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Anemia in Elderly Koreans

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Recently, the geriatric population in Korea has grown to comprise approximately 10% of the total population, and anemia has become a significant problem among elderly patients. Many elderly patients have anemia due to nutritional deficiency, chronic inflammation, or comorbid diseases; however, in a significant fraction of the patients with anemia, the cause remains obscure. Anemia of any degree is recognized as a significant independent contributor to morbidity and mortality in elderly patients. This article summarizes the patterns of anemia in Korean geriatric patients.

Key Words: Anemia, Korean elderly, anemia pattern

INTRODUCTION

Hematologic disorders in elderly individuals often present difficult diagnostic and therapeutic dilemmas to practitioners. Practitioners must decide whether the presence of a hematologic disorder is indicative of a true disease state and how aggressively such findings should be pursued.

There is a fairly widespread assumption that mild to moderate anemia may develop due to the aging process alone. However, anemia and other disorders of the hematopoietic system in an elderly person require the same evaluation of the underlying mechanism as that one would carry out in a younger patient, and evaluation for reversible causes of anemia may be warranted. Occult bleeding, malignancy, anemia associated with chronic disorders, or rarer conditions may be found. In disorders for which effective treatment exists, the response in an elderly person will be as successful as in younger patients.[1]

CHANGES IN NORMAL HEMATOPOIESIS WITH AGE

Bone marrow cellularity decreases by approximately one third after 65 years of age as part of a decline in marrow activity with advancing age that begins at around the age of 30.[2] While renewal of peripheral blood cells remains normal with advancing age, except in times of excess stress, there is a reduction in bone marrow stem cell reserves and proliferative capacity with age. Elderly patients may not respond to bleeding with the same degree of reticulocytosis as younger patients.[3]

The mean hemoglobin level is 1 g/dL lower in elderly females compared with younger females and 2 g/dL lower in elderly males compared with younger males.[4] Most normal elderly men continue to maintain normal hemoglobin levels even in old age. If there is a significant decline in hemoglobin below the normal adult range in an elderly individual, especially below 10.5 g/dL, practitioners must assume that a pathologic process is present until proven otherwise. In Korea, Song, et al.[5] reported geriatric male and female hemoglobin levels of 13.9 g/dL and 12.7 g/dL, respectively. Our study[6] revealed that the mean hemoglobin level among men was 14.8 g/dL, which was significantly different than the control level of 15.5 g/dL (p<0.001). The hemoglobin level among geriatric women was 12.9 g/dL, which was also significantly different than the control level of 12.6 g/dL (p=0.038).

Subclinical alternations, such as slight increases in red cell size[7] and membrane viscosity,[8] have been noted among elderly patients. In Korea, our study[9] revealed a mean MCV in geriatric men of 94.7±4.3 fl (range, 86.3-103.1 fl), which was significantly higher than that of the control men (93.7±3.8 fl, p=0.03). In geriatric women, the mean MCV was 91.7±3.5 fl (range, 84.8-98.6 fl) with no significant difference when compared to controls (91.3±3.7 fl, p=0.421). These findings may be due to somewhat shortened red cell life span and slight decrements in enzyme content and metabolic activity in elderly patients.[10]

A 20-40% increase in the erythrocyte sedimentation rate in the elderly[11] may be due to associated chronic disease, subclinical alternations in plasma proteins, or both; therefore, its utility as a screening test is limited.

HEMATOPOIETIC DISORDERS

Anemia is the most frequently encountered hematologic problem in the elderly. It is a sign of an underlying problem and may be primary or secondary in nature. According to WHO criteria, anemia is defined as a hemoglobin level less than 13 gm/dL in men and 12 gm/dL in women. Among presumably healthy individuals over the age of 65, 12-25% of the population has a hemoglobin level below the usual limit.[12] Clinically, in men and women with a hemoglobin level less 12 gm/dL, an etiology is determined in the majority of cases,[13] such as chronic disorders (inflammation, infection, neoplasm), chronic kidney disease and nutritional deficiencies (iron, folate/vit B_{12}). However, specific causes of anemia are often unknown though a bone marrow examination and other tests would have revealed some other causes such as myelodysplasia, thus prompting the use of the term anemia of senescence[14] or senile anemia.

Guralnik[15] estimated in the third National Health and Nutrition Examination Survey (NHANES Ⅲ) that a substantial proportion (one third) of anemia is of indeterminate causes.

Impaired erythropoietin (EPO) responsiveness of the hematopoietic stem cell has been implicated in the pathophysiology of anemia in elderly patients.[16] Our data also revealed inappropriately low EPO levels.[17] Another mechanism for the impaired EPO response associated with unexplained anemia in the elderly population has been postulated to be due to elevated proinflammatory markers such as an iron regulatory hormone, hepcidin;[18] however, there was no clear association between them.[19] Analysis of the relationship between vitamin D deficiency and anemia in older individuals in the NHANES Ⅲ did not reveal any significant correlation.[20]

The classic signs and symptoms of pallor, weakness, and fatigue may be present in the anemic elderly patient. The initial manifestations may be symptoms of specific end organ dysfunction, behavioral changes and confusional states, ischemic chest pain, congestive heart failure, pulmonary decompensation, syncope, or falls.

A relatively small improvement in hemoglobin level may produce dramatic symptomatic improvement. Transfusion should be performed over 3-4 hours to avoid precipitation of angina or congestive heart failure. An elevated reticulocyte count represents an appropriate response to anemia by the bone marrow and may suggest a hemolytic process, blood loss, or recent recovery from a toxin or nutritional deficiency. Low reticulocyte count is accompanied by hypoproliferative anemia and aplastic anemia.

Anemia can be morphologically categorized as microcytic, normocytic, or macrocytic.

MICROCYTIC ANEMIA

Iron deficiency anemia (IDA) and the anemia of chronic disease (ACD) in their later phases are microcytic. MCV, serum iron, and transferin saturation are decreased in IDA, and serum ferritin is decreased in IDA but not in ACD. RDW is increased in IDA, but not in ACD.[21] Sometimes, serum iron and total iron binding capacity are not reliable indices in the elderly, due to their wide fluctuations in disease states and the tendency for serum iron to decrease with age in the absence of true iron deficiency.[22] Low serum ferritin is di-

agnostic of iron deficiency, but may be falsely elevated by liver disease or inflammatory disorders.[23] If serum ferritin is nondiagnostic, soluble transferrin receptor measurement is available, even though scarsely anemia must be assessed by bone marrow aspiration.

IDA

In Korea, our study revealed a low mean hemoglobin level of 7.8±2.2 g/dL and a decreased serum iron level of 22.7±12.3 μg/dL with a decreased transferrin saturation of 6.7±4.1%. There was no increase in TIBC (357.2±83.2 μg/dL), and ferritin levels were decreased to 18.9±14.6 ng/dL among men and 9.2±6.3 ng/dL among women with an upper limit of 37 ng/dL.[24]

Causes of iron deficiency include decreased absorption, perhaps with gastric achlorhydria, prior gastrectomy or, rarely, dietary iron deficiency as in the case of tea-and-toast lady syndrome. Most cases are due to gastrointestinal blood losses secondary to drugs, peptic ulcer disease, stomach cancer, colon carcinoma, diverticulitis, or vascular abnormalities. Treatment can generally be accomplished with ferrous sulfate 300 mg for six months which can be administered as a liquid suspension or parenterally as necessary such as in malabsorbtion or when cannot tolerate oral iron supplementation.

ACD

Anemia of chronic disease is due to hepcidin, which block the release of iron from the reticuloendothelial system, thereby resulting in abnormal iron utilization. Serum EPO level is not increased sufficiently relative to the severity of the anemia, because of inflammatory cytokines.[25] Our study of serum erythropoietin also revealed an inappropriately low response to this type of anemia.[26] This type of anemia is quite common in the elderly, owing to the high incidence of chronic inflammatory disease in this age group.

Measurement of serum iron and total iron binding capacity does not reliably distinguish ACD from iron deficiency anemia. Serum ferritin levels may not be decreased, therefore, bone marrow examination may be needed to exclude hypoproliferative anemia. Underlying problems, such as chronic inflammatory states, infections, or neoplastic disorders, should be corrected.

Thalassemia minor, which is very rare in Korea, involves genetically-determined abnormal globin chain synthesis that results in decreased hemoglobin production. A blood film and hemoglobin assay are needed for diagnosis.

The incidence of sideroblastic anemia is increasing in the elderly. This type of anemia is characterized by increased serum iron, increased saturation, and elevated serum ferritin. In the bone marrow, iron-laden red cell precursors, ring sideroblasts, are noted. Sideroblastic anemia may be secondary to pyridoxine deficiency, drugs, or alcohol, but in the elderly, it also occurs in an acquired idiopathic form, such as refractory anemia with ringed sideroblasts of the myelodysplastic syndrome. Treatment is symptomatic.

MACROCYTIC ANEMIA

In the elderly, macrocytic megaloblastic anemia is most frequently due to a deficiency of folic acid or vitamin B_{12}. Although such types of anemia constitute a small percentage of anemia cases, they are of considerable importance because of their correctability.

Serum methylmalonic acid and homocysteine levels are very sensitively increased at early stage of folate or vit B_{12} deficiency even in their normal blood levels.

Folic acid deficiency is found more often than vitamin B_{12} deficiency.[23] Elderly people often fail to meet the daily requirement of 50 μg of folic acid because of decreased food intake. Body stores of folate are limited and may be exhausted within weeks to months, and folate metabolism may be affected adversely by alcohol ingestion.[27] Serum folate levels less than 3 ng/mL usually indicate deficiency, but are not always helpful because 10% of presumably healthy elderly individuals have been found to have the levels below the normal limit.[6] Red blood cell folate concentration is more valuable, and a level less than 102.6 ng/mL is defined as deficient. Folic acid deficiency is readily corrected by administering 1 mg of folic acid orally per day.

Vitamin B_{12} deficiency in the elderly is seen in the setting of pernicious anemia, which is due to a lack of intrinsic factor production by the gastric parietal cells. Chronic atrophic gastritis, previous gastrectomy, or disease of the terminal ileum can also produce vitamin B_{12} deficiency in the elderly. The normal lower limit in the elderly is uncertain because of the progressive decrease in serum B_{12} levels with advancing age. Typically, patients at levels less than 180 pg/mL are considered deficient. A Shilling test can hardly be per-

formed. After treatment with vitamin B_{12}, a brisk reticulocyte response can be seen within 5-7 days.

In Korean geriatric patients, our data revealed that 75.7% were anemic among patients with a serum folate level less than 3 ng/mL, and 93.8% were anemic among patients with a serum vitamin B_{12} level less than 180 pg/mL.[28]

NORMOCYTIC NORMOCHROMIC ANEMIA

Blood loss should always be initially suspected as the cause of this type of anemia. The elderly patient should not be expected to report melena, and a blood film and reticulocyte count are essential. Early iron deficiency anemia or anemia of chronic disease may be normocytic. Vitamin B_{12} and folate deficiency may not be associated with macrocytosis if there is concurrent iron deficiency.

A blood film with microspherocytes suggests undiscovered hereditary spherocytosis which is occasionally but mostly immune hemolytic anemia; the drug-induced type is more common in the elderly. A normocytic hypoproliferative anemia with abnormal burr cells on the blood film may be seen in chronic renal disease. Hyperthyroidism and other endocrine insufficiencies are commonly associated with this type of anemia in the elderly.

CONCLUSIONS

Anemia has recently become a significant problem in elderly Koreans. The exact etiologies of anemia should be identified, and it should be treated appropriately according to various causes of anemia. There is a need for further efforts to understand the pathogenesis of anemia among the elderly in order to improve outcomes.

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