CLINICAL VIGNETTE

Evaluation of Microcytic Anemia

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Introduction

Anemia is common in clinical practice with various etiologies. We present a case of microcytic anemia and discuss the approach to evaluation, diagnosis, and treatment.

Presentation

A 28-year-old Italian female with no significant past medical history presented for evaluation of microcytic anemia. She initially presented to a new primary care physician for her annual exam. She reported menorrhagia and ice cravings. She was previously treated with OCPs to regulate menstruation but stopped this several years ago. She reported anemia since at least high school and has been prescribed oral iron several times in the past, but anemia never resolved. Family history includes her mother with anemia. Labs included hemoglobin (Hgb)10.5, mean corpuscular volume (MCV) 66, RBC 5.0, RDW 18.2, absolute reticulocyte count 1.0, iron 65, TIBC 342, %sat 19, and ferritin 8 confirming iron deficiency. Patient tolerated oral iron well with repeat labs Hgb 11.0, MCV 72, RBC 6.1, RDW 15.0, iron 80, TIBC 250, %sat 32, and ferritin 70. Hemoglobin electrophoresis revealed Hgb A 92.3%, Hgb A2 5.4%, Hgb F 2.3% confirming beta thalassemia trait.

Discussion

The evaluation of anemia is multifaceted and includes both clinical and laboratory evaluation. In this patient, pertinent clinical information included history of menorrhagia, pica symptoms, chronicity of anemia, and family history of anemia. Pertinent laboratory information included hemoglobin and RBC indices.

The most common causes of microcytic anemia include iron deficiency and thalassemia. The initial evaluation of microcytic anemia includes CBC, peripheral smear, reticulocyte count, iron studies, ferritin, and consideration of hemoglobin analysis. Typically, iron studies to evaluate for iron deficiency are obtained in all adults with unexplained anemia especially if anemia is microcytic, RBC is decreased, reticulocyte count is low, or if clinically suspicious for iron deficiency. In this patient, hemoglobin analysis was also sent given her ethnicity, family history, and personal history of ineffective oral iron treatment. Interestingly, this patient had two separate etiologies contributing to her microcytic anemia: iron deficiency anemia and beta-thalassemia minor.

Iron deficiency is a common cause of microcytic anemia. Iron deficiency can be related to insufficient intake, abnormal absorption, and blood loss. In this patient, menorrhagia is the likely cause of her iron deficiency. Common symptoms include fatigue, dyspnea on exertion, headache, restless leg syndrome, and pica. Pica refers to a desire to eat non-food substances; such as, clay, dirt, paper products, or ice. Pica for ice, also known as pagophagia, is considered specific for iron deficiency.[1]

Iron studies typically reveal low iron, increased total iron-binding capacity, low transferrin saturation, and low ferritin. Diagnostic criteria for iron deficiency include a transferrin saturation ≤19 % or a serum ferritin <30 ng/mL.[2] Iron deficiency anemia is also associated with low RBC count and reticulocyte count. The peripheral smear may reveal microcytic hypochromic RBCs with pencil cells and variable RBC size. First-line therapy for uncomplicated iron deficiency is oral iron. Oral iron is commonly associated with GI side effects including nausea and constipation. Alternate-day dosing appears to result in equivalent or better iron absorption than daily dosing, usually with fewer adverse effects.[3] As such, this patient was treated with 1 tab oral iron every other day. If oral iron is not tolerated or cannot keep up with iron losses, then treatment with IV iron is appropriate.

Thalassemia trait also presents as a microcytic anemia and is often misdiagnosed as iron deficiency anemia. In adults, the most common hemoglobin is Hgb A which is a tetramer that consists of two alpha and two beta subunits. If there is a mutation in the beta subunit, then there will be a decrease in Hgb A levels and an increase in alternative Hgb levels including Hgb A2 (alpha and delta subunits) and Hgb F (alpha and gamma subunits). Thus, beta thalassemia minor is diagnosed when hemoglobin analysis reveals a decreased Hgb A, increased Hgb A2, and increased Hgb F.[4] Iron deficiency modulates the synthesis of HbA2 and can result in reduced HbA2 levels in patients with iron deficiency anemia. Thus, patients with beta-thalassemia and concomitant iron deficiency can show normal HbA2 levels.[5] If suspicion is high for beta thalassemia, then it may be necessary to repeat hemoglobin analysis after iron repletion.

Beta thalassemia minor is a benign carrier condition in which the patient is heterozygous for a single beta thalassemia mutation. It is prevalent in southern Europe along the Mediterranean.

Presentation most often includes asymptomatic mild microcytic anemia identified incidentally on routine labs.[6] Other RBC indices include elevated RBC and normal to slightly elevated reticulocyte count. Peripheral smear may reveal microcytic hypochromic RBCs and target cells.[4] Evidence of hemolysis is usually absent. There is no recommended intervention or monitoring for beta thalassemia minor. The diagnosis is important for preconception counseling as the genetic mutation can be passed down from parent to child. Further, it is appropriate to test first degree relatives.

Conclusion

Microcytic anemia is commonly encountered in clinical practice and a careful evaluation is needed to identify the cause. This patient was found to have both iron deficiency and beta thalassemia trait. Hemoglobinopathies are often overlooked and treated as iron deficiency anemia. Close follow-up and clinical suspicion are necessary to fully evaluate.

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