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Thrombocytopenia beyond Cirrhosis-A Case of Helicobacter pylori associated ITP

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Abstract

Thrombocytopenia is a frequent hematologic abnormality in patients with chronic liver disease (CLD), commonly attributed to hypersplenism, portal hypertension, and impaired thrombopoietin production. However, when thrombocytopenia presents acutely or with bleeding manifestations, alternative etiologies must be considered. We report the case of a 64-year-old male with alcohol-related CLD and newly diagnosed hepatocellular carcinoma (HCC), who presented with profound thrombocytopenia and mucocutaneous bleeding. Standard evaluations for hepatic, infectious, and marrow-related causes were unremarkable. Subsequent identification of Helicobacter pylori infection, coupled with a favorable response to eradication therapy and corticosteroids, confirmed the diagnosis of H. pylori-associated immune thrombocytopenic purpura (ITP). This case underscores the importance of a systematic diagnostic approach to thrombocytopenia, particularly in the presence of confounding comorbidities. It further highlights the potential role of H. pylori as a modifiable trigger in secondary ITP and supports current recommendations for routine screening in endemic regions.

Keywords: Immune thrombocytopenic purpura, Chronic liver disease, Helicobacter pylori, Hepatocellular carcinoma, Thrombocytopenia, Eradication therapy

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia, resulting from the accelerated destruction of platelets and impaired megakaryocyte function in the absence of other hematologic abnormalities [1]. While ITP is often idiopathic in nature, a substantial proportion of cases are classified as secondary, with underlying triggers such as autoimmune disorders, viral infections (HIV, hepatitis C), malignancies, and certain bacterial infections—including Helicobacter pylori(H. pylori)—playing a pathogenic role[2,3]. The discovery of a causal association between H. pylori infection and secondary ITP has significantly altered the diagnostic and therapeutic approach to thrombocytopenia, particularly in endemic regions such as Asia and Southern Europe [4]. Eradication therapy has demonstrated platelet count recovery in up to 50% of H. pylori-positive ITP patients, suggesting an immunologically mediated cross-reactivity between bacterial antigens and platelet glycoproteins [5,6].

Chronic liver disease (CLD) adds further complexity to the evaluation of thrombocytopenia due to multifactorial mechanisms including hypersplenism, diminished thrombopoietin synthesis, and portal hypertension-associated sequestration[7]. Moreover, in patients with concurrent hepatocellular carcinoma (HCC), thrombocytopenia is more typically attributed to tumor-related factors such as marrow infiltration or a paraneoplastic syndrome, although thrombocytosis is more commonly reported in HCC[8].

We report a diagnostically challenging case of a 64-year-old male with CLD and incidentally diagnosed HCC, who presented with acute thrombocytopenia and mucocutaneous bleeding. Initial work-up for tropical infections, marrow infiltration, and liver-related causes was unremarkable. The subsequent detection of H. pylori infection, coupled with a favorable response to eradication therapy and corticosteroids, confirmed the diagnosis of H. pylori-associated secondary ITP. This case underscores the importance of a comprehensive diagnostic approach to thrombocytopenia, especially in patients with confounding comorbidities such as CLD and malignancy.

Case Presentation

A 64-year-old male, a professional driver and reformed alcoholic for the past five years, presented to the emergency department with complaints of fever, generalized myalgia, and bleeding from multiple sites including the oral cavity and rectum, along with reddish discoloration of urine. His past medical history was significant for alcohol-related chronic liver disease (CLD) with portal hypertension, for which he had been under regular follow-up. He was also a known hypertensive and had completed treatment for pulmonary tuberculosis six years prior. Two weeks before presentation, he had sustained a minor road traffic accident and was managed conservatively.

On presentation, the patient was hemodynamically stable. Neurological examination revealed preserved higher mental functions. Mucosal bleeding from the oral cavity was noted, though there were no signs of petechiae or purpura on the skin. Abdominal examination did not reveal hepatosplenomegaly or ascites.

Initial laboratory investigations revealed severe thrombocytopenia (25,000/mm^3), with preserved hemoglobin and leukocyte counts. Peripheral smear demonstrated erythrocytosis with thrombocytopenia. Liver function tests showed mildly elevated transaminases. Coagulation profile showed mildly prolonged prothrombin time (PT) and elevated INR. Renal function and electrolytes were within normal limits except for mild hyponatremia. Infectious screening including Dengue, Leptospira, HIV, HBsAg, and HCV was negative. ANA was also negative.

Imaging and Diagnostic Work-Up

Ultrasound abdomen revealed a coarse liver echo texture with a hyperechoic lesion in the right lobe, splenomegaly, and features of portal hypertension. Serum alpha-fetoprotein (AFP) level of 821 ng/mL. Contrast-enhanced CT abdomen raised suspicion for hepatocellular carcinoma (HCC) with portal vein thrombosis. MRI liver with hepatobiliary protocol confirmed a heterogeneous lesion in the right lobe with restricted diffusion and portal vein thrombosis, classified as LI-RADS TIV as shown in Figure 1. Liver biopsy confirmed presence of poorly differentiated HCC as shown in figure 2. In view of persistent thrombocytopenia unresponsive to transfusions, a bone marrow biopsy was performed, which showed normocellular marrow with trilineage hematopoiesis and no malignant infiltration as in figure 3. Table 1 shows the summary of the intial laboratory and imaging investigations.

Therapeutic Intervention

Suspecting immune-mediated thrombocytopenia, the patient was started on intravenous corticosteroids. A modest improvement in platelet counts was noted. Evaluation for secondary ITP revealed high titers of IgG antibodies against *Helicobacter pylori*. Upper GI endoscopy showed antral gastritis, and biopsy confirmed mucosal inflammation consistent with H. pylori infection as in figure 4. Although rapid urease testing (RUT) could not be performed, the patient was started on H. pylori eradication therapy with a triple-drug regimen (proton pump inhibitor, amoxicillin, and clarithromycin).

Clinical Course and Outcome

Following eradication therapy, there was a sustained improvement in platelet count, allowing tapering and eventual discontinuation of corticosteroids. A liver biopsy confirmed poorly differentiated HCC. The patient was discharged with oncological follow-up and supportive management. At follow-up, platelet levels remained stable without further need for immunosuppression.

Discussion

Thrombocytopenia is a common hematological abnormality observed in patients with chronic liver disease (CLD), typically attributed to hypersplenism, reduced thrombopoietin production, and bone marrow suppression [2, 9]. However, in cases where thrombocytopenia is profound, persistent, or acute, accompanied by bleeding manifestations especially in the absence of hepatosplenomegaly a broader differential must be considered, including immune thrombocytopenic purpura (ITP).

ITP is characterized by immune-mediated platelet destruction and impaired production in the absence of other causes of thrombocytopenia[10]. Although most cases of ITP are idiopathic, secondary causes—including infections (HIV, HCV), autoimmune conditions (e.g., systemic lupus erythematosus), malignancies, and drugs—should be excluded before labeling a case as primary ITP [3].

This case was diagnostically complex due to the co-existence of CLD, portal hypertension, and a newly diagnosed hepatocellular carcinoma (HCC), which initially directed the clinical suspicion toward hypersplenism and marrow infiltration as potential causes of thrombocytopenia. However, imaging ruled out significant splenomegaly and marrow biopsy demonstrated normal trilineage hematopoiesis without infiltration, prompting consideration of an immune-mediated etiology.

The patient showed a positive response to corticosteroid therapy, supporting a diagnosis of ITP. The subsequent discovery of elevated *Helicobacter pylori* (H. pylori) IgG antibodies, endoscopic gastric mucosal biopsy showing the

evidence of inflammation and the patient's response to eradication therapy further confirmed *H. pylori*-associated secondary ITP.

The association between *H. pylori* and ITP has been well-documented in various geographic regions, particularly in Asia and Southern Europe [4,7]. Eradication of *H. pylori* in patients with ITP has been associated with platelet recovery in approximately 30–60% of cases, depending on genetic and regional factors [6]. The exact mechanism linking *H. pylori* to ITP is not fully understood but is hypothesized to involve molecular mimicry between *H. pylori* antigens and platelet glycoproteins (e.g., GPIIb/IIIa), leading to the formation of cross-reactive autoantibodies[1].

While *H. pylori*-associated ITP is more commonly described in the absence of significant comorbidities, this case highlights that the condition may occur even in the background of CLD and malignancy, both of which are independently associated with thrombocytopenia. HCC has occasionally been associated with paraneoplastic thrombocytopenia, but more frequently with thrombocytosis due to interleukin-6 production[8]. The absence of bone marrow infiltration and the patient's favorable response to *H. pylori* eradication therapy argued against a paraneoplastic cause.

Another noteworthy aspect is the importance of a high index of clinical suspicion. The diagnosis of *H. pylori*-associated ITP was considered only after a detailed evaluation excluded more common causes. This approach prevented unnecessary escalation of immunosuppressive therapy and directed effective antimicrobial treatment.

The response to eradication therapy also emphasizes the value of routine *H. pylori* testing in ITP patients, even when other plausible causes of thrombocytopenia exist. International guidelines now recommend *H. pylori* testing and treatment in all newly diagnosed ITP patients, particularly in endemic areas [8,10].

Table-2 highlights the novelty of the case occurring in the context of CLD and HCC while reinforcing consistency with recent literature in diagnostic approaches and positive outcomes after therapy.

Conclusion

This case underscores the importance of considering immune-mediated causes of thrombocytopenia, even in patients with confounding conditions such as chronic liver disease and malignancy. The identification and successful treatment of *H. pylori*-associated ITP in this complex clinical context reinforce the value of a comprehensive, evidence-informed diagnostic approach. This case adds to the growing recognition of infection-driven autoimmunity and supports routine *H. pylori* evaluation in atypical thrombocytopenia.

Conflict of Interest- Nil

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Table 1-Laboratory and Imaging Investigations

Parameter	Value	Normal Range
Hemoglobin	17.4 g/dL	13 – 16 g/dL
MCV	83.4 fL	80 – 100 fL
PCV	48.9%	42 ± 6%
Total Leukocyte Count	6900 /mm³	4000 – 11,000 /mm³
Differential Count	P58, L39	-
Platelet Count	15,000 /mm³	150,000 – 450,000 /mm³
Peripheral Smear	Erythrocytosis with thrombocytopenia	-
Prothrombin Time	19.4 s	9 – 13 s
INR	1.6	0.8 – 1.2
Aptt	31.3 s	25 – 45 s
Fibrinogen	433 mg/dL	<498 mg/dL
D-Dimer	0.8 µg/mL	<0.5 µg/mL
Urea	24 mg/dL	7 – 20 mg/dL
Creatinine	0.9 mg/dL	0.7 – 1.2 mg/dL
Sodium	132 mEq/L	135 – 145 mEq/L
Potassium	3.7 mEq/L	3.5 – 5.5 mEq/L
Total Bilirubin	1.9 mg/dL	0.1 – 1.2 mg/dL
Direct Bilirubin	0.5 mg/dL	0.1 – 0.3 mg/dL
SGOT (AST)	70 U/L	<40 U/L
SGPT (ALT)	53 U/L	<40 U/L
ALP	140 U/L	40 – 147 U/L
Total Protein	7.5 g/dL	6 – 8 g/dL
Albumin	3.2 g/dL	3.5 – 5.5 g/dL
C reactive Protein	15.2 mg/L	<6 mg/L
Random Blood Sugar	152 mg/dL	-
Alpha Feto Protein	821 ng/mL	<10 ng/mL
Anti Nuclear Antibody	Negative	-
HIV/HBsAg/HCV	Negative	-
RBCs in Urine	Plenty	Nil
Pus Cells	0–2/hpf	<5/hpf
Epithelial Cells	Occasional	Occasional
Dengue/Leptospira Serologies	Negative	-
USG Abdomen	CLD, hyperechoic lesion, splenomegaly	-
CECT Abdomen	HCC with portal vein thrombosis	-
MRI Abdomen	Heterogeneous lesion (LI-RADS TIV)	-
Upper GI Endoscopy	Antral gastritis	-
Bone Marrow Biopsy	Trilineage hematopoiesis, no malignancy	-
Liver Biopsy	Poorly differentiated HCC	-

Table 2- Recent Cases of H. pylori-Associated ITP

Author (Year)	Population / Setting	Comorbidity	H. pylori Diagnosis	Platelet Response
Present Case (2025)	64-year-old male, India	CLD + Hepatocellular Carcinoma	IgG serology; endoscopy + biopsy	Sustained normalization after eradication + steroids
Asiimwe et al.[11]	70-year-old male,	Post-influenza	Known H. pylori;	Platelets normalized within

(2023)	Uganda	vaccination	not tested during event	3 days of eradication
Sadia et al.[12] (2022)	Adult female, Pakistan	None reported	Gastric biopsy + stool antigen	Full recovery post triple therapy
Suetsugu et al.[13] (2023)	Adult, Japan	Membranous nephropathy	Gastric biopsy	ITP resolved post eradication

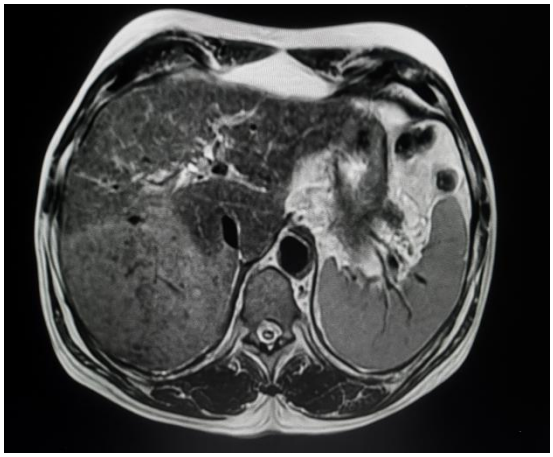

Figure 1- MRI abdomen showing a large heterogenous signal intensity in the right lobe of liver ion the background of cirrhosis. LIRADS – TIV

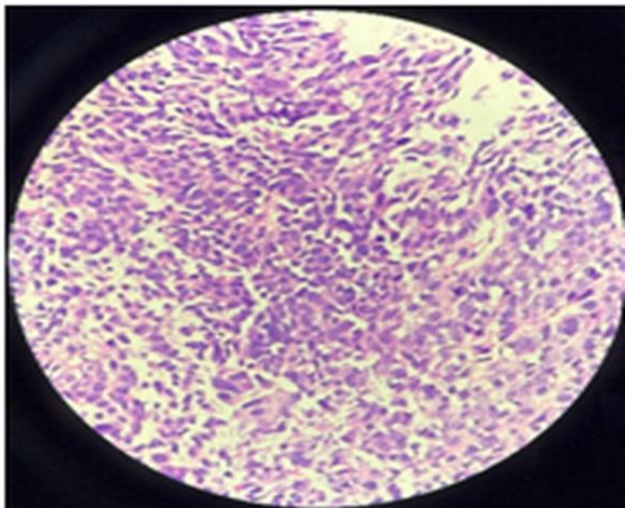

Figure 2- Liver biopsy showing infiltrating poorly differentiated carcinoma arising from the liver.

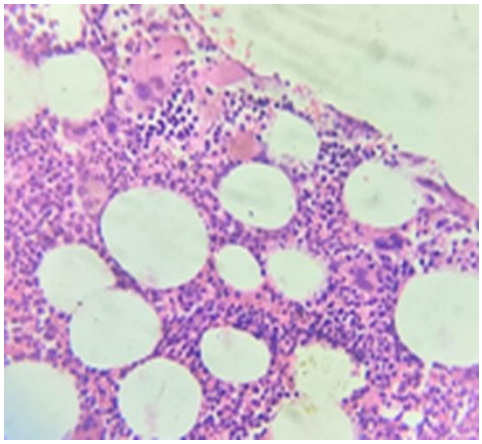

Figure 3- Bone marrow biopsy showing trilineage haematopoiesis with no malignant cell infiltration.

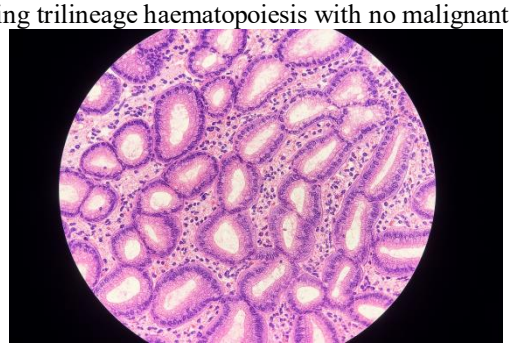

Figure 4-Gastric biopsy showing lymphoplasmacytic inflammatory infiltration of lamina propria.