Survival rates are decreased in patients with B symptoms, lymph node mass >7 cm in diameter, and high or intermediate histologic grade. Despite that, pathogenesis of lymphoma in the setting of Sjögren's syndrome remains to be elucidated, and genetic alterations involved in chronic inflammatory, B-cell activation and the type I interferon pathways, as well as epigenetic abnormalities, have been shown to be significant contributors.

Recent data reveal an increased risk for multiple myeloma as well for Sjögren's syndrome patients with anti-Ro52, anti-Ro60, or anti-La autoantibodies. In line with observations in rheumatoid arthritis and systemic lupus erythematosus, patients with Sjögren's syndrome also display an increased risk of cardiovascular disease.

Routine laboratory tests in Sjögren's syndrome can reveal leukopenia and infrequently lymphopenia. In two-thirds of patients, elevated erythrocyte sedimentation rate, hypergammaglobulinemia, antinuclear antibodies, rheumatoid factors, and antibodies against Ro52/Ro60 and La autoantigens are detected. Anticentromere autoantibodies are present in Sjögren's patients with a clinical picture similar to that of limited scleroderma **(Chap. 360)**, while the presence of antimitochondrial antibodies may connote liver involvement in the form of autoimmune cholangitis **(Chap. 346)**. Autoantibodies to 21-hydroxylase are found in patients with a blunted adrenal response, while autoantibodies to citrullinated peptides are seen in Sjögren's patients with arthritis. Anticalponin-3 antibodies have been recently associated with the occurrence of peripheral neuropathies.

■ DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Sjögren's syndrome should be suspected if a patient presents with eye and/or mouth dryness, major salivary gland enlargement, or systemic manifestations such as Raynaud's phenomenon, palpable purpura, or symptomatology of renal tubular acidosis. A careful history of medications causing dryness should be obtained. Recently, cases of Sjögren's syndrome were triggered by PD-1/PD-L1 checkpoint inhibitors.

The workup should include eye tests that might reveal keratoconjunctivitis sicca, salivary flow tests or ultrasonography, and