

Macrocytic Anemia: Causes, Diagnosis, and Clinical Management

Introduction

Macrocytic anemia is a hematologic disorder characterized by enlarged red blood cells, reflected as an increased mean corpuscular volume (MCV) on laboratory testing. It is a common cause of anemia with diverse etiologies, ranging from nutritional deficiencies to bone marrow disorders and medication-induced effects. Understanding the underlying mechanisms is essential for accurate diagnosis, appropriate treatment, and prevention of complications such as neurologic deficits and cardiovascular stress.

Etiology and Pathophysiology

Macrocytic anemia is broadly classified into megaloblastic and non-megaloblastic types.

Megaloblastic anemia arises from impaired DNA synthesis, often due to vitamin B12 or folate deficiencies. In these cases, red blood cell precursors show characteristic nuclear-cytoplasmic asynchrony, leading to ineffective erythropoiesis. Common causes include pernicious anemia, dietary deficiency, malabsorption syndromes, and certain medications like methotrexate.

Non-megaloblastic anemia is associated with conditions that affect red blood cell maturation without DNA synthesis defects. Causes include liver disease, alcohol use, hypothyroidism, and myelodysplastic syndromes.

Additional contributors, such as chronic medications, chemotherapy, and metabolic disorders, can further exacerbate macrocytosis.

Diagnosis and Clinical Implications

Diagnosis of macrocytic anemia begins with a complete blood count showing elevated MCV and peripheral blood smear examination. Laboratory evaluation of vitamin B12, folate, liver function, and thyroid status helps identify the underlying etiology. Bone marrow studies may be necessary in atypical or refractory cases.

Clinical manifestations vary depending on severity and cause, ranging from fatigue, pallor, and dyspnea to neurologic symptoms in B12 deficiency, such as numbness, paresthesia, and cognitive impairment. Timely identification and correction of the underlying cause are critical to prevent long-term complications.

Conclusion

Macrocytic anemia is a heterogeneous disorder with potentially serious consequences if left untreated. Differentiating between megaloblastic and non-megaloblastic forms is essential for targeted therapy. Advances in diagnostic testing and a structured clinical approach allow for early detection, appropriate supplementation, and management of underlying causes. Continued research and awareness are necessary to optimize patient outcomes and prevent long-term sequelae.

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