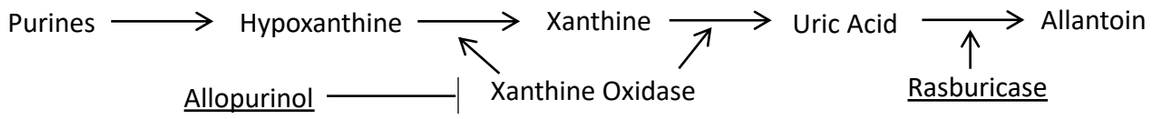
TUMOR LYSIS SYNDROME

Tumor lysis syndrome (TLS) occurs when the rapid breakdown of tumor cells results in the release of intracellular contents causing electrolyte disturbances and acute renal failure. It can occur spontaneously or after starting treatment. Incidence rates vary, but in-hospital mortality rates may be as high as 20%.

Pathophysiology and Risk Factors



* Allopurinol is a xanthine oxidase inhibitor that prevents the formation of uric acid. Rasburicase is recombinant xanthine oxidase that can break down existing uric acid and allow it to be safely excreted in the urine. See the metabolic pathway above.

Pathophysiology

Cellular breakdown results in the following:

- Release of K^+ and $PO4^-$ into the circulation which cannot be adequately cleared by the kidneys.
- Formation of calcium phosphate crystals, leading to hypocalcemia.
- Release of purines which are metabolized to uric acid via the pathway above.

Acute kidney injury (AKI) results from several mechanisms:

- Uric acid deposition in the renal tubules
- Precipitation of calcium phosphate crystals
- Changes in the renal vasculature.

Risk Factors

Tumor-Related:

- Hematologic malignancies
- Large tumor burden
- Rapid tumor proliferation
- Chemosensitive malignancy

Patient-Related:

- Pre-existing AKI or chronic kidney disease (CKD)
- Hypovolemia
- Electrolyte abnormalities or hyperuricemia at baseline
- Nephrotoxic medications

Risk Stratification by Disease

High-Risk (TLS Risk > 5%)

- Acute leukemia with WBC ≥ 100 x 10^9/L
- ALL with WBC ≤ 100 x 10^9/L and LDH ≥ 2x ULN
- DLBCL, T-cell lymphomas, and transformed lymphomas with elevated LDH and bulky disease
- Neuroblastoma, germ-cell tumors, small-cell lung cancer

Intermediate-Risk (TLS Risk 1-5%)

- AML with WBC 25-100 x 10^9/L
- ALL with WBC ≤ 100 x 10^9/L and LDH ≤ 2x ULN
- CLL being treated with targeted therapies or biologics
- DLBCL, T-cell lymphomas, and transformed lymphomas with normal LDH and bulky disease

Clinical Presentation and Diagnosis

Clinical Presentation

The clinical presentation can vary from generalized malaise, nausea, vomiting and muscle cramps to life-threatening symptoms including tetany, seizures, congestive heart failure, and cardiac arrhythmias.

Laboratory Diagnosis of TLS

Two or more of the following:

Uric acid : ≥ 476µmol/l or ↑ 25%

Potassium: ≥ 6.0mmol/l or ↑ 25%

Phosphate: ≥ 1.45mmol/l or ↑ 25%

Calcium: ≤ 1.75mmol/l or ↑ 25%

Clinical Diagnosis of TLS

Laboratory TLS plus any of the following;

Creatinine ≥ 1.5x ULN

New onset seizure

Cardiac arrhythmia or sudden death

Prevention and Treatment

Patients At Risk of TLS

Supportive Measures:

- All patients should receive IV fluid hydration to maintain urine output
- Urinary alkalinisation is not recommended
- Check bloodwork at least Q12H

Uric Acid-Lowering Therapy:

- Intermediate risk patients can be given allopurinol prophylaxis for up to 7 days → 300mg PO daily
- High risk patients should receive rasburicase prophylaxis → 4.5mg IV x 1 and reassess
- Allopurinol should be held in patients receiving rasburicase as it may impact rasburicase effectiveness

Patients with Established TLS

Supportive Measures:

- Target urine output of 100 ml/m^2/h with IV fluids
- Do not give furosemide unless volume overload present
- Dialysis indications = refractory electrolyte abnormalities or volume overload → Intermittent hemodialysis is the preferred modality for severe electrolyte disturbances
- Asymptomatic hypocalcaemia should not be treated
- Check bloodwork Q4-6H

Uric Acid-Lowering Therapy:

- Rasburicase 4.5mg IV x 1 should be given with duration and dosing adjustment dependent on clinical response