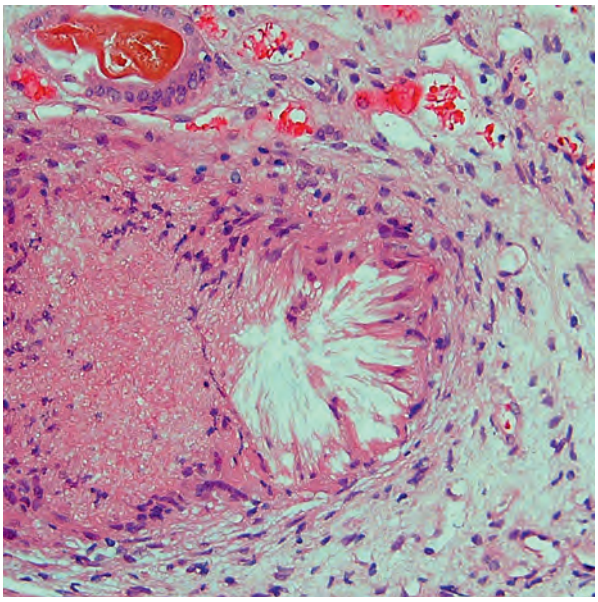

Figure 20-34 Granulomatous inflammation and fibrosis outline the slender urate crystals in the renal medulla.

hyperuricemia. The monosodium urate crystals deposit in the acidic milieu of the distal tubules and collecting ducts as well as in the interstitium, and form distinct birefringent needle-like crystals either in the tubular lumens or in the interstitium (Fig. 20-34). The urate deposits evoke a mononuclear response that contains foreign-body giant cells. This lesion is called a *tophus* (Chapter 26). Tubular obstruction by the urates causes cortical atrophy and scarring. Clinically, urate nephropathy is a subtle disease associated with tubular defects that may progress slowly. Some individuals with gout who develop a chronic nephropathy have evidence of increased exposure to lead.

- *Nephrolithiasis:* uric acid stones are present in 22% of individuals with gout and 42% of those with secondary hyperuricemia (see later discussion of renal stones).

Hypercalcemia and Nephrocalcinosis

Disorders associated with hypercalcemia, such as hyperparathyroidism, multiple myeloma, vitamin D intoxication, metastatic cancer, or excess calcium intake (milk-alkali syndrome), may induce the formation of calcium stones and deposition of calcium in the kidney (nephrocalcinosis). Extensive degrees of calcinosis, under certain conditions, may lead to chronic tubulointerstitial disease and renal insufficiency.

The earliest functional defect is an inability to concentrate the urine. Other tubular defects, such as tubular acidosis and salt-losing nephritis, may also occur. With further damage, a slowly progressive renal insufficiency develops. This is usually due to nephrocalcinosis, but many of these patients also have calcium stones and secondary pyelonephritis.

Acute Phosphate Nephropathy

Extensive accumulations of calcium phosphate crystals in tubules can occur in patients consuming high doses of select oral phosphate solutions in preparation for colonoscopy. These patients are not hypercalcemic, but the excess phosphate load, perhaps complicated by dehydration, causes marked precipitation of calcium phosphate, typically presenting as renal insufficiency several weeks after the exposure. Patients with acute and reversible injury typically recover partial renal function.

Light-Chain Cast Nephropathy ("Myeloma Kidney")

Nonrenal malignant tumors, particularly those of hematopoietic origin, affect the kidneys in several ways (Table 20-10). The most common involvements are tubulointerstitial, caused by complications of the tumor (hypercalcemia, ureteral obstruction) or therapy (irradiation, hyperuricemia, chemotherapy, hematopoietic cell transplantation, infections in immunosuppressed patients). We limit the discussion here to the tubulointerstitial lesions in *multiple myeloma* patients.

Overt renal insufficiency occurs in half of those with multiple myeloma and related lymphoplasmacytic disorders. Several factors contribute to renal damage:

- *Bence-Jones proteinuria and cast nephropathy*. The main cause of renal dysfunction is related to Bence-Jones (light-chain) proteinuria, and correlates with the degree of proteinuria. Two mechanisms seem to account for the renal toxicity of Bence-Jones proteins. First, some Ig light chains are directly toxic to epithelial cells, apparently because of their intrinsic physicochemical properties. Second, Bence-Jones proteins combine with the urinary glycoprotein (Tamm-Horsfall protein) under acidic conditions to form large, histologically distinct tubular casts that obstruct the tubular lumens and induce a characteristic inflammatory reaction (light-chain cast nephropathy).
- *Amyloidosis* of AL type, formed from free light chains (usually of λ type), which occurs in 6% to 24% of individuals with myeloma.
- *Light-chain deposition disease*. In some patients, light chains (usually of κ type) deposit in GBMs and mesangium in nonfibrillar forms, causing a glomerulopathy (described earlier), and in tubular basement membranes, which may cause tubulointerstitial nephritis.
- *Hypercalcemia* and *hyperuricemia* are often present in these patients.

Table 20-10 Renal Disease Related to Nonrenal Neoplasms

Direct or Metastatic Tumor Invasion of Renal Parenchyma
Ureters (obstruction) Artery (renovascular hypertension)
Hypercalcemia
Hyperuricemia
Amyloidosis (Al, Light-Chain Type)
Excretion of Abnormal Proteins (Multiple Myeloma)
Glomerulopathies
Membranous nephropathy, secondary (carcinomas) Minimal-change disease (Hodgkin disease) Membranoproliferative glomerulonephritis (leukemias and lymphomas) Monoclonal immunoglobin/light-chain deposition disease (multiple myeloma)
Effects of Radiation Therapy, Chemotherapy, Hematopoietic Cell Transplantation, Secondary Infection