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Anemia in patients with solid tumors

Abstract

Anemia frequently complicates the clinical scenario in patients with solid tumors. Intensified by the tumor's metabolic demands, inflammation, and treatment regimens, anemia detrimentally impacts quality of life and clinical outcomes. This review delves into the multifaceted pathophysiology, including molecular and genetic insights, diagnostic approaches, contemporary management strategies, and therapeutic advancements. Emphasis is placed on translational research and emerging treatments.

Keywords: anemia, inflammation, síndrome, deficiency

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Introduction

Cancer-associated anemia (CAA) in patients with solid tumors is a prevalent and debilitating condition that warrants comprehensive clinical attention. Its multifactorial etiology involves direct tumor effects, systemic inflammation, nutritional deficiencies, and treatment-induced bone marrow suppression. Understanding the molecular and genetic underpinnings of CAA is crucial for developing targeted therapies. This article aims to provide a thorough analysis of the current understanding, diagnostic methods, and innovative treatments for anemia in the context of solid tumors.

Pathophysiology

The etiology of anemia in patients with solid tumors is intricate, involving multiple pthological mechanisms and molecular pathways:

Chronic inflammation

Cytokine-mediated effects: Inflammatory cytokines such as IL-6, TNF-alpha, and IL-1β play significant roles in mediating anemia. These cytokines inhibit erythropoietin production and responsiveness, disrupt iron homeostasis by upregulating hepcidin, and impair erythroid progenitor cell survival. Hepcidin, in particular, binds to ferroportin on cell membranes to promote its internalization and degradation, decreasing iron absorption and release from storage sites.

Genetic insights: Polymorphisms in genes encoding for these cytokines and their receptors have been associated with variability in anemia severity among cancer patients. For example, polymorphisms in the IL-6 gene are linked to changes in hepcidin levels and iron metabolism.[1,2]

Nutritional deficiencies

Cancer can induce a catabolic state leading to cachexia and malabsorption syndromes, compromising the intake and utilization of critical hematopoietic nutrients, specifically iron, vitamin B12, and folate.

Bone marrow infiltration

Solid tumors, particularly metastatic cancers such as breast and prostate cancer, may infiltrate the bone marrow, disrupting normal hematopoiesis. This can be assessed via bone marrow biopsy revealing tumor cells and associated fibrosis.[3]

Blood loss

Tumors located in the gastrointestinal or genitourinary tract can cause chronic bleeding. Furthermore, coagulopathies frequently observed in malignancies may exacerbate blood loss.

Chemotherapy and radiation therapy

These treatments induce bone marrow suppression, diminishing the production of erythrocytes. Platinum-based chemotherapies (e.g., cisplatin) are notorious for their nephrotoxic effects, leading to reduced erythropoietin production.[4]

Clinical manifestations

Patients with anemia associated with solid tumors frequently present with:

General fatigue and weakness Affects daily functioning and reduces quality of life.

Dyspnea: Particularly with exertion, caused by reduced oxygen-carrying capacity.

Palpitations and tachycardia: As compensatory mechanisms to maintain oxygenation.

Pallor: Visible in mucous membranes and skin.

Signs of heart failure: In extreme cases, particularly in patients with pre-existing cardiovascular conditions.

Diagnosis

An integrated approach is necessary for diagnosing anemia in cancer patients:

a) **Complete blood count (CBC):** Evaluates hemoglobin, hematocrit, mean corpuscular volume (MCV), and red blood cell (RBC) indices.

b) **Reticulocyte count:** Indicates bone marrow activity.

c) **Iron studies:** Including serum ferritin, iron, and transferrin saturation, to delineate iron deficiency anemia from anemia of chronic disease (also referred to as anemia of inflammation).

d) **Vitamin levels:** Measurements of serum vitamin B12 and folate to identify deficiencies.

e) **Inflammatory markers:** CRP and erythrocyte sedimentation rate (ESR) levels can indicate chronic inflammation.

f) **Bone marrow examination:** Indicated in cases of unexplained anemia or when malignancy-driven marrow infiltration is suspected.

Molecular and genetic insights

Innovative research has identified molecular targets crucial for the development of therapeutics:

Hepcidin regulation: Hepcidin is a key therapeutic target. RNA interference and monoclonal antibodies against hepcidin or its regulatory pathways (e.g., BMP/SMAD signaling) have shown promise in preclinical models.[5]

Erythropoiesis stimulating agents (ESAs): Genetic variants influencing the erythropoietin (EPO) receptor's activity or the JAK2/STAT5 signaling pathway may alter the response to ESAs, necessitating personalized treatment approaches.

Management

Managing anemia in cancer patients requires multimodal strategies:

a) **Erythropoiesis stimulating agents (ESAs):** These agents, including epoetin alfa and darbepoetin alfa, stimulate erythropoiesis. However, their use is controversial due to potential risks such as increased thromboembolic events and possible tumor progression. Recent guidelines recommend cautious use, primarily in palliative settings or when transfusions are contraindicated.[6,7]

b) **Iron supplementation:** Intravenous iron sucrose or ferric carboxymaltose is preferred over oral iron due to better efficacy and tolerance, especially in cases of functional iron deficiency.[8]

c) **Red blood cell transfusions:** Critical for managing severe symptomatic anemia. Transfusion thresholds should be individualized based on clinical symptoms and comorbidities.

d) **Nutritional support:** To address deficiencies, supplementation of iron, vitamin B12, and folate is necessary. Parenteral supplementation may be required in cases of malabsorption or severe deficiency.

e) **Treatment of underlying causes:** Effective cancer therapy, managing chronic bleeding, and treating comorbid conditions like renal insufficiency are essential components.

Modern therapeutic approaches

Recent advances include

Targeted therapies and immunotherapy: New classes of drugs, such as immune checkpoint inhibitors (e.g., pembrolizumab) and tyrosine kinase inhibitors (e.g., sunitinib), have specific profiles with varying impacts on hematopoiesis.[9]

Gene therapy: Experimental treatments involving gene editing technologies like CRISPR/Cas9 are being explored for correcting genetic abnormalities contributing to anemia.[10]

Hepcidin antagonists and anticalins: These novel agents aim to modulate the hepcidin-ferroportin axis, offering a potential cure for anemia of chronic disease.[11]

Conclusion

Anemia in patients with solid tumors significantly impacts patient outcomes and quality of life. A comprehensive understanding of its pathophysiology, incorporating molecular and genetic insights, is essential for effective management. Advances in diagnostic and therapeutic modalities offer promising avenues for improving patient care. Ongoing research holds the key to novel treatments, aiming for better management of anemia in this vulnerable patient population.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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