Renal Disease

Urine acidification abnormalities of the distal renal tubule leading to complete or incomplete distal renal tubular acidosis are the most common manifestation of renal involvement, but overt renal disease is less common. Glomerular diseases such as membranoproliferative glomerulonephritis and membranous nephropathy can occur in patients with SS and SLE overlap or those with cryoglobulinemia and hypocomplementemia.

Cardiovascular System

Although pericardial effusion can be seen on the echocardiogram, primary SS patients rarely have acute pericarditis. Placental transmission of maternal anti-Ro/SSA and anti-La/SSB antibodies can cause neonatal lupus and fatal fetal congenital heart block. In women with these antibodies, there is 5% risk of their first child being born with heart block. This risk rises to 15% with subsequent pregnancies. Fetal heart rate monitoring in the antenatal period is essential.

Neuromuscular Disease

Peripheral neuropathy occurs in about 10% of patients with SS and can precede sicca symptoms. Diagnosis of small fiber neuropathy may require quantitative sudomotor autonomic reflex testing or measurement of epidermal nerve density by biopsy. Cranial nerves, particularly the trigeminal and optic nerves, can be involved as a consequence of vasculitis. Although the frequency of central nervous system involvement remains controversial, focal or diffuse brain lesions and multiple sclerosis–like syndromes have been reported. Myalgia is very common, but symptomatic inflammatory myopathy is rare.

Lymphoproliferative Disease

Patients with SS are predisposed to develop lymphoma (primarily B cell in origin). Risk factors include cutaneous vasculitis, peripheral neuropathy, rheumatoid factor, cryoglobulinemia, and hypocomplementemia. Development of new masses with constitutional symptoms or persistent lymph node enlargement should raise concern for malignancy.

Gastrointestinal and Hepatobiliary Disease

Dysphagia commonly results from dryness of the pharynx and esophagus. Lymphocytic infiltration, predominantly by $CD4^+$ T cells, may cause chronic atrophic gastritis, achlorhydria, and pernicious anemia. Although liver involvement in primary SS patients is rare, histologic features show a clear association between SS and hepatic abnormalities. However, other causes of abnormal liver function test results in SS, particularly hepatitis C infection and drug toxicity, should be considered.

Diagnosis and Differential Diagnosis

Although there are no established diagnostic criteria for SS, classification criteria were developed for use in research. The American-European Consensus Group (AECG) classification is most widely accepted, and it requires demonstration of the following:

1. Signs and symptoms of inadequate tear production and decreased salivary gland function
2. Detection of autoantibodies (anti-Ro/SSA or anti-La/SSB, or both)
3. Exclusion of underlying diseases that may mimic SS, including head and neck irradiation, hepatitis C, acquired immune deficiency syndrome, preexisting lymphoma, sarcoidosis, graft-versus-host disease, and anticholinergic drug use.

A provisional classification was proposed by American College of Rheumatology and the Sjögren International Collaborative Clinical Alliance investigators (ACR-SICCA), but it has not been validated completely. The MAIN differences between the AECG and ACR-SICCA criteria are that ocular or oral dryness symptoms are not required in the latter and the ACR criteria do not distinguish between primary and secondary forms of SS.

The diagnosis of SS is made on the basis of compatible clinical and laboratory features and after the exclusion of other causes of sicca symptoms. Various tests are used to evaluate the objective glandular component of the disease. To confirm keratoconjunctivitis sicca, the Schirmer test, the rose bengal test, and tear breakup time can be used. Salivary gland scintigraphy with uptake of technetium-99m, parotid sialography, and measurement of unstimulated production of saliva (i.e., Saxon test) may provide objective evidence of xerostomia. A labial salivary gland biopsy is often essential in evaluating patients with suspected SS, particularly when the patients lack anti-Ro/SSA or anti-La/SSB antibodies. Rheumatoid factor and ANAs are commonly detected, and patients may be erroneously diagnosed with rheumatoid arthritis. Common laboratory findings include anemia, thrombocytopenia, leukopenia, raised ESR, monoclonal gammopathy, and hypergammaglobulinemia.

Other conditions can produce keratoconjunctivitis sicca symptoms, xerostomia, or lacrimal and salivary gland enlargement. The differential diagnosis of SS must consider infectious diseases such as diffuse infiltrative lymphadenopathy syndrome associated with HIV, hepatitis B and C, human T-cell lymphotropic virus infection, syphilis, and infection with mycobacteria, and it must take into account infiltrative diseases such as sarcoidosis and amyloidosis. Anticholinergic side effects from many drugs, including over-the-counter products, should be considered during assessment of dry eyes and dry mouth. Sicca symptoms may result from overlap syndromes, which may have features of SS and SLE or of SS and scleroderma.

Treatment

No cure for SS is available. Because of the diverse symptoms of SS, several medications are used to ameliorate the symptoms outlined in Table 85-4. Patients with moderate to severe involvement may require systemic medical therapy, including the use of immunosuppressive and biologic agents. There is no evidence that azathioprine, low-dose steroids, cyclosporine, infliximab, or methotrexate are useful. Hydroxychloroquine normalizes the ESR and immunoglobulin levels, but it does not increase the salivary flow rate significantly. Many clinicians use it to treat rash, fatigue, myalgia, and arthralgia. B-cell and anticytokine or antichemokine-directed therapies are active areas of research.

Prognosis

Primary and secondary forms of SS are characterized by chronic courses and different rates of progression. Systemic involvement