Anemia of Chronic Disease

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Key Points
➢ Mild anemia ➢ Causative factor: Substances released from activated monocytes ➢ Chronic kidney disease also leads to anemia

Definition: The anemia of chronic disease (ACD) is defined as a mild anemia associated with a chronic inflammatory, infectious or neoplastic illness and with a characteristic disturbance of iron metabolism.[1]

Cause: Many of the findings in ACD can be accounted for by release of a monokine called leukocyte endogenous mediator (LEM), endogenous pyrogen, or interleukin-1. This substance is released from "activated" monocytes. Bacterial endotoxins, certain lymphokines and phagocytic challenges are among the factors stimulating its biosynthesis. LEM induces fever, leukocytosis, biosynthesis. LEM induces fever, leucocytosis, a variety of biochemical changes collectively known as the "acute phase response." It is proposed that ACD results from the long-term elaboration of LEM and that release of this material is the common pathogenetic factor found in the illnesses that are associated with ACD. Some suggest that the hypoferremia associated with ACD is probably caused by defective release of iron from cells--particularly from macrophages, but also from hepatocytes and intestinal epithelium. Two possible mechanisms for this abnormality have been proposed: Liberation of lactoferrin from neutrophilic leukocytes and induction of apoferritin synthesis.[1] Neither mechanism has been established. Erythrokinetic studies in ACD have detected a modest reduction of erythrocyte survival without an adequate compensatory increase in the rate of red cell production. The reduced erythrocyte survival is probably related to an increase in phagocytic activity by activated macrophages. Impaired bone marrow response is partly related to the restricted iron supply, but there is substantial evidence for an additional defect in erythropoietin secretion. In some malignant diseases, there is evidence of an additional abnormality: impaired marrow response to a normal amount of erythropoietin. The nature of the erythropoietic defects and the relation of LEM to them remain to be established.[2] Chronic kidney disease (CKD) is a widespread health problem in the world and anemia is a common complication. Anemia conveys significant risk for cardiovascular disease, faster progression of renal failure and decreased quality of life. Patients with CKD can have anemia for many reasons, including but not invariably their renal insufficiency. These patients require a thorough evaluation to identify and correct causes of anemia other than erythropoietin deficiency. The mainstay of treatment of anemia secondary to CKD has become erythropoiesis-stimulating agents (ESAs). The use of ESAs does carry risks and these agents need to be used judiciously. Iron deficiency often co-exists in this population and must be evaluated and treated. Correction of iron deficiency can improve anemia and reduce ESA requirements. Partial, but not complete, correction of anemia is associated with improved outcomes in patients with CKD.[3] To determine the possible association between anemia and clinical and echocardiographic cardiac disease, a cohort of 432 end-stage renal disease patients (261 on hemodialysis and 171 on peritoneal dialysis) who started dialysis therapy between 1982 and 1991 were followed prospectively for an average of 41 months. Baseline demographic, clinical, echocardiographic

assessments were performed, as well as monthly serial clinical and laboratory tests while the patients were on dialysis therapy. The mean (±SD) hemoglobin level during dialysis therapy was 8.8 ± 1.5 g/dL. After adjusting for age, diabetes, and ischemic heart disease, as well as for blood pressure and serum albumin levels measured serially, each 1 g/dL decrease in mean hemoglobin was independently associated with the presence of left ventricular dilatation on repeat echocardiogram (odds ratio, 1.46; *P* = 0.018) and the development of de novo (relative risk [RR] = 1.28; *P* = 0.018) and recurrent (RR = 1.20; *P* = 0.046) cardiac failure.[4] Most patients with chronic kidney disease eventually become anemic. We should view the management of anemia in these patients as part of the overall management of the many clinically relevant manifestations of chronic kidney disease. Erythropoiesis-stimulating agents (ESAs) are safe and should be used, as treating anemia may forestall some of the target-organ damage of chronic kidney disease. [5] The differential diagnosis includes other underproduction anemias, such as those caused by vitamin and mineral deficiencies, renal failure, endocrinopathies, and myelodysplasia, it generally is easily distinguished from these conditions. Nevertheless, an understanding of the pathogenesis of this condition, as well as a means of alleviating the anemia when the chronic disorder persists, has remained elusive. Recently, major advances have occurred toward understanding the pathogenesis of the anemia of chronic disease and its treatment, and these advances are reviewed.[4]

References:

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