patients with relapsed Hodgkin's disease in whom one or two courses of chemotherapy has failed. The role of autologous bone marrow transplantation in other tumors is evolving. Results in patients with breast cancer and multiple myeloma appear promising. The treatment of other solid tumors has shown excellent response rates, but unfortunately, positive response has tended to be of brief duration.

BRIAN J. BOLWELL, MD
Department of Hematology and Oncology

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TURNING BACK GROUP A STREPTOCOCCI

Acute rheumatic fever has become resurgent in this country in the last 5 years, with outbreaks that included an epidemic in Salt Lake City, Utah, and smaller clusters in Columbus and Akron, Ohio. Acute rheumatic fever is the only clearly preventable cause of heart disease; yet, worldwide it causes 15 to 20 million new cases of heart disease every year, and it is responsible for 25% to 40% of all cardiac disease.

Because of the resurgence, it is necessary to maintain a high index of suspicion and re-examine our diagnostic approach to group A beta hemolytic streptococcal infection. In the recent outbreaks, the affected patients were primarily from suburban, middle-class, small families. Only one-third had sore throats that required medical attention in the early stages of the disease, when acute rheumatic fever can be most effectively prevented.

Tests are available for rapid, in-office diagnosis of streptococcal infection; these kits work by direct detection of the antigen in the throat. Although they are highly specific, they have a sensitivity of only 60% to 70%. Therefore, if the test is negative, a throat culture is mandatory.

RISK FACTORS

Only upper respiratory streptococcal infection is associated with acute rheumatic fever. High antistreptolysin O (ASO) titers (200 Todd units/mL) and prolonged exudative pharyngitis increase the risk, and there appears to be a familial predisposition to the disease.

In an epidemic setting, acute rheumatic fever may develop in 3% of individuals with streptococcal pharyngitis. The risk is much lower in a nonepidemic setting—about 0.3%. Because the prevalence—even in an epidemic setting—is only 3%, a positive throat culture alone does not necessarily provide useful information about the likelihood of acute rheumatic fever. Carriers without active infection further confound the picture.

DIAGNOSIS

The diagnosis of acute rheumatic fever may be elusive, especially to younger clinicians who have never seen a case. The manifestations are diverse and there is no specific diagnostic test, although the T. Duckett Jones criteria are generally accepted. The presence of two major criteria *or* one major criterion and two minor criteria along with evidence of preceding streptococcal infection makes the diagnosis probable.

The major criteria are carditis (the only feature with a potential for long-term disability or death), chorea, polyarthritis, erythema marginatum, and subcutaneous nodules. Minor criteria are previous acute rheumatic fever or rheumatic heart disease, arthralgia, fever, and acute phase reactions that include elevated sedimentation rate, positive CRP, elevated white blood cell count, and prolonged P-R interval.

In adults, carditis occurs in only 15% of patients and tends to be mild and transient. Even when carditis does occur, it is often asymptomatic, although manifestations may range from just a widened P-R interval up to and including congestive heart failure.

Arthritis is a major feature in adults and usually involves large, lower-extremity joints. Severity ranges from subacute arthralgias to frank arthritis. Synovial fluid analysis yields no findings specific to rheumatic fever, but is useful to rule out other types of arthritis.

Erythema marginatum is an unusual finding that presents as evanescent, primarily vasomotor lesions and may continue for several weeks. Subcutaneous nodules are associated with severe carditis and persist for a few weeks after the onset of disease.

Sydenham's chorea, although rare, is by itself thought

to be diagnostic of acute rheumatic fever. There may be no laboratory evidence of inflammation or streptococcal infection but, on long-term follow-up, significant cardiac disease may be found in many of these patients.

Hepatic dysfunction may be a prominent feature of rheumatic fever, and the salicylates used in treatment can cause further elevations in transaminase or symptoms of hepatitis. Abdominal pain and epistaxis are notable presenting symptoms. Pulmonary findings, including edema, atelectasis, infiltrates, and emboli also may occur. Renal disease and aseptic meningitis also have been reported.

A battery of three serologic tests on a serum sample obtained within 2 months of the onset of presumed acute rheumatic fever will help to support the diagnosis. In most instances of acute rheumatic fever, measurement of ASO titer, anti-DNAse B, and antihyaluronidase will demonstrate evidence of immunologically significant streptococcal infection.

TREATMENT AND PROPHYLAXIS

Acute rheumatic fever is generally a self-limited disorder. Most patients, even if untreated, recover after several months, but about 5% develop a chronic form. Salicylate therapy may hasten resolution of arthritis and myocarditis, and steroid therapy is recommended for patients with severe carditis. But neither modality will reverse any cardiac valvular damage that was sustained before starting therapy.

Recurrence is an immunologically derived insult, and is therefore more likely in patients with high ASO titers and preexisting heart disease. The risk of recurrence increases with each succeeding episode. Exposure to populations that harbor the organism also increases the likelihood. The disease recapitulates itself with recurrence; that is, if carditis was a prominent feature of the first episode, then it will be a part of future episodes.

Continuous antibiotic prophylaxis is needed to prevent streptococcal infections and, therefore, recurrence of acute rheumatic fever. The most effective regimen consists of a single injection of 1,200,000 units of benzathine penicillin G every 4 weeks. Erythromycin, 250 mg twice daily is an acceptable alternative in patients unable to take penicillin.

PHILIP I. LERNER, MD
Director, Division of Infectious Disease
The Mt. Sinai Medical Center
Cleveland, Ohio

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