At an Increased Risk: Tumor Lysis Syndrome

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Patients at highest risk for tumor lysis syndrome (TLS) often are diagnosed with bulky, rapidly proliferating hematologic tumors, such as acute leukemia and non-Hodgkin lymphoma (Kaplow & Hardin, 2007). Patients with solid tumors, such as mediastinal masses which are highly sensitive to chemotherapy, also may develop TLS, although it is more common in patients undergoing treatment for leukemia and lymphoma. TLS occurs from the effect of chemotherapy or radiation on rapidly dividing cells. Patients with elevated lactic dehydrogenase (LDH), dehydration, and renal insufficiency are at greatest risk for developing TLS (Brant, 2002). Advances in cancer treatment, such as those in bone marrow transplantation, require the use of high-dose chemotherapy, which may demonstrate an increase in the incidence of TLS.

TLS is a rapidly developing oncologic emergency characterized by electrolyte and metabolic disturbances that are fatal without timely identification and management. Patients present with hyperuricemia, hyperphosphatemia, hypocalcemia, and hyperkalemia. Electrolyte disturbances can cause acute renal and multisystem organ failure (see Figure 1).

Pathophysiology

TLS occurs from the rapid release of intracellular components during cell death. Cancer cells have an abnormally high amount of potassium, phosphorus, and nucleic acid (Kaplow & Hardin, 2007). When cancer cells are destroyed by chemotherapy or radiation, they spill their intracellular components into the bloodstream, causing an influx of potassium, phosphorus, and nucleic acid which the kidneys are not able to efficiently excrete, leading to hyperuricemia, hyperphosphatemia, hypocalcemia, and hyperkalemia. Hyperuricemia occurs when the liver converts nucleic acids into uric acid; hypocalcemia develops as serum calcium binds to elevated amounts of phosphorus within the bloodstream (Kaplow & Hardin).

Clinical Findings

Laboratory findings will demonstrate electrolyte imbalances such as hyperuricemia (more than 6.0 mg/dl), hyperphosphatemia (more than 4.5 mg/dl), hypocalcemia (less than 8.5 mg/dl), and hyperkalemia (more than 5.5 mEq/l) (McCance & Heuther, 2006). Hyperkalemia generally is the first electrolyte imbalance, followed by hyperphosphatemia, and leads to hypocalcemia and hyperuricemia (Agnani, Gupta, Atray, & Vachharajani, 2006). Multisystem organ failure may occur because of these metabolic findings. TLS has the ability to affect the renal, gastrointestinal, cardiac, and neuromuscular systems.

Renal

Hyperuricemia occurs when uric acid crystals and calcium phosphate salts obstruct renal flow, causing renal failure (Kaplow & Hardin, 2007). Patients will have increased uric acid and creatinine levels, indicating renal failure. Physical symptoms consist of flank pain, gross hematuria, cloudy urine, oliguria, lethargy, nausea, and vomiting (Murphy-Ende & Chernecky, 2002). Weight gain and edema also may be present.

Gastrointestinal

Hyperkalemia causes nausea, vomiting, and diarrhea (Cope, 2004). Anorexia, abdominal cramping, and pain also may occur because of the elevated potassium (McCance & Heuther, 2006). Decreased levels of serum calcium may cause intestinal cramping and increased bowel activity (McCance & Heuther).

Cardiac

Serum potassium levels more than 5.3 mEq/l may cause irregular heart arrythmias and hypotension (Murphy-Ende & Chernecky, 2002). Often the dysrhythmias are atrial in origin (Kaplow & Hardin, 2007). Hyperkalemia causes electrocardiogram changes such as tall T waves, flattened P waves, prolonged PR intervals, widened QRS complexes, and depressed ST segments (Murphy-Ende & Chernecky). The presence of a prolonged QT interval may indicate hypocalcemia.

Neuromuscular

Hyperkalemia causes neuromuscular irritability, muscle weakness, or paralysis, and hypocalcemia causes neuromuscular excitability (McCance & Heuther, 2006). A decreased level of serum calcium also may cause seizures and tetany (McCance & Heuther).

Medical Management

To prevent morbidity and mortality, early recognition and management of TLS are of primary concern. Patients at

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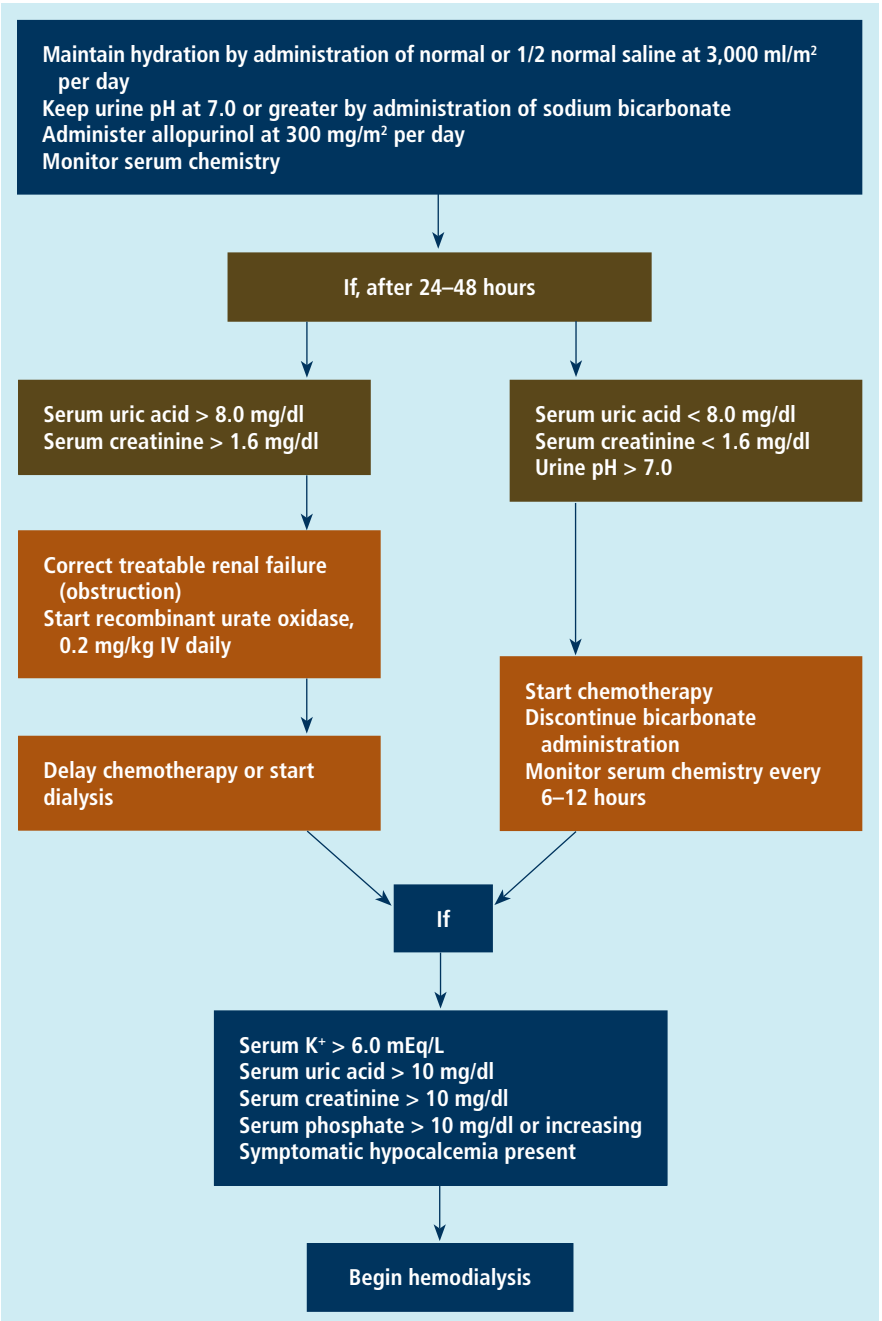

Figure 1. Patient Management for Tumor Lysis Syndrome

Note. From *Harrison's Principles of Internal Medicine* (17th ed., p. 1737), by A.S. Fauci, D.L. Kasper, E. Braunwald, S.L. Hauser, D.L. Longo, J.L. Jameson, et al., 2008, New York: McGraw-Hill Professional. Copyright 2008 by the McGraw-Hill Companies, Inc. Reprinted with permission.

increased risk for TLS should be identified early and preventive measures should be initiated prior to beginning treatment. At-risk patients often are diagnosed with acute leukemias, aggressive lymphomas, and solid tumors that are highly chemosensitive (Brant, 2002). Patients with baseline renal failure and an elevated LDH are at greater risk for developing TLS prior to any cancer treatment.

Preventive Measures

Before treatment begins, patients are given allopurinal orally to prevent uric acid formation. Although more expensive than allopurinal, rasburicase also can be given as a pretreatment one to two days prior to therapy initiation. Rasburicase converts uric acid into allantoin, which is more soluble in urine and easily excreted through the kidneys (Brant, 2002). Aggressive hydration and the addition of diuretics enhance urinary excretion. IV solutions containing sodium bicarbonate help alkalinize urine, increasing uric acid solubility and, therefore, decreasing precipitation in the renal tubules (Kaplow & Hardin, 2007). Serial electrolyte monitoring is essential once treatment has begun. Electrolyte monitoring should begin prior to treatment initiation and then every 6–12 hours for early TLS identification (Cantril & Haylock, 2004). Although symptoms of TLS may occur up to seven days after initial treatment, patients are at greatest risk during the first 6–48 hours (Gucalp & Dutcher, 2006).

Treatment Measures

Depending on the severity of the electrolyte imbalance, medical management will begin and treatment options initiated (see Table 1). Hyperkalemia is managed with the use of sodium polystyrene sulfonate, diuretics, IV glucose and insulin infusions, IV calcium gluconate, or dialysis (McCance & Heuther, 2006). Hyperphosphatemia and hypocalcemia can be treated with IV 10% calcium gluconate, oral phosphate binders (aluminum hydroxide), dietary restriction of phosphorus intake, or dialysis (McCance & Heuther). Management of hyperuricemia consists of aggressive hydration with D5 1/2 normal saline (3–6 l/m² per day), 50–100 mEq of sodium bicarbonate per liter for urinary alkalinization to keep the urine pH at 7–7.5, diuretics, allopurinol 200–400 mg/m² IV daily or 300–800 mg per day orally, or rasburicase 0.20mg/kg IV daily (Brant, 2002). Dialysis would be required if electrolyte imbalances continued and renal failure was imminent.

Nursing Management

Identifying and initiating prevention measures prior to the first course of treatment for high-risk patients will help avoid TLS. Continued monitoring for side effects related to TLS is essential. Maintenance of IV fluids, strict intake and output monitoring, daily weights, and continued assessment for fluid overload is required (Kaplow & Hardin, 2007). Nurses should be familiar with the signs and symptoms of hyperuricemia, hyper-

Table 1. Treatment Measures for Tumor Lysis Syndrome

ELECTROLYTE IMBALANCE	TREATMENT
Hyperkalemia	Administration of sodium polystyrene sulfonate, IV diuretics, IV glucose or insulin infusions, IV calcium gluconate, or dialysis (McCance & Heuther, 2006)
Hyperphosphatemia and hypocalcemia	Infusion of IV 10% calcium gluconate, oral phosphate binders such as aluminum hydroxide, dietary restriction of phosphorus intake, or dialysis (McCance & Heuther, 2006)
Hyperuricemia	Aggressive hydration with dopamine receptor-5 1/2 normal saline (3–6 l/m^2 per day), 50–100 mEq of sodium bicarbonate per liter for urinary alkalinization to keep urine pH at 7–7.5, IV diuretics, allopurinol 200–400 mg/m^2 IV daily or 300–800 mg per day orally, or rasburicase 0.20 mg/kg IV daily (Brant, 2002). If imbalance continues or renal failure is imminent, perform dialysis.

phosphatemia, hypocalcemia, and hyperkalemia. TLS should be reviewed with the patient and family prior to, during, and after treatment.

Case Study

P.C., a 58-year-old woman, was diagnosed with acute myeloid leukemia and began induction chemotherapy of cytarabine and daunorubicin. Her baseline bloodwork consisted of a white blood cell count of 155,000/mcl (85% blast cells), LDH of 98 U/L, creatinine of 0.9 mg/dl, potassium of 4.2 mEq/l, phosphorus of 3.7 mg/dl, calcium of 8.0 mg/dl, and uric acid of 4.5 mg/dl. P.C. was started on allopurinol 300 mg orally twice daily 24 hours prior to initiating her induction chemotherapy and received two doses. Repeated bloodwork was drawn 12 hours after chemotherapy began, and LDH increased to 110 U/L, creatinine to 1.2 mg/dl, potassium to 5.3 mEq/l, phosphorus to 4.0 mg/dl, uric acid to 6.5 mg/dl, and calcium dropped to 7.5 mg/dl. P.C.'s bloodwork significantly changed 24 hours after chemotherapy initiation. Her LDH was 550 U/L, creatinine 2.3 mg/dl, potassium 5.9 mEq/l, phosphorus 4.9 mg/dl, calcium 6.0 mg/dl, and uric acid 9.7 mg/dl. P.C. had become increasingly lethargic and hypotensive and electrocardiogram changes demonstrated tall T waves and a prolonged QT interval. P.C. complained of nausea and had become disoriented and confused. A significant decrease in urine output was noted after eight hours. The physician was notified immediately and vigorous hydration of dopamine receptor-5 1/2 normal saline with 50 mEq sodium bicarbonate, IV rasburicase (0.20 mg/kg IV), IV 10% calcium gluconate, IV glucose or insulin infusions, and IV diuretics to promote dieresis were ordered. A Foley catheter was placed and hematuria was present. The patient was transferred to the critical care unit for closer observation and the chemotherapy was placed on hold.

Serial bloodwork was ordered every four hours over the next three days. Uric acid levels decreased to 4.0 mg/dl and remained less than 7.0 mg/dl after day one of treatment for TLS. Other electrolyte imbalances resolved and renal function improved. Within five days, creatinine levels returned within normal range and induction chemotherapy was resumed.

Conclusion

TLS is an oncologic emergency in which nurses have the ability to be proactive through prevention and early intervention. As patient advocates, nurses must identify patients at greatest risk of developing TLS. Monitoring for signs and symptoms of renal insufficiency and electrolyte imbalances is essential for early identification, treatment, and management. Nurses must be competent in their ability to recognize high-risk patients and the signs and symptoms, treatment options, and management of TLS. Nurses are instrumental in preventing morbidity and mortality for patients at risk of or suffering from TLS.

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Spot on tumor lysis syndrome . . .

To learn more about how tumor lysis syndrome affects pediatric patients with non-Hodgkin lymphoma, visit www.cancer.org/docroot/cri/content/cri_2_2_4x_how_is_childhood_non-hodgkins_lymphoma_treated_9.asp.