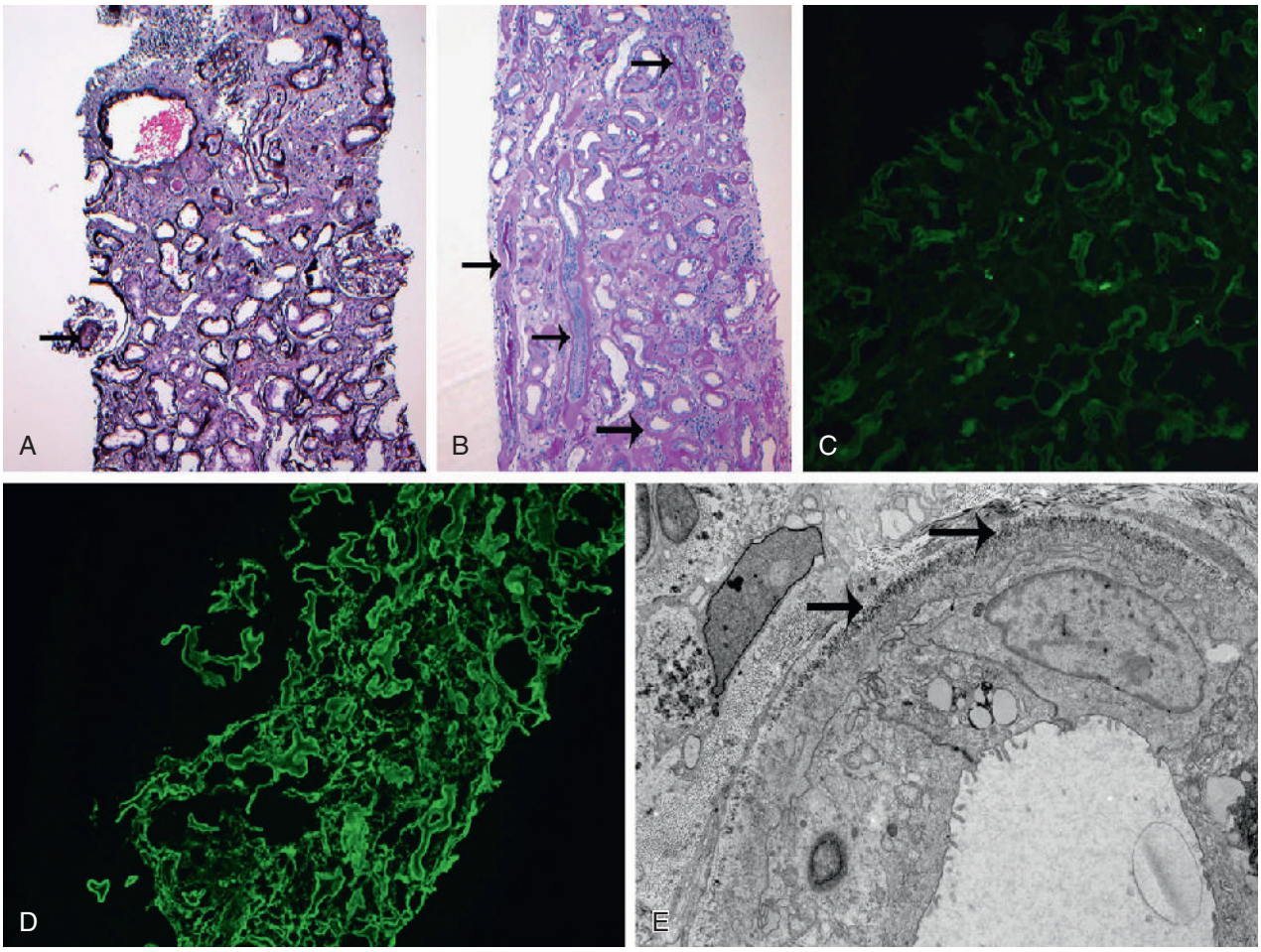

FIGURE 28-13 Light chain deposition disease. **A,** Light microscopy shows glomeruli with silver-positive mesangial nodules *(arrow)* and thickened tubular basement membranes (silver methenamine, ×10). **B,** Periodic acid–Schiff staining shows thickened, wavy tubular basement membranes *(arrow)* (×10). Immunofluorescence studies found negative staining for λ light chains (**C**) and bright staining for κ light chains (**D**) along the tubular basement membranes (both ×10). **E,** Electron microscopy shows granular, punctate, electron-dense deposits *(arrows)* along the tubular basement membranes (×5800).

predominant neurologic involvement suggests a diagnosis of TTP, and predominant renal involvement points to HUS. In most cases, the clinical presentations are very similar, making it difficult to distinguish between HUS and TTP on clinical grounds alone. Other causes of thrombotic microangiopathy include malignant hypertension, drugs (e.g., cocaine, quinidine, ticlopidine), autoimmune diseases (e.g., SLE, scleroderma, antiphospholipid antibody syndrome), malignancy, HIV infection, and antibody-mediated rejection.

Kidney biopsy in HUS and TTP reveals microthrombi in glomerular capillaries and arterioles, and mesangial expansion with loose granular material, called *mesangiolysis*, may be seen in HUS and TTP and in malignant hypertension or autoimmune diseases (Fig. 28-14). Malignant hypertension and autoimmune diseases may also show thickening and intimal fibrosis of arteries and onion-skinning (i.e., laminated deposition of basement membrane–type material) of the vessel walls. Thrombi are common and may occlude the vascular lumen.

Hemolytic Uremic Syndrome

Two subtypes of HUS are recognized: a sporadic or diarrhea-associated form (D+ HUS) and an atypical or non–diarrhea-associated form (D− HUS). D+ HUS is the most frequently encountered form, and it is linked strongly to ingestion of meat contaminated with enterohemorrhagic *Escherichia coli* or other infectious agents. The bacterium produces a Shiga-like toxin that binds to a glycolipid receptor on renal endothelial cells and triggers activation of the alternative complement cascade, leading to endothelial damage. Therapy for D+ HUS is supportive. Children with D+ HUS have a good prognosis (90% recover renal function), but older patients have increased mortality rates and unfavorable long-term renal survival.

Atypical or D− HUS represents 10% to 15% of the cases of HUS and is more common in adults. The disease results from genetic mutations or autoantibodies against complement factors or complement factors regulating proteins (i.e., C3, factor B, factor H, factor I, MCP, CFHR1, and CFHR3) that control the activity of C3 convertase of the alternative complement pathway. The resulting defective control of C3 convertase leads to widespread activation of the complement cascade.

The complement inhibitor eculizumab has been approved for the treatment of patients with atypical HUS. Eculizumab and plasma infusion may also be considered in the treatment of