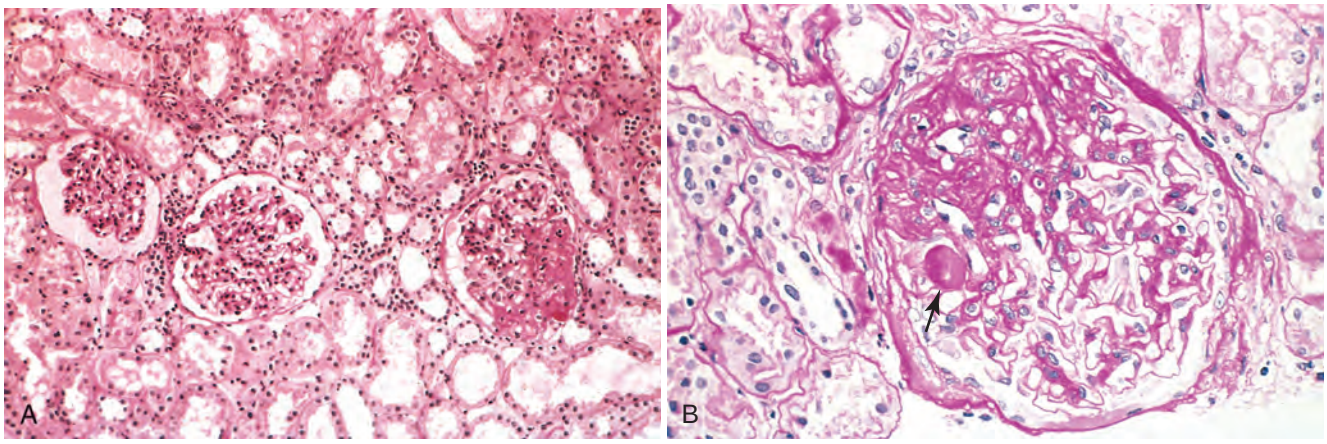

Figure 20-14 Focal segmental glomerulosclerosis, PAS stain. **A,** Low-power view showing segmental sclerosis in one of three glomeruli (at 3 o'clock). **B,** High-power view showing hyaline insudation *(arrow)* and lipid (small vacuoles) in sclerotic area.

Renal ablation FSGS, a secondary form of FSGS, occurs as a complication of glomerular and nonglomerular diseases causing reduction in functioning renal tissue. Particularly striking examples where this occurs are reflux nephropathy and unilateral agenesis. These may lead to progressive glomerulosclerosis and renal failure. The pathogenesis of FSGS in this setting is described earlier in this chapter.

MORPHOLOGY

By light microscopy the **focal and segmental lesions may involve only a minority of the glomeruli** and may be missed if the biopsy specimen contains an insufficient number of glomeruli (Fig. 20-14*A*). In the sclerotic segments there is collapse of capillary loops, increase in matrix and segmental deposition of plasma proteins along the capillary wall (hyalinosis), which may become so pronounced as to occlude capillary lumens. Lipid droplets and foam cells are often present (Fig. 20-14*B*). Glomeruli that do not show segmental lesions usually appear normal on light microscopy but may show increased mesangial matrix. On electron microscopy both sclerotic and nonsclerotic areas show **diffuse effacement of foot processes**, and there may also be focal detachment of the epithelial cells and denudation of the underlying GBM. By immunofluorescence microscopy IgM and C3 may be present in the sclerotic areas and/or in the mesangium. In addition to the focal sclerosis, there may be pronounced hyalinosis and thickening of afferent arterioles. With the progression of the disease, increased numbers of glomeruli become involved and sclerosis spreads within each glomerulus. In time, this leads to total (i.e., global) sclerosis of glomeruli, with pronounced tubular atrophy and interstitial fibrosis.

A morphologic variant of FSGS, called **collapsing glomerulopathy,** is characterized by retraction and/or collapse of the entire glomerular tuft, with or without additional FSGS lesions of the type described above (Fig. 20-15). A characteristic feature is proliferation and hypertrophy of glomerular visceral epithelial cells. This lesion may be idiopathic, but it also has been associated with some drug toxicities (e.g., pamidronate), and it is the most characteristic lesion of HIV-associated nephropathy. Collapsing glomerulopathy is typically associated with prominent tubular injury with formation of microcysts. It has a particularly poor prognosis.

Clinical Course. There is little tendency for spontaneous remission in idiopathic FSGS, and responses to corticosteroid therapy are variable. In general, children have a better prognosis than adults do. Progression to renal failure occurs at variable rates. About 20% of patients follow an unusually rapid course, with intractable massive proteinuria ending in renal failure within 2 years. Factors associated with rapid progression include the degree of proteinuria, the degree of renal insufficiency at diagnosis, and histologic subtype (the collapsing variant has an unfavorable course; the tip variant has a relatively good prognosis). Recurrences are seen in 25% to 50% of patients receiving allografts.

HIV-Associated Nephropathy

HIV infection can directly or indirectly cause several renal complications, including acute renal failure or acute

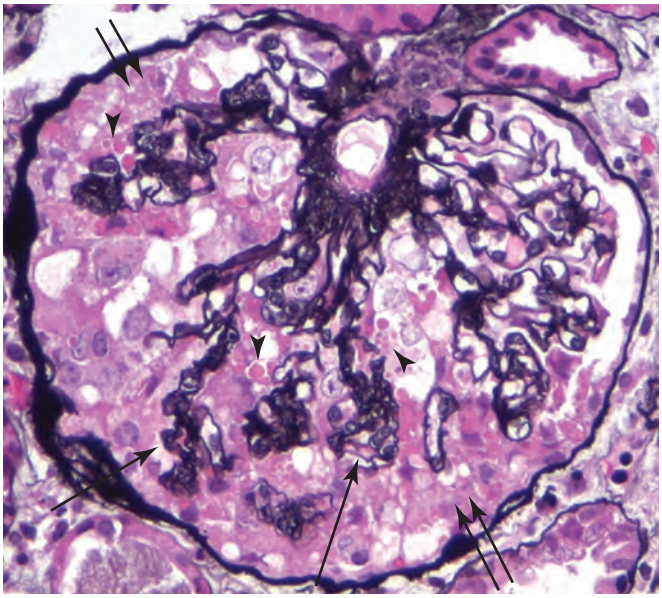

Figure 20-15 Collapsing glomerulopathy. Visible are retraction of the glomerular tuft *(arrows),* narrowing of capillary lumens, proliferation and swelling of visceral epithelial cells *(double arrows),* and prominent accumulation of intracellular protein absorption droplets in the visceral epithelial cells *(arrowheads).* Silver methenamine stain. (Courtesy Dr. Jolanta Kowalewska, Cedars-Sinai Medical Center, Los Angeles, Calif.)