2.1 CASE HISTORY

A 26-year-old woman presents with a short history of joint pain, a skin rash on her face and tiredness. On investigation she is also found to have urine abnormalities with both blood and protein excretion. Serological tests show that she has circulating antibodies to nuclear antigens including double-stranded DNA and a nucleic acid associated protein Rho. These features, especially the autoantibody profile, are diagnostic of systemic lupus erythematosus (SLE).

One of the most important prognostic features of SLE is the type, extent and activity of the renal involvement so a renal biopsy was done. Biopsy specimens from affected tissues may show a range of severity and acuteness, the assessment of which is an important part of the practice of histopathology of SLE. The biopsy specimens showed deposition of immune complexes in the wall of the glomerular capillaries (Figure 2.16A). The immune complexes contained IgG, IgM, IgA, and complement components. On light microscopy 80% of glomeruli were affected by an inflammatory process with infiltration by neutrophils and macrophages (Figure 2.16B). 30% of the glomeruli had crescents. This means that this woman's renal disease is of lupus nephritis type 4 with significant activity.

She started treatment with cyclophosphamide and steroids. Our understanding of the pathogenesis of SLE informs this therapy. Cyclophosphamide specifically targets the B lymphocytes that produce the autoantibody and the steroids suppress the activity of the effector neutrophils and macrophages. After 6 months of therapy the young woman is well with no blood and protein in her urine, her joint symptoms have improved and she does not have a skin rash.

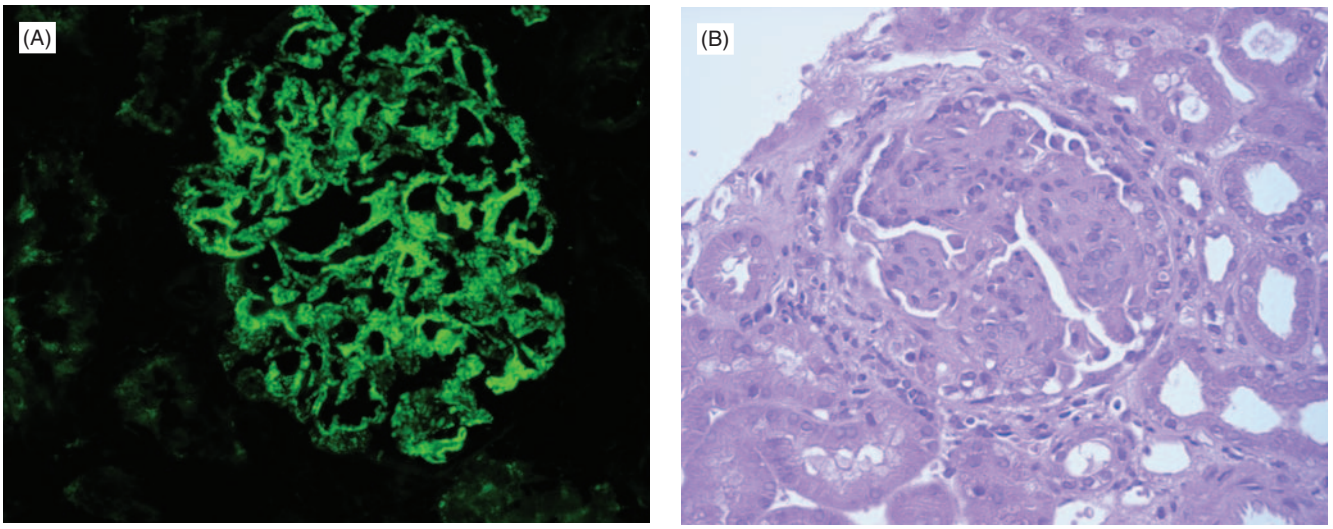

FIGURE 2.16 In the glomerulonephritis associated with systemic lupus erythematosus there is deposition of complement-activating immune complexes – IgG illustrated by immunofluoresence (A), with consequent infiltration by inflammatory cells (B).

blood and become deposited in the microcirculation of key tissues such as skin, joints and especially kidney. In these locations complement activation occurs, neutrophils and, in a chronic setting, macrophages infiltrate the tissues and elicit damage (see Case History 2.1 above).

Primary biliary cirrhosis is a chronic progressive disease of the liver with good evidence of an autoimmune aetiology. Although autoantibodies to mitochondria are present, the pattern of destruction of intrahepatic bile ducts is typical of a type 4 hypersensitivity. Autoreactive T lymphocytes directed against antigens on the epithelium of the bile duct trigger the activation of macrophages and formation of a granulomatous response. With the granulomas there is progressive destruction of bile ducts, obstruction to biliary secretion and fibrosis leading to cirrhosis and liver failure.

Attempts to suppress the autoimmune response and the inflammatory destruction of tissue form the basis of the medical management of these disorders. Understanding the type of autoimmune reaction and the type of hypersensitivity underlying the tissue injury is important in directing the rational treatment of autoimmune disease.

Immunodeficiency and Immunosuppression

Immunodeficiency may be primary or secondary, the primary immunodeficiencies being inherited abnormalities associated with a failure of development of components of the immune system, whereas secondary immunodeficiency occurs as a result of disease or its treatment.