Narrative review

Anemia in malignancies: Pathogenetic and diagnostic considerations

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Objectives: The aim of this paper is to review the pathogenesis and diagnostic approaches to anemia in cancer patients.
Methods: PubMed was queried for various combinations of anemia and cancer-related terms using appropriate filters for articles and practice guidelines published in the last 5 years. Specific searches were conducted for individual pathogenetic mechanisms and malignancies of specific anatomic sites.
Results: Anemia is the commonest hematological manifestation of cancer, afflicting 40–64% of patients treated for malignancies. Pathophysiologically, cancer-related anemia can be classified into four broad but overlapping categories: hypoproliferative anemia including the common anemia of inflammation/chronic disease, hemolytic anemia, miscellaneous etiologies, and uncertain etiologies. Anemia incidence increases with the administration of chemotherapy/radiotherapy. It reduces the quality of life and shortens survival in cancer patients. A positive correlation is observed between anemia and tumor hypoxia. Experimentally, hypoxemia enhances tumor growth and resistance to therapy by stimulating angiogenesis, acquisition of genomic mutations, and increasing resistance to apoptosis as well as to the killing effects of chemo/radiotherapy-generated free radicals.
Discussion: Diagnostic approaches to the anemic cancer patient begin with a detailed clinical history and physical examination. Peripheral blood morphology and reticulocyte count are also helpful. Patients with unexplained anemia are evaluated by standard approaches also used in patients of similar age without malignancy. Serum iron profile and bone marrow examination are often required in difficult cases. This review focuses on major aspects of the pathogenesis of the individual entities. Diagnostic approaches and uncommon causes including hemophagocytic lymphohistiocytosis, acquired hemoglobinopathies, and myelodysplasia are also discussed.

Keywords: Anemia, Cancer, Chemotherapy, Chronic disease, Etiopathogenesis, Hypoxia, Malignancy, Radiotherapy

Introduction

Cancer is the commonest cause of mortality in developed countries and the second leading cause of mortality in the developing world. Global estimates for 2008 pointed to 12.7 million cancer cases and 7.6 million cancer deaths.[1,2] Anemia is a major public health problem affecting 1.62 billion people worldwide. A World Health Organization (WHO) Global Database on Anemia for 1993–2005 pegged the prevalence of anemia worldwide at 25%.[3]

Anemia is the commonest hematological manifestation of cancer and a majority of cancer patients are anemic.[4] Anemia may at times be the sole manifestation of cancer and a diagnostic work-up of anemia may unmask a hidden malignancy like a gastrointestinal tract adenocarcinoma (refractory iron deficiency anemia (IDA) may be sole manifestation), hairy cell leukemia (HCL), or a myelodysplastic syndrome (MDS). The commonest anemia in patients with malignancies is anemia of inflammation/chronic disease,[4] although other causes depending on the site may be also common (e.g. blood loss in stomach, bladder, uterine, and cervical malignancies). Multiple etiologies are encountered in many cases. In the current era of multimodality cancer therapy, the prevalence of treatment-related anemia is likely to be increasing even though definite estimates are difficult.

We review here the pathogenetic and etiological approaches to anemia in cancer patients. For this, we queried PubMed for various combinations of the terms anemia, cancer, malignancy, diagnosis, and pathogenesis using the following filters: reviews, systematic reviews, articles published in the last 5 years, and practice guidelines. Subsequently, specific

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