dyspnoea on exertion and decrease schooling performance. He had no other significant personal or family past medical history.

On admission detailed examination was done and vitals show

- Pulse: 124 bpm
- Blood pressure: 98/60 mm-hg
- SpO_2: 97% on room air
- Respiratory Rate: 26 /min

General examination suggests patient is pale, icteric. He also has pigmented knuckles.

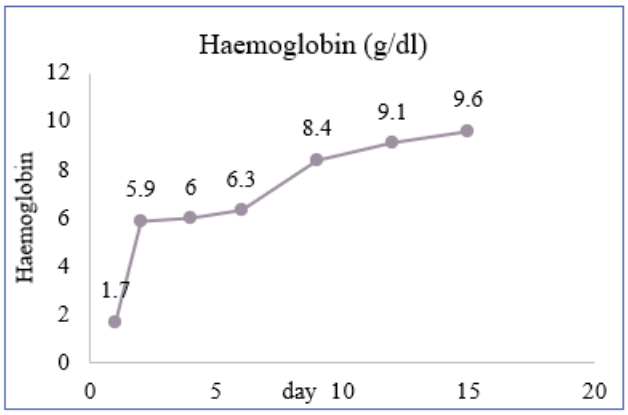
Systemic examination founds systolic murmur in the pulmonary area without any palpable organomegaly.

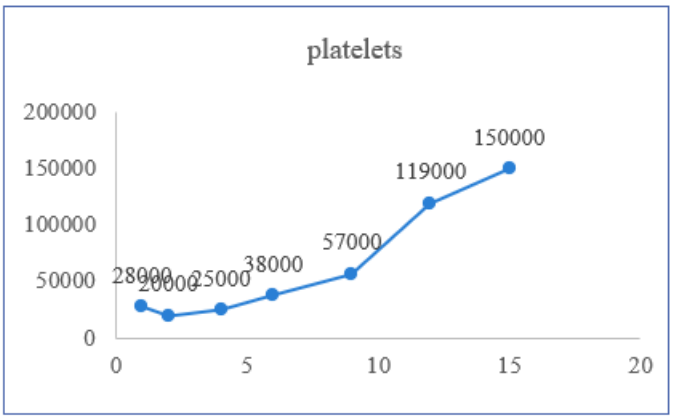
Figure 1: Hyperpigmented knuckles

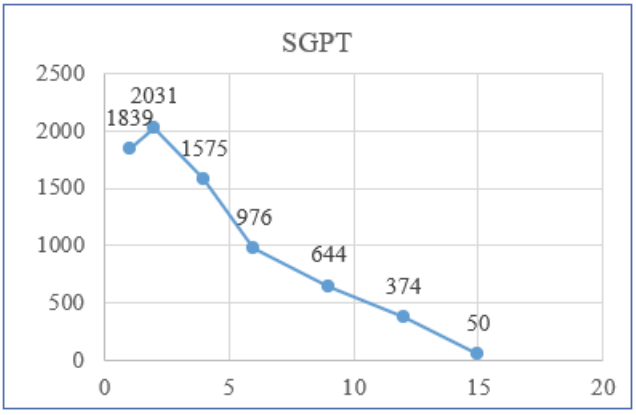
Initial blood workup shows the findings as follows:

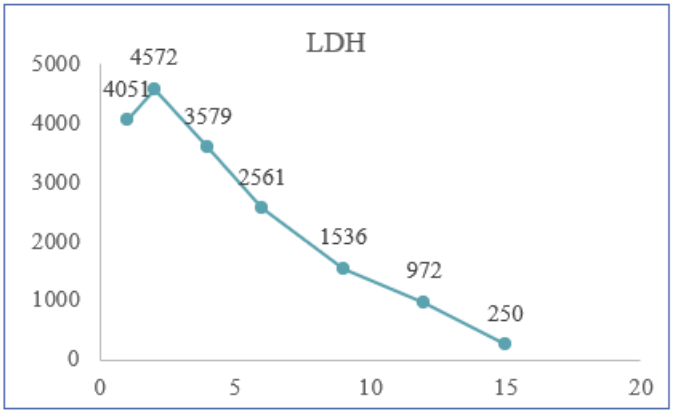
S No.	Tests	Value	Normal Range
1	Haemoglobin (gm/dl)	1.7	11.0-16.0
2	WBC (cells/mm^3)	6.16 x 10^3	4.00-10.0 x 10^3
3	APC (cells/mm^3)	28000	1.5-3.0 x 10^5
4	RDW (%)	28	11.0-16.0
5	RETIC COUNT (%)	1.57	1.5-2.5
6	URINE RBC (cells/HPF)	8 -10	Zero
7	SGPT (IU/L)	1839	0-40
8	SGOT (IU/L)	387	0-40
9	GGT (IU/L)	17.00	0-54
10	Total Billirubin (mg/dl)	7.3	0.1-1.2
11	Indirect Billirubin (mg/dl)	5.7	0.1-0.8
12	FDP (mcg/ml)	20	0-5
13	INR	2.59	1
14	PRTHROMBIN TIME (sec)	36.3	10-14
15	AMMONIA (umol/L)	71	0-30
16	LDH (IU/L)	4051	21-274

- DCT, dengue, G6PD deficiency, HAV, HEV, HBV, HCV, HIV all tests done to rule out other hepatic and haemolytic causes.
- As initially patient having haematuria, significant thrombocytopenia, and raised FDP we consider as a disseminated intravascular coagulation due to any liver aetiology.
- As initial treatment plan we transfuse 2 packed red blood cells, 3 fresh frozen plasma, 4 platelet rich concentrate. We serially monitor patient's vitals and general condition for initial 48 hours. No any warning signs detected and no any worsening in patient's condition. Haematuria begins to resolves after 48 hours and resolved on 4th day.
- After stabilization we send special investigation to identify the hepatic pathology, it suggests normal levels of IgG, ANA, AMA, 24-hour urinary copper level. For low Vitamin B_{12} level, to rule out pernicious anaemia we sent Anti-IF antibodies, and it turns out to be Positive. During hospital stay we transfuse 4 packed red blood cells, 4 platelet rich concentrate and 14 fresh frozen plasma as a blood product.









1) The typical pattern of AST and ALT elevation in IH is a peak within the first 24 hours, then levels drop down to half of the peak seen within 48 hours, then slowly return to baseline over the next 10–15 days.
2) Lactate dehydrogenase (LDH) also elevates to a significantly higher level than that seen in viral hepatitis.[2] the B_{12} deficiency (HEMOLYSIS) and the hypoxemia of the liver, both known to increase LDH level.

Pathophysiology:

Ischemic hepatitis results from reduced hepatic blood flow, primarily through the hepatic arterial and portal venous systems. The liver receives oxygen-rich arterial blood and nutrient-rich, low-oxygen portal blood, offering dual protection against ischemia. Zones 1 and 2 of the liver acinus receive the most oxygen, while zone 3 is more vulnerable to hypoxia due to lower oxygen levels. Hepatic arterial buffer response, mediated by adenosine, regulates hepatic arterial flow based on

portal blood flow changes. Conditions like heart failure, shock, and severe respiratory failure can lead to hepatocyte hypoxia and necrosis. Cellular hypoxia triggers ATP depletion, metabolic pathway failure, and irreversible cellular injury, exacerbated by oxidative stress during reperfusion.

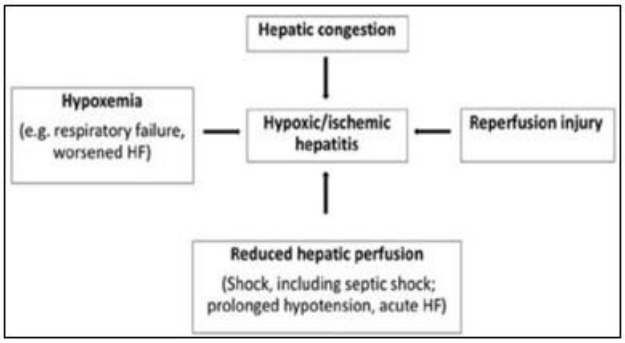


Figure 2: Pathophysiology

3. Discussion

Diagnosis is based on 3 parameters:

1) A state of reduced oxygen delivery to the liver.
2) A significant and transient increase in serum transaminases.
3) The exclusion of other causes of liver injury like viral or medication or toxin induced hepatitis.[5]

ALT/LDH RATIO: [6]

- AST and LDH level rising most sharply and peaking in the first 12-48 hrs, while the rise and peak ALT is not as dramatic.
- Aminotransferase levels falls by >50% within 72 hrs than normalise by around 10 days.
- Increase in LDH level tend to be massive and ALT/LDH ratio of <1.5 distinguishes ischemic injury from other form of acute hepatitis.
- LDH is raised because of either haemolysis caused due to B_{12} deficiency or arterial hypoxic injury to liver.

Differential Diagnosis:

1) Acute Viral Hepatitis
2) Toxic Hepatitis [Drugs, Medication, Acetaminophen]
3) Autoimmune Hepatitis
4) Liver Trauma

4. Prognosis

- Prognosis of patients with IH 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 IH but is related to the underlying disease.[7]
- there is no reported mortality of IH secondary to PERNICIOUS anaemia considering the rarity of this clinical entity, we postulate it may be comparative considering the similarity in pathophysiology and the severity of the anaemia that could very well be compared with any severely decompensated chronic condition or shock state.

5. Outcome

The patient was transferred to the general medicine floor where he stayed for 5 additional days until His haemoglobin levels improved. Liver enzyme trend was consistent with the typical pattern of IH. he was discharged and asked for follow after 2 weeks.

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