

Pathophysiology, Clinical Consequences, and Treatment of Tumor Lysis Syndrome

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Tumor lysis syndrome is an oncologic emergency that is characterized by severe electrolyte abnormalities and, frequently, by acute renal failure. The syndrome typically occurs in patients with lymphoproliferative malignancies, most often after initiation of treatment. The pathophysiology involves massive tumor cell lysis resulting in the release of large amounts of potassium, phosphate, and uric acid. Deposition of uric acid and calcium phosphate crystals in the renal tubules may lead to acute renal failure, which is often exacerbated by concomitant intravascular volume depletion. The kidney normally excretes these products, and consequently preexisting renal failure exacerbates the metabolic derangements of tumor lysis syndrome. Standard

treatment aims to clear high plasma levels of potassium, uric acid, and phosphorus; correct acidosis; and prevent acute renal failure by way of aggressive intravenous hydration; lowering serum potassium levels; use of allopurinol; urinary alkalinization; or renal replacement therapy (if necessary). Allopurinol is the standard of care for treating hyperuricemia of malignancy, but is associated with drawbacks. Recombinant urate oxidase (rasburicase), which recently became available in the United States, provides a safe and effective alternative to allopurinol for lowering uric acid levels and preventing uric acid nephropathy. *Am J Med.* 2004;116:546–554. ©2004 by Excerpta Medica Inc.

Tumor lysis syndrome is an oncologic emergency that is characterized by severe metabolic derangements. It typically occurs in patients with lymphoproliferative malignancies who are exposed to chemotherapy, radiation, or corticosteroids, but can occur spontaneously in the absence of treatment (1). The syndrome is associated frequently with acute renal failure; this may be more frequent and predict worse clinical outcomes in the spontaneous form of the syndrome than in the treatment-related form (1–5). Patients with preexisting acute or chronic renal insufficiency are predisposed to developing the syndrome and are more vulnerable to its effects.

Tumor lysis syndrome was first reported in 1929 in patients with chronic leukemia (6). In 1977, Crittenden and Ackerman described the first case of both spontaneous tumor lysis syndrome and acute renal failure due to uric acid nephropathy in a patient with disseminated gastrointestinal carcinoma (1). Tumor lysis syndrome is most commonly observed following chemotherapy for high-grade lymphoproliferative malignancies such as

acute lymphocytic leukemia and Burkitt lymphoma (7–10). It has also been reported in many different types of solid tumors, including lung and breast carcinoma (2,11–31). Risk factors include large tumor burdens, lactate dehydrogenase levels above 1500 IU, extensive bone marrow involvement, and high tumor sensitivity to chemotherapeutic agents (7).

With increasingly effective antitumor regimens, there is an increased likelihood of tumor lysis syndrome in a wider range of malignant diseases. Various chemotherapeutic agents have been implicated, including cisplatin, etoposide, fludarabine, intrathecal methotrexate, and paclitaxel (32–34). In addition, rituximab (35), ionizing radiation (36), interferon α (37), and endocrine therapies such as corticosteroids and tamoxifen (18,38–40) have been implicated. These agents increase renal risk because of their increased antitumor activity, rather than a direct toxicity of the renal tubules.

METABOLIC ABNORMALITIES AND CONSEQUENCES

Hyperkalemia

Hyperkalemia may appear from 6 to 72 hours after the initiation of chemotherapy (10) and is the most serious manifestation of tumor lysis syndrome (Table 1). Potassium is generally concentrated intracellularly. Cell lysis results in the liberation of large amounts of intracellular potassium into extracellular fluid. Chronic kidney disease, acute renal failure, or concurrent acidosis may ex-

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Table 1. Characteristic Electrolyte Abnormalities Encountered in Tumor Lysis Syndrome and Their Clinical Consequences

Electrolyte	Pathophysiology	Clinical Consequence	Treatment Options
Potassium	Rapid expulsion of intracellular K^+ into the circulation due to cell lysis.	Adverse skeletal and cardiac manifestations (e.g., ventricular arrhythmia, weakness, paresthesias)	Insulin/glucose, sodium bicarbonate, inhaled beta-agonist, K-binding resins, dialysis, calcium gluconate
Phosphate	Release of intracellular PO_4^- due to cell lysis. May be compounded by renal dysfunction.	Muscle cramps, tetany, arrhythmias, seizures	Dialysis, phosphate binders
Calcium	Precipitation of the calcium phosphate complex due to the rapid increase in the phosphorous concentration.	Muscle cramps, tetany, arrhythmias, seizures, renal failure (acute nephrocalcinosis)	Calcium gluconate (treatment should be reserved for those with neuromuscular irritability)
Uric acid	Cell lysis leads to increased levels of purine nucleic acids into the circulation that are metabolized to uric acid.	Renal failure (uric acid nephropathy)	Hydration, dialysis, xanthine oxidase inhibitors, alkalization of urine, urate oxidase

acerbate hyperkalemia as the excretory capacity of the kidney can be overwhelmed by transcellular shifts due to potassium release from lysing cells as well as acidosis. Symptoms of hyperkalemia include weakness, paresthesias, muscle cramps, nausea, vomiting, diarrhea, and anorexia. Severe hyperkalemia (>7.0 mg/dL or $\Delta K^+ >2.0$ mg/dL) can adversely affect skeletal and cardiac muscle function. Electrocardiographic changes include widening of the QRS complex and peaked T waves. Hyperkalemia must be corrected rapidly before potentially fatal ventricular arrhythmias occur.

Hyperphosphatemia and Hypocalcemia

Hyperphosphatemia develops from 24 to 48 hours following initiation of chemotherapy (10). Release of intracellular phosphate can exceed the renal threshold for phosphate excretion, leading to hyperphosphatemia (Table 1). Malignant hematologic cells may contain up to four times more intracellular phosphate compared with normal mature lymphoid cells (10). Additionally, acute destruction of tumor cells during chemotherapy prevents the rapid reuse of phosphate for newly synthesized tumor cells. Precipitation of calcium phosphate occurs when the solubility product of calcium and phosphate is exceeded, possibly leading to hypocalcemia. Muscle cramps, tetany, cardiac arrhythmia, and seizures can result. Acute nephrocalcinosis, or precipitation of calcium phosphate in the renal tubules with an inflammatory response, may lead to acute renal failure. Calcium and phosphate abnormalities should be identified and treated early.

Hyperuricemia

Hyperuricemia develops from 48 to 72 hours following initiation of treatment (10) (Table 1). Tumor cell lysis releases purine nucleic acids, which are metabolized into

uric acid (Figure 1). Malignant cells carry a large burden of nucleic acid products due to their high cellular activity and turnover. The high turnover rate of neoplastic cells leads to ongoing DNA catabolism. The breakdown of purine nucleotides yields high amounts of hypoxanthine. Xanthine oxidase catalyzes the conversion of hypoxanthine into uric acid (Figure 1, step A). After spontaneous or cytotoxic therapy-induced lysis, large amounts of uric acid are produced, leading to rapid increases in plasma and renal tubular concentrations.

The pathophysiology of acute renal failure in tumor lysis syndrome is multifactorial. Two major synergistic mechanisms are volume depletion and uric acid nephropathy. In the presence of an acidic pH in the collecting ducts and increasing concentration of uric acid (Figure 2C), the threshold at which uric acid precipitates into crystals may be reached. These crystals obstruct urine flow in the tubules, leading to uric acid nephropathy, which is more common in patients with volume depletion. Patients with malignancies are often volume depleted from poor oral intake, vomiting, diarrhea, insensible losses (from fever or tachypnea), or procedures requiring fasting. Volume depletion is indicated by history and by several laboratory parameters, including an elevated blood urea nitrogen:creatinine ratio, high urine osmolality, and elevated urine specific gravity.

A decrease in intravascular volume leads to prerenal state as well as an increase in tubular uric acid concentration. The normal kidney responds to volume depletion by autoregulation to maintain intraglomerular flow and filtration fraction. However, in patients with tumor lysis syndrome, the high uric acid load and hyperphosphatemia may overwhelm the ability of the nephron to autoregulate (Figure 2A). The resultant decline in tubular

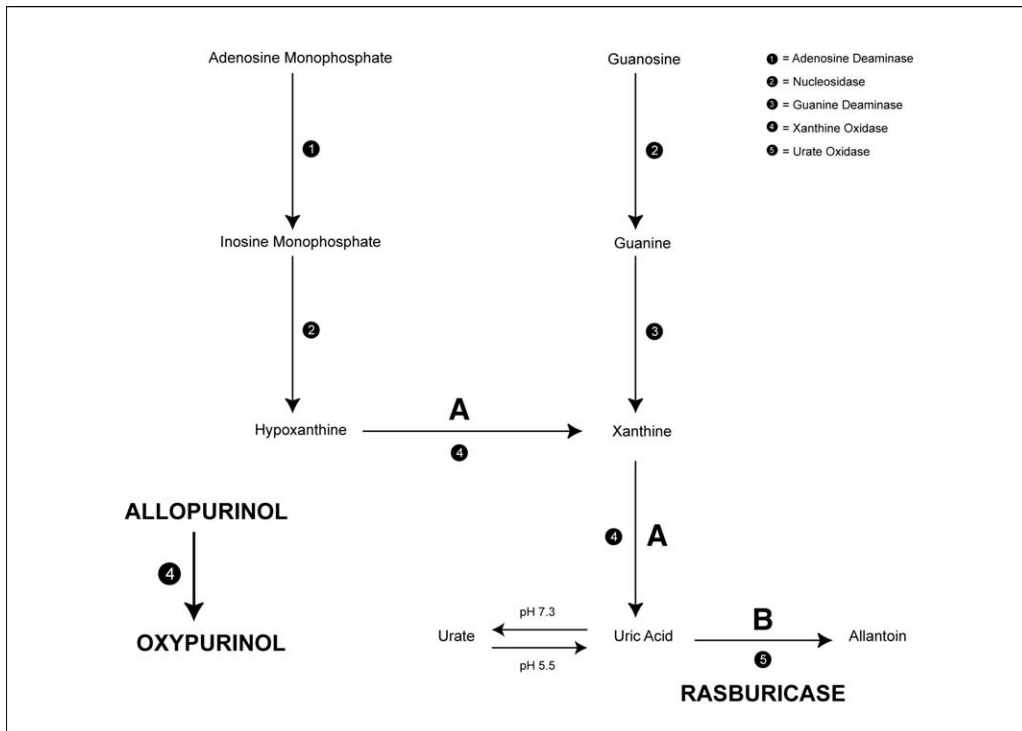


Figure 1. Purine nucleic acid degradation and the formation of uric acid. A: Uric acid formation is inhibited by allopurinol and its metabolite oxypurinol by the inhibition of the enzyme xanthine oxidase. B: Rasburicase, an analog of the enzyme urate oxidase, catalyzes the conversion of uric acid to allantoin. Reprinted with the permission of The Cleveland Clinic Foundation.

flow may precipitate uric acid, leading to uric acid nephropathy. It should be noted, however, that the absence of uric acid crystals in the urine does not rule out uric acid nephropathy. In the setting of acute renal failure and suspected uric acid nephropathy, the use of a random urine measurement to determine the presence of uric acid nephropathy may be appropriate (41). A uric acid:creatinine ratio greater than 1.0 is suggestive of uric acid nephropathy, whereas a ratio less than 0.6 to 0.75 suggests renal failure of another etiology. Acute tubular necrosis should always be considered in the differential diagnosis of acute renal failure in a patient with malignancy. Patients at risk of tumor lysis syndrome are also susceptible to other forms of renal injury owing to prolonged periods of hypotension or to exposure to nephrotoxic agents such as antimicrobial agents, chemotherapy, or contrast media. Ischemic tubule cells exhibit disruption in the mechanisms involved in maintaining cell adhesion, polarity, and solute transport. Damaged tubule cells may slough off into the lumina, resulting in obstruction of nephron flow (Figure 2B). These events further amplify the injury resulting from tumor lysis syndrome–associated acute renal failure. Early identification and treatment may limit the spectrum of manifestations of the syndrome.

PREVENTION AND TREATMENT

The principles of management should address three critical areas: hydration, metabolic abnormalities, and supportive treatment of renal failure.

Hydration

Hydration should begin 2 days prior to, and continue 2 to 3 days after, chemotherapy. Volume expansion with isotonic saline reduces serum concentrations of uric acid, phosphate, and potassium (32,42). Excluding patients who are at risk of volume overload, aggressive fluid administration has been recommended in all patients presumed to be at risk of the syndrome (42–45). As a result of increased renal blood flow, glomerular filtration rate, and urine volume, the concentration of solutes in renal tubules is decreased, making precipitation less likely.

Hyperkalemia

The major goals of the treatment of acute hyperkalemia are cardiac membrane stabilization, intracellular shift of potassium, and reduction of total potassium load. Membrane stabilization is achieved with 10% calcium gluconate to prevent life-threatening cardiac arrhythmias (8,9). Its duration of action, however, is short lived, and treatment may need to be repeated. Insulin promotes the

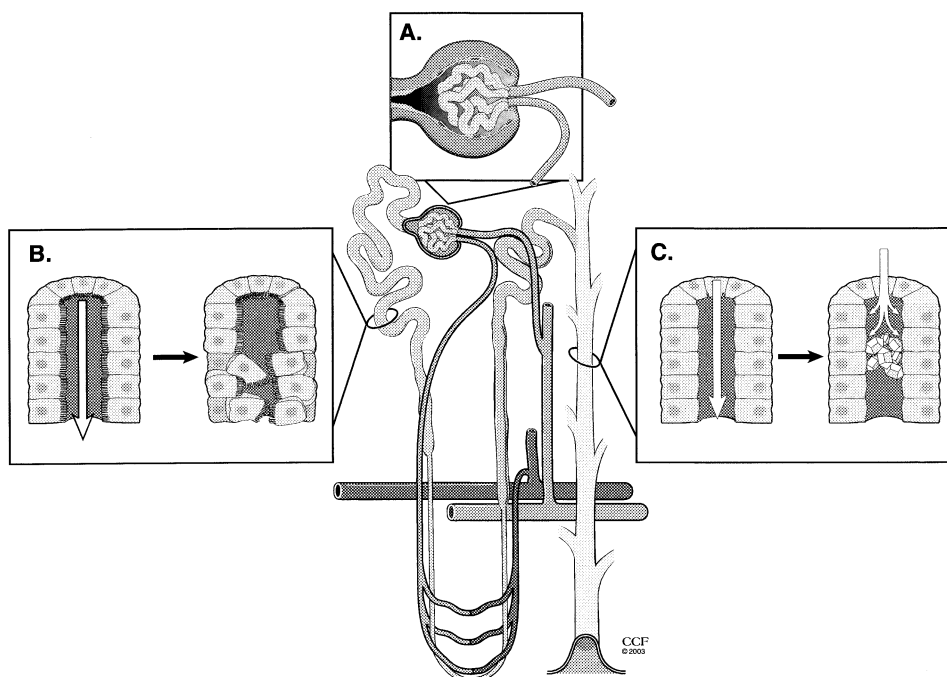


Figure 2. Potential mechanisms of renal injury in acute tumor lysis syndrome. A: The glomerulus. A reduction in glomerular filtration rate mediated by preexisting volume depletion or cytokine-mediated alterations in renal perfusion. B: Renal tubules. Ischemic acute tubular necrosis with impairment of solute transport, disruption of cell adhesions and polarity, and sloughing of cells into lumina resulting in partial or total obstruction of nephron flow. C: Distal tubule/cortical collecting duct. Increasing urine concentration and acidity in the distal portions of the nephron favor precipitation of uric acid crystals and monosodium urate crystals that cause extensive obstruction of the renal collecting ducts. Reprinted with the permission of The Cleveland Clinic Foundation.

intracellular shift of potassium, and is administered with dextrose to prevent hypoglycemia. Inhaled β_2 -agonists may also produce an intracellular shift of potassium (46). Isotonic sodium bicarbonate can be used to reduce metabolic acidosis and also to shift potassium intracellularly (9). However, sodium bicarbonate should be administered judiciously in patients with acute renal failure since it can lead to inappropriate volume expansion. Net potassium excretion can be achieved by several methods. Diuretics facilitate the renal excretion of potassium. Potassium-binding resins, such as sodium polystyrene sulfonate, exchange sodium for potassium cations in the gastrointestinal tract (9,45). Since resins typically require a longer time to effect removal, faster methods of lowering potassium such as dialysis may be required, especially in the setting of acute renal failure (11,42).

Hyperuricemia

The cornerstone of prevention and treatment of hyperuricemia includes both inhibiting the formation of uric acid as well as increasing its renal clearance (Table 2).

Urinary alkalinization increases the solubility of uric acid. At a physiologic pH, more than 98% of uric acid exists in the plasma as its ionized salt, urate (42); in an acidic urinary filtrate environment, uric acid will precipitate

in the renal tubule (54). Alkalinization with sodium bicarbonate increases uric acid solubility by increasing the percentage of ionized uric acid in urine (55).

The goals of urinary alkalinization should be to raise the urine pH to >7.0 . Isotonic sodium bicarbonate in 0.45% normal saline with 5% dextrose should be infused at a rate of 150 to 300 mL/h to achieve effective diuresis and urinary alkalinization (56). Since calcium and phosphate can precipitate at an alkaline pH and worsen renal failure (55,57), sodium bicarbonate should be administered judiciously and discontinued when serum uric acid normalizes. In some cases, increasing urinary flow rates alone may be as effective as urinary alkalinization for decreasing the risk of uric acid nephropathy associated with tumor lysis syndrome (58).

Xanthine oxidase catalyzes the formation of both hypoxanthine and xanthine (19) (Figure 1). Allopurinol (Watson Laboratories, Corona, California) is a structural analog of hypoxanthine and a competitive inhibitor of xanthine oxidase (42). Rundles et al demonstrated the effects of xanthine oxidase inhibitors on uric acid metabolism in patients with chronic granulocytic leukemia (59). Subsequently, DeConti and Calabresi studied 33 patients with neoplastic disease (47). All of the 24 patients

Table 2. Experience Using Pharmacologic Agents to Prevent or Reverse Hyperuricemia in Tumor Lysis Syndrome

First Author (Reference)	Drug	Study Description	Types of Neoplasms	Efficacy	Adverse Events
DeConti (47)	Allopurinol	33 cases demonstrating a dose-related reduction in uric acid in patients treated with allopurinol.	Myeloproliferative disorders, lymphomas, and chronic and acute leukemias	Consistent dose-related drop in serum uric acid levels.	2 patients developed podagra. Acute renal failure in 1 patient.
Masera (48)	Nonrecombinant urate oxidase (Uricozyme)	30 pediatric patients compared with matched historical controls treated with allopurinol.	Acute leukemia	Significant decrease in uric acid levels by urate oxidase vs. allopurinol at day 2 ($P < 0.01$) and following two courses of therapy ($P < 0.0001$).	5 patients from the allopurinol group developed uric acid nephropathy.
Chua (49)	PEG-uricase	1 patient with severe allopurinol allergy and non-Hodgkin's lymphoma with hyperuricemia.	Non-Hodgkin's lymphoma	Demonstrated a drop in plasma uric acid levels without antigenicity and a longer duration of action than urate oxidase.	No adverse reactions.
Pui (50)	Nonrecombinant urate oxidase (Uricozyme)	126 pediatric patients compared with matched historical controls treated with allopurinol.	Acute lymphoblastic leukemia	Significant decrease in uric acid levels by urate oxidase vs. allopurinol ($P < 0.001$). Significant difference in time to decrease in uric acid by urate oxidase vs. allopurinol at day 1 ($P < 0.001$).	6 patients in the urate oxidase group developed allergic reactions. Renal function was preserved significantly better in the urate oxidase group with BUN ($P < 0.001$) and creatinine ($P < 0.01$).
Smalley (51)	Intravenous allopurinol	1176 patients over 21 years who could not tolerate oral allopurinol.	39% non-Hodgkin's lymphoma, 34% acute leukemia	Prevented an increase in uric acid levels in 93% patients. Partial or complete return of uric acid levels to normal in 91% of patients treated.	10 patients developed mild allergic reactions to allopurinol. 10 patients developed uric acid nephropathy despite adequate intravenous allopurinol therapy.
Pui (52)	Rasburicase	245 patients treated with rasburicase for prophylaxis or treatment of hyperuricemia.	71% acute leukemia	Compared with baseline values, serum uric acid levels decreased significantly ($P < 0.001$) with rasburicase.	9 patients developed mild allergic reactions. 10 patients required hemodialysis while being treated with rasburicase.
Goldman (53)	Rasburicase vs. allopurinol	Comparison of 52 patients assigned randomly to allopurinol or rasburicase.	Leukemia or lymphoma (at high risk of tumor lysis)	Significant decrease in uric acid levels by rasburicase vs. allopurinol ($P < 0.0001$) at 4 hours after the first dose.	1 patient taken off rasburicase when hemolysis occurred. Not powered to determine differences in renal failure or need for dialysis.

BUN = Blood urea nitrogen; PEG = polyethylene glycol.

who received allopurinol showed a consistent reduction in uric acid levels. The dose of oral allopurinol for tumor lysis syndrome ranges up to 800 mg/d. An intravenous form is available for patients who either are unable to take oral medications or have conditions in which intravenous administration is preferred (45,51,60). Allopurinol has a half-life of 60 to 180 minutes. Its active metabolite, oxypurinol, is also an effective inhibitor of xanthine oxidase and remains active for 18 to 30 hours (9). Since oxypurinol is cleared renally, its half-life can be prolonged substantially in patients with renal insufficiency (42). In addition, thiazide diuretics also delay excretion of oxypurinol (61). A decrease in plasma urate levels can be seen by 2 to 3 days. It should be noted that inhibition of uric acid synthesis by allopurinol increases plasma and urinary xanthine levels (19). Since xanthine (pKa 7.4) is less soluble in urine than uric acid (pKa 5.5), allopurinol therapy may lead to precipitation of xanthine in the renal tubules and renal failure (42,62). However, this potential complication has rarely been reported in the literature.

In addition to its limiting production, uric acid can also be converted to a more soluble form to facilitate excretion. Urate oxidase catalyzes the oxidation of uric acid to allantoin, which is five times more soluble than uric acid (Figure 1B) (63). This enzyme occurs in most species except higher primates, due to a nonsense mutation (64). Nonrecombinant urate oxidase has been used in Europe since 1975 for the prophylaxis of acute tumor lysis syndrome (65). The use of urate oxidase was limited by a high incidence of anaphylaxis, but the addition of polyethylene glycol has reduced this risk (66). Subsequently, a recombinant form of urate oxidase, rasburicase (Elitek; Sanofi-Synthelabo Inc., New York, New York), was developed using a complementary DNA fragment from *Aspergillus flavus* in *Saccharomyces cerevisiae* (67–69). Rasburicase has recently been approved in the United States.

Rasburicase is both efficacious and well tolerated (53,70). In a randomized comparison with allopurinol in 52 pediatric patients at high risk of tumor lysis, Goldman et al demonstrated that rasburicase significantly reduced plasma uric acid levels within 4 hours after the first dose (86% vs. 12% reduction, $P < 0.0001$) (53). No renal failure requiring renal replacement therapy occurred in the rasburicase group, and no antirasburicase antibodies were detected at day 14 of treatment. Rasburicase does not require adjustment with decreased creatinine clearance (69,70). Although the Food and Drug Administration has warned about the risk of hypersensitivity reactions, including anaphylaxis, a study showed that the risk of hypersensitivity reaction (consisting of bronchospasm and hypoxemia) was considerably lower with rasburicase than with nonrecombinant urate oxidase (50). In patients with glucose-6-phosphate dehydrogenase deficiency, hemolytic anemia may occur due to the inability to metabolize hydrogen peroxide produced during the formation

of allantoin (Figure 1B) (52,69,71). Rare adverse drug reactions such as nausea and vomiting have been reported with rasburicase (50). Rasburicase may interfere with serum uric acid estimation due to the continued breakdown of uric acid following sample collection. This may be avoided by promptly placing the blood sample in an ice bath (69).

Hypocalcemia

Asymptomatic hypocalcemia should not be treated due to the risk of exacerbating calcium phosphate precipitation (72). Intravenous calcium gluconate is indicated for symptomatic hypocalcemia. Hypocalcemia usually resolves with treatment of the concomitant hyperphosphatemia.

ACUTE RENAL FAILURE AND THE ROLE OF RENAL REPLACEMENT THERAPY

Dialysis is indicated when the resolution of tumor lysis–induced acute renal failure is unlikely, or whenever life-threatening electrolyte disorders or volume overload occurs. Renal replacement therapy must be instituted promptly and aggressively once conservative measures have been proven to be inadequate. General principles include normalization of potassium, calcium, phosphorus, and uric acid levels to avoid further renal insults and to reduce the likelihood of arrhythmias. Renal replacement therapies may also reduce nitrogenous waste products and afford flexibility in management of nutrition and fluid balance (56).

Dialytic support is used primarily to correct the metabolic abnormalities seen in tumor lysis syndrome and potentially limit further renal injury. There are many forms of renal replacement therapy; each differs in its efficiency in correcting fluid and electrolyte abnormalities.

The concept of clearance is useful when attempting to compare the efficacy of different forms or techniques of dialytic support in various groups of patients. Clearance can be defined as the volume of blood that is purified of a solute per unit of time. The clearance of a solute depends on a number of variables, both patient specific and technique dependent, which may vary greatly between patient groups or between therapies. This heterogeneity makes precise predictions of the potential effectiveness of any one technique difficult. Although the final prescription of dialysis therapy should be determined only with careful consideration of the clinical situation, a general appreciation of the differences achieved by each type of dialysis support is useful. Interestingly, within each form of dialysis therapy, the clearance of any particular solute appears similar in patients with tumor lysis syndrome and in patients with other forms of renal failure (5,73–77).

The solutes that are most often affected in tumor lysis syndrome are cleared more efficiently with hemodialysis than with peritoneal dialysis (73,78). Although intermittent therapy is considered to be more efficient than continuous therapy per unit time, continuous therapies can be more effective overall by virtue of the extension of therapy over time afforded with these approaches (5,74).

Intermittent hemodialysis is a rapid means of addressing fluid and electrolyte perturbations, and in the United States it is readily available in the hospital setting. Multiple individual treatments utilizing high blood flow and high dialysate flows, with laboratory-directed alterations of potassium and calcium concentrations in dialysate fluid, provide the best means of rapidly correcting electrolyte levels (73). Absolute clearance rates vary and are dependent on blood flow achieved, but generally reflect those obtained in other patients with renal disease. Clearance of uric acid ranged from 70 to 145 mL/min in one report (73), which is similar to that observed in chronic dialysis patients (77). Certain abnormalities (e.g., hyperphosphatemia) are relatively difficult to control with intermittent hemodialysis, even with the use of high flux membranes and high blood flows. Therefore, it is recommended that patients receive intermittent hemodialysis every 12 to 24 hours depending on the initial magnitude of derangement and the subsequent clinical course.

Peritoneal dialysis can be an alternative to intermittent hemodialysis, although the need to place a peritoneal catheter is a major obstacle in patients with abdominal involvement of their tumor burden. Clearance rates with peritoneal dialysis are lower than with hemodialysis; rates of uric acid clearance ranged from 6.7 to 9.5 mL/min in one report (73,78), similar to those observed in chronic peritoneal dialysis patients (76) and substantially less efficient than rates obtained with intermittent dialysis (73). The extended time available for treatment on continuous peritoneal dialysis can somewhat compensate for this reduced efficiency, but can be a limitation in patients with immediately life-threatening metabolic disorders.

The types of continuous renal replacement therapy include hemofiltration, hemodialysis, and hemodiafiltration, all of which require close monitoring, typically in an intensive care unit. Clearance of solutes is highly variable and depends on the specific prescription for each of these methods. For comparative purposes, in patients with tumor lysis syndrome, uric acid clearance has been reported at 39 mL/min in continuous arteriovenous hemodialysis and 45 mL/min in continuous veno-venous hemodiafiltration (5,79). These rates were observed in patients treated with high dialysate or high replacement fluid flow rates, and as such are higher than clearance estimates in other patients treated with lower rates (74,80). Experience with continuous therapies in the treatment of tumor lysis syndrome is generally favorable, although it is not known if they are much more effective than intermittent

therapy (5,79–83). Continuous renal replacement therapy has been utilized as a prophylactic adjunct to the treatment of patients at high risk of tumor lysis syndrome in select cases, with some encouraging results (44,84).

CONCLUSION

Tumor lysis syndrome is a life-threatening condition in which rapid destruction of tumor cells leads to hyperuricemia, hyperphosphatemia, hyperkalemia, hypocalcemia, or, often, acute renal failure. Early identification of patients at risk and prevention of its development is critical. The syndrome is seen most frequently in patients with lymphoproliferative malignancies, but also in those with solid tumors. Tumor lysis syndrome is seen most often following chemotherapy induction of tumor cells, which initiates massive cell death and lysis of cell contents. During chemotherapy, patients who are at risk of the syndrome should be monitored closely through daily weights and assessments of urine output. Uric acid, lactate dehydrogenase, creatinine, potassium, phosphate, and calcium levels should be measured frequently. Acute renal failure may occur from intravascular volume depletion or from deposition of uric acid and calcium phosphate crystals in the tubules, resulting in uric acid nephropathy. The metabolic and electrolyte disturbances of tumor lysis syndrome may be concurrently exacerbated by renal failure. Patients may be treated with allopurinol, hydration, urinary alkalinization, or hemodialysis. Rasburicase, which was recently approved in the United States, may be more effective than allopurinol because it oxidizes uric acid to the soluble product allantoin, preventing or reversing nephropathy from uric acid or xanthine. Failure of medical therapies to control abnormalities of the tumor lysis syndrome is an urgent indication for renal replacement therapy. Without prompt and proper management, derangements of the tumor lysis syndrome can result in death. Early recognition and treatment will decrease the risk of fatal complications.

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