Q&A column, 4/16

Editor: Frederick L. Kiechle, MD, PhD

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Submit a Question

Q. We review peripheral blood smears and sometimes provide recommendations. For microcytic anemia with high red blood cell count, iron study and hemoglobin electrophoresis are suggested to rule out hemoglobinopathy. But for cases of microcytosis with high RBC count but without anemia, should we give the same recommendation as for an anemic patient?

A. I find microcytosis to be a fascinating and sometimes oversimplified issue. As the question suggests, the differential diagnosis for microcytic anemia versus microcytosis without anemia contains overlapping entities. An increase in RBC count relative to the hemoglobin level can be used as a factor to consider; in combination with microcytosis and a relatively normal red cell distribution width, these are traditionally termed "thalassemic indices." Typically, when iron deficiency is the cause of microcytosis, the RBC count is decreased proportionately to the hemoglobin and hematocrit. When thalassemia is present, there may be an increased or at least a relatively increased (greater than three times the Hgb level) RBC count in relation to the hemoglobin and hematocrit. Many hemoglobin disorders result in microcytic anemia. In addition, a number of them are associated with normal hemoglobin levels and the only indication is the microcytosis and possibly an increased RBC count. In these situations, the recommendation to exclude a hemoglobinopathy or thalassemia is appropriate because many common alpha and beta thalassemias, as well as other hemoglobin conditions such as large beta globin cluster deletions (hereditary persistence of fetal hemoglobin, delta beta thalassemia, epsilon gamma delta beta thalassemia) and hemoglobin variants (Hb E, Hb C, compensated unstable variants), can be present. Additional causes of microcytosis with normal hemoglobin levels include polycythemic conditions (polycythemia vera, congenital erythrocytosis mutations, and high oxygen affinity hemoglobin variants) with coincident iron deficiency.

Many polycythemic patients undergo therapeutic chronic phlebotomy to control the elevated hemoglobin levels through iatrogenic iron deficiency. In polycythemia, iron deficiency counterbalances the abnormally increased RBC production, and the opposing conditions result in a targeted (usually normal) hemoglobin level with increased RBC count, although the RDW can be variably elevated, likely due to the introduction of reticulocytes.

In summary, for patients with increased RBC count and microcytosis but normal hemoglobin values, the differential diagnosis most commonly includes a hemoglobin disorder or a polycythemic disorder with coincident iron deficiency.

Even in the absence of anemia, the proper evaluation of unexplained microcytosis is often clinically useful. A definitive identification of a hemoglobin disorder is required for genetic counseling purposes, and discouraging unnecessary chronic iron supplementation is important in thalassemia patients because they are prone to iron overload.

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Q. How do most hospital labs perform and report post-vasectomy semen checks?

A. Traditionally, after examination of a fresh, uncentrifuged specimen for motile sperm, the semen would then be centrifuged and examined for the presence of nonmotile sperm. The British Andrology Society and the 3rd (1992) and 4th (1999) editions of the *WHO Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction* specifically recommended centrifugation of azoospermic semen samples as part of the routine post-vasectomy semen analysis.

Recently, however, the American Urological Association issued guidelines specifically requesting post-vasectomy semen analysis be performed on uncentrifuged specimens only, stating that centrifugation is not necessary to confirm that only rare nonmotile sperm are present. The AUA cited literature examining uncentrifuged azoospermic semen specimens compared with centrifuged specimens (n=2,014 samples) and concluded that uncentrifuged semen analysis is a reliable method of identifying samples with more than 100,000 sperm/mL. The sensitivity of the uncentrifuged sample was 99.3 percent and the negative predictive value was 99.8 percent. While up to one-third of post-vasectomy specimens may contain a small number of immotile sperm, the clinical significance is thought to be low, and the position of the AUA is that these findings often result in unnecessary follow-up and procedures.

Nevertheless, many laboratories continue to concentrate semen post-vasectomy, based on previous recommendations. The current reproductive laboratory checklist from the CAP incorporates either process as follows (RLM.03984): "For azoospermic and post-vasectomy seminal fluid specimens, the laboratory clearly communicates the findings of the assay and either employs a concentrating technique on seminal fluid or includes a comment in the patient report indicating that a concentrating technique was not performed."

1. Hancock P, McLaughlin E; British Andrology Society. British Andrology Society guidelines for the assessment of post vasectomy semen samples (2002). *J Clin Pathol.* 2002;55:812–816.
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4. Steward B, Hays M, Sokal D. Diagnostic accuracy of an initial azoospermic reading compared with results of post-centrifugation semen analysis after vasectomy. *J Urol*. 2008;180:2119–2023.

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