Laboratory Testing in Pediatric Rheumatology

Jay Mehta, MD, MS

KEYWORDS

• Pediatric rheumatology • Diagnosis • Laboratory testing
• Biologic markers • Autoantibodies • Prognosis

Although pediatric rheumatic disorders are primarily diagnosed through history and physical examination, laboratory studies are valuable adjuncts to the care of patients with such disorders. Laboratory evaluations can assist in the screening of patients for inflammatory disorders, confirm diagnoses, allow for monitoring of disease activity and response to therapy, and suggest prognoses and risk of morbidities associated with rheumatic diseases.

Which laboratory tests are ordered should be dictated by a thorough history and physical examination, rather than by the indiscriminate use of a rheumatology screen. Although commonly ordered tests such as the complete blood count (CBC), antinuclear antigen (ANA), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are useful in the appropriate clinical setting, they lack specificity and abnormal values may be found in the well child. This review provides an overview of the usefulness and interpretation of both the commonly ordered tests ordered by the general pediatrician as well as those frequently used in the pediatric rheumatology clinic for diagnosis and disease monitoring.

CBC

The CBC provides information about the 3 major cellular components of whole blood. Rheumatic diseases may be associated with alterations in each of them.

Red Blood Cell Count

Anemia is seen in many of the rheumatic diseases and can be multifactorial. An anemia of chronic disease is usually normocytic, but may be microcytic, and can be associated with any inflammatory disease. The cause likely relates to cytokine-mediated shortened red blood cell (RBC) survival and impaired bone marrow response to erythropoietin.[1] Another major contribution to the anemia of chronic

Division of Pediatric Rheumatology, Albert Einstein College of Medicine, Children's Hospital at Montefiore, 3415 Bainbridge Avenue, Bronx, NY 10467, USA
E-mail address: jmehta@montefiore.org

Pediatr Clin N Am 59 (2012) 263–284
doi:10.1016/j.pcl.2012.03.008 **pediatric.theclinics.com**
0031-3955/12/$ – see front matter

disease is the inflammation-induced activation of the interleukin 6 (IL-6)-hepcidin axis, which leads to decreased intestinal iron absorption and decreased iron release from stores.[2] This condition must be distinguished from iron-deficiency anemia, which can also be seen in any of the rheumatic diseases. **Table 1** contrasts these 2 conditions based on commonly used serum parameters. Complicating factors include the frequent coexistence of these 2 conditions and the fact that ferritin is an acute phase reactant so it may be normal, or even increased, in iron deficiency. Measurement of the soluble transferrin receptor, which is gaining acceptance, may help to more reliably distinguish anemia of chronic disease from iron-deficiency anemia.[3]

Autoimmune hemolytic anemia may be seen in systemic lupus erythematosus (SLE) and related conditions (ie, Sjögren syndrome and mixed connective tissue disease [MCTD]). This diagnosis is made through a positive direct Coombs test and evidence of hemolysis (decreased hemoglobin or hematocrit, increased reticulocyte count, increased serum lactate dehydrogenase (LDH), increased unconjugated bilirubin, decreased haptoglobin, and hemoglobinuria). Nonimmune-mediated hemolysis is seen in the macrophage activation syndrome (MAS) (see later discussion) and thrombotic thrombocytopenic purpura.

White Blood Cell Count

SLE and related conditions frequently cause leukopenia, specifically lymphopenia and neutropenia. These abnormalities may confer an increased risk of infection in patients with SLE.[4–6] Increased white blood cell (WBC) counts can be seen in other inflammatory diseases, and particularly increased counts may be seen in systemic juvenile idiopathic arthritis (sJIA; often >30,000 cells/mm^3). Malignancies can cause either increased or depressed WBC counts, and they must be considered in any patient who presents with WBC abnormalities.

Platelet Count

Because of their role as an acute phase reactant, platelets are frequently modestly increased in the rheumatic diseases. Significant increases (occasionally more than 1,000,000 cells/mm^3) may be seen in sJIA, Kawasaki disease, or Takayasu arteritis. SLE and related conditions often cause thrombocytopenia, and a depressed platelet count in the face of signs of systemic inflammation or arthritis should raise suspicion for these diseases or for malignancy. Thrombocytopenia may also be seen in the antiphospholipid antibody syndrome (APS) and in thrombotic thrombocytopenic purpura.

Table 1
Distinguishing features of anemia of chronic disease and iron-deficiency anemia

Parameter	ACD	IDA
MCV	Normal (can be ↓ in prolonged disease)	↓
Serum iron	↓	↓
Transferrin	↓	↑
Ferritin	Normal or ↑	↓ (can be normal if ACD+IDA)
STfR-ferritin index	<1.0	>2.0 (can also indicate ACD+IDA)
Transferrin saturation %	Normal (can be ↓)	↓

Abbreviations: ACD, anemia of chronic disease; IDA, iron-deficiency anemia; MCV, mean corpuscular volume; STfR, soluble transferrin receptor.