URIC ACID AND RENAL DISEASE

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**FIGURE 11-12**

Uric acid contributes to the risk of kidney stones in several ways. Pure uric acid stones occur in patients with hyperuricosuria, particularly when the urine is acidic. Thus, therapy involves both allopurinol and alkalinization with potassium alkali salts. Hyperuricosuria also promotes calcium oxalate stone formation. In these patients, calcium nephrolithiasis can be prevented by therapy with allopurinol. The mechanism may involve heterogenous nucleation of calcium oxalate by uric acid microcrystals, binding of endogenous inhibitors of calcium crystallization, or “salting out” of calcium oxalate by urate [4].

Acute uric acid nephropathy occurs most often in the setting of brisk cell lysis from cytotoxic therapy or radiation for myeloproliferative or lymphoproliferative disorders or other tumors highly responsive to therapy. Uric acid nephropathy can uncommonly occur spontaneously in malignancies or other states of high uric acid production. Examples are infants with the Lesch-Nyhan syndrome who have excessive uric acid production resulting from deficiency of hypoxanthine-guanine phosphoribosyltransferase deficiency and, rarely, adults with gout who become volume-contracted and whose urine is concentrated and acidic. The mechanism involves intratubular obstruction by crystals of uric acid in the setting of an acute overwhelming load of uric acid, particularly in acidic urine. In recent years, the widespread use of an effective prophylactic regimen for chemotherapy has made acute uric acid nephropathy much less common [15]. This regimen includes preparation of the patient with high-dose allopurinol, volume-expanding the patient to maintain a dilute urine, and alkaline diuresis. In patients whose tumor lysis leads to hyperphosphatemia, however, it is important to discontinue urinary alkalinization or else calcium phosphate precipitation may occur. Occasionally, patients will develop renal failure despite these measures. In such patients, hemodialysis is preferable to peritoneal dialysis because of the higher clearance rates for uric acid. Frequent hemodialysis, even multiple times per day, may be necessary to prevent extreme hyperuricemia and facilitate recovery of renal function. A modification of continuous arteriovenous hemodialysis has recently been reported to be effective in management of these patients [16].

Chronic gouty nephropathy is a term referring to deposition of sodium urate crystals in the renal interstitium, with an accompanying destructive inflammatory reaction. As a specific entity with intrarenal tophi, gouty nephropathy appears to have become uncommon. It appears clear that long-standing hyperuricemia alone is not sufficient to cause this condition in most patients, and that renal failure in patients with hyperuricemia or gout is almost always accompanied by other predisposing conditions, particularly hypertension or exposure to lead [17].

Familial hyperuricemic nephropathy is an entity that now has been reported in over 40 kindreds. It is characterized by recurrent gout, often occurring in youth and even childhood; hyperuricemia; and renal failure. Histopathology reveals interstitial inflammation and fibrosis, almost always without evidence of urate crystal deposition, although this has been found in two patients. In contrast to gouty nephropathy, hypertension usually is absent until renal failure is advanced. The hyperuricemia appears to reflect decreased renal excretion of urate rather than overproduction of urate. Although hyperuricemia precedes and is disproportionate to any degree of renal failure, the role, if any, that uric acid plays in the pathogenesis of the renal failure remains unclear. There is no consensus among authors regarding the potential value of allopurinol in this disease. The inheritance follows an autosomal dominant pattern, but, beyond this, the genetics of the disease are not understood [18,19].