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HEMATOLOGICAL DISORDERS IN LIVER CIRRHOSIS: MODERN CONCEPTS OF PATHOGENESIS, DIAGNOSTICS, AND CLINICAL SIGNIFICANCE IN THE CONTEXT OF THE REBALANCED HEMOSTASIS CONCEPT

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Abstract: Liver cirrhosis is a chronic progressive disease accompanied by profound morphological and functional alterations of the hepatobiliary system. Hemostatic disorders represent a characteristic component of cirrhosis and include anemia, thrombocytopenia, leukopenia, and coagulopathy. Contemporary research demonstrates that the hemostatic system in cirrhosis is not in a state of complete hypocoagulation, as previously believed. Instead, a condition of "rebalanced hemostasis" develops, in which impaired production of procoagulants and anticoagulants maintains a fragile equilibrium, predisposing patients to both bleeding and thrombosis. This article summarizes current data on the mechanisms of hematological disorders, diagnostic approaches, and therapeutic strategies, including discussion of the roles of thrombopoietin, hepcidin, coagulation factors, hypersplenism, and portal hypertension. Understanding these processes is essential for optimizing patient management and guiding treatment decisions.

Keywords: liver cirrhosis, anemia, thrombocytopenia, coagulopathy, rebalanced hemostasis, thrombopoietin, hypersplenism.

Introduction

Liver cirrhosis represents the end stage of many chronic liver diseases and is characterized by progressive replacement of functional parenchyma with fibrous tissue and formation of regenerative nodules. These structural alterations lead to impairment of essential hepatic functions, including metabolic, synthetic, and detoxification processes. Hematological disorders play a significant role in the pathophysiology of cirrhosis, affecting prognosis, contributing to complications, and influencing treatment strategies.

The liver synthesizes most coagulation factors, fibrinolytic proteins, and regulates platelet production and iron metabolism. Therefore, hepatic insufficiency is accompanied by complex disturbances in hematopoiesis and hemostasis. For a long time, patients with cirrhosis were thought to be predominantly in a state of hypocoagulation and at high risk of bleeding. However, recent studies have revealed that the hemostatic system in cirrhosis exists in a state of dynamically unstable equilibrium — a rebalanced hemostasis — in which both hemorrhagic and thrombotic events are possible.

Anemia in Liver Cirrhosis

Anemia occurs in the majority of patients with decompensated cirrhosis. Its pathogenesis is multifactorial:

Chronic blood loss
Associated with portal hypertension, esophageal and gastric varices, portal gastropathy, and hemorrhoids.

Hypersplenism
The enlarged spleen actively destroys blood cells.

Iron deficiency and impaired iron metabolism
The liver regulates synthesis of hepcidin — the key hormone of iron homeostasis.
In cirrhosis, hepcidin levels decrease → impaired iron release from stores → functional iron deficiency develops even when iron reserves are adequate.

Anemia of chronic inflammation
Elevated pro-inflammatory cytokines suppress erythropoiesis.

Hydrolysis
May occur in severe alcoholic cirrhosis or immune-mediated processes.

Clinically, anemia worsens organ hypoxia, reduces exercise tolerance, and negatively affects survival.

Thrombocytopenia

Thrombocytopenia is one of the most characteristic laboratory markers of cirrhosis.

Mechanisms:

Hypersplenism → increased platelet sequestration and destruction.

Decreased hepatic synthesis of thrombopoietin.

Immune-mediated platelet destruction in some cases.

Bone marrow suppression due to chronic inflammation and nutritional deficiency.

Modern therapy includes **TPO receptor agonists (eltrombopag, avatrombopag)**, which reduce the need for platelet transfusions before invasive procedures.

Leukopenia

Leukopenia primarily results from hypersplenism and neutrophil sequestration.
It increases susceptibility to bacterial infections — a major cause of decompensation.
Use of **G-CSF** is limited to severe infectious complications.

Coagulopathy and the Concept of Rebalanced Hemostasis

Traditionally, coagulopathy in cirrhosis was attributed to decreased clotting factor synthesis and elevated INR.
However, **INR does not reflect actual bleeding risk**.

Modern understanding:

Reduced synthesis of both procoagulants and anticoagulants (protein C, protein S, antithrombin III).

Increased von Willebrand factor and decreased ADAMTS-13 → increased thrombosis risk.

Fibrinolysis may be either suppressed or enhanced depending on disease stage.

Thus, hemostasis in cirrhosis is unstable: **patients may bleed and thrombose simultaneously**.

Major thrombotic complications:

Portal vein thrombosis

Deep vein thrombosis

Pulmonary embolism

Diagnostics

Method	**Purpose**
CBC	detection of anemia, thrombocytopenia, leukopenia
Ferritin, transferrin	evaluation of iron metabolism
Coagulation tests (PT, INR, aPTT)	assessment of hepatic synthetic function
TPO level	assessment of thrombopoiesis regulation
Imaging (Ultrasound, CT)	detection of splenomegaly and thrombosis

Treatment

Disorder	**Therapeutic Approach**
Anemia	control of bleeding source, IV iron, transfusion
Thrombocytopenia	TPO receptor agonists; splenectomy in refractory cases

Disorder	Therapeutic Approach
Leukopenia	infection prevention
Coagulopathy	FFP only when bleeding occurs; anticoagulation in thrombosis

Liver transplantation remains the only radical treatment.

Conclusion

Hematological disorders in liver cirrhosis reflect a complex interplay of inflammation, portal hypertension, impaired hepatic synthetic function, and dysregulation of hematopoiesis. The modern concept of rebalanced hemostasis has shifted understanding of bleeding and thrombotic risks in cirrhotic patients. Comprehensive evaluation and multidisciplinary management are critical for optimizing treatment strategies.

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