Question 25

In a transfusion-dependent patient with idiopathic acquired sideroblastic anaemia, the most appropriate treatment for prevention of transfusional iron overload is:

A. vitamin C.
B. phlebotomy.
C. desferrioxamine.
D. ethylene-diamine tetra-acetic acid (EDTA).
E. pyridoxine.

Acquired idiopathic sideroblastic anemia (AISA) generally occurs in middle-aged and older individuals, although younger persons including children are not spared. The anemia develops insidiously and may be discovered during a routine examination or in association with an unrelated complaint. Older individuals more often experience symptoms of fatigue and angina, especially if there is coexisting coronary artery disease. Apart from pallor, hepatosplenomegaly is found in one-third to one-half of patients. With advanced iron overload, often after repeated transfusions, symptoms and signs of liver decompensation, as well as heart failure and arrhythmia, may occur.

Diagnosis

- In women, the hematologic phenotype in PSA or RARS is often indistinguishable from X-linked sideroblastic anemia; this latter disorder should therefore be excluded.
- Complete blood count — The anemia is usually moderate and normocytic or macrocytic, with a variable population of hypochromic cells on the blood smear. Particularly characteristic are occasional siderocytes: hypochromic red cells with basophilic stippling that stains positive for iron.
- Leukocyte and platelet counts are often within the normal range in patients with AISA. The presence of moderate leukopenia and/or thrombocytopenia tends to be associated with other myelodysplastic features, such as the pseudo-Pelger anomaly. Leukocytosis and/or thrombocytosis are least common, and may reflect the presence of a myeloproliferative disorder.
- Free erythrocyte protoporphyrin — The free erythrocyte protoporphyrin is characteristically increased, up to about 300 µg/dL (normal: 20 to 65). However, in some patients, values have ranged from 1055 to 10,514 µg/dL, and some have experienced photosensitivity.
- Iron studies — Serum iron and ferritin levels reflect the commonly associated iron overload, as in hereditary sideroblastic anemia.
- Bone marrow examination — Bone marrow aspiration shows the presence of erythroid hyperplasia, commonly with mild megaloblastic changes. The marrow macrophage iron content is increased and, in contrast to the hereditary form, ring sideroblasts are evident at all stages of maturation; their presence establishes the diagnosis.

Management — Available treatment measures are supportive, as in hereditary sideroblastic anemia. However, a response to pyridoxine supplements is not expected. Curative treatment with hematopoietic cell transplantation, with the attendant risks, is considered an option for younger individuals, as in the other myelodysplastic syndromes.

- Erythropoietin and G-CSF
- Chemotherapeutic agents
- Transfusion — If anemia is symptomatic or progresses to a symptomatic stage, regular red cell transfusions are necessary, especially in the presence of advanced age and/or other comorbid conditions, such as coronary artery disease.
- Removal of excess iron — Phlebotomy or deferoxamine are used to control the iron overload.
- Risk of splenectomy — Similar to patients with hereditary sideroblastic anemia, splenectomy should be avoided at all costs.

Iron overload — The associated iron overload requires treatment for optimal prognosis, thereby minimizing or averting morbidity from parenchymal organ damage. Based on the severity of iron overload (eg, serum ferritin >500 µg/L), best documented by liver biopsy, an iron depletion program must be instituted. This is accomplished in one of two ways: therapeutic phlebotomy or iron chelation.

Therapeutic phlebotomy — Graded phlebotomies can be performed in patients who have responded to pyridoxine supplements, and in all others with mild or moderate anemia (ie, hemoglobin >9 g/dL) when there are no contraindications to therapeutic phlebotomy, such as congestive heart failure. After initial de-ironing, maintenance phlebotomies are continued on a regular basis for life, in order to prevent reaccumulation of iron.

Iron chelation therapy — In patients who have more severe anemia, and in those who require regular red cell transfusions, and thus cannot undergo phlebotomy, chelation of the excess iron with deferoxamine is performed. This agent, a siderophore, is poorly absorbed from the gastrointestinal tract and must be given parenterally. It avidly binds non-protein-bound, non-heme-bound iron that is in a transit phase within cells to form ferrioxamine, which freely exits cells and is readily excreted in urine and bile.
A. vitamin C.
Supplement as part of multivitamin
B. phlebotomy.
Correct – primary therapy
C. desferrioxamine.
Useful in conjunction with phlebotomy
D. ethylene-diamine tetra-acetic acid (EDTA).
EDTA is used for the treatment of sideroblastic anaemia proven to be caused by Lead poisoning
E. pyridoxine.
Pyridoxine (Vitamin B6) has been shown to be effective in hereditary sideroblastic anaemia