

# TUMOR LYSIS SYNDROME

## RISK FACTORS FOR TUMOR LYSIS SYNDROME

- Baseline hyperuricemia
- Bulky tumor burden (> 10 cm)
- Concentrated acidic urine pH
- Elevated serum LDH
- Elevated WBC (leukemia)
- First course chemotherapy in patients with bulky disease
- Hematological malignancies with a high proliferative index
- Preexisting renal dysfunction
- Volume depletion

## MALIGNANCIES THAT ARE COMMONLY ASSOCIATED WITH TUMOR LYSIS SYNDROME

- Acute leukemia
- Chronic leukemia
- Multiple myeloma
- Non-Hodgkin's lymphoma, high grade (Burkitt's lymphoma)
- Other non-Hodgkin's lymphomas

## SOLID TUMORS RARELY ASSOCIATED WITH TUMOR LYSIS SYNDROME

- Breast cancer
- Germ cell tumors
- Hepatocellular cancer
- Leiomyosarcoma
- Lung cancer (more common in SCLC)
- Medulloblastoma
- Metastatic colon cancer
- Metastatic melanoma
- Neuroblastoma
- Ovarian cancer
- Rhabdomyosarcoma
- Soft-tissue sarcoma
- Vulval cancer

## DRUG THERAPY ASSOCIATED WITH TUMOR LYSIS SYNDROME

- Alemtuzumab
- Rituximab

NOTE: In patients with a high tumor burden, any agent – including benign agents such as steroids may cause Tumor Lysis Syndrome.

Adapted from: Huen AO. Tumor Lysis Syndrome: Prevention and Management Strategies. *Oncology Special Edition* 2005;8:90 – 6.

# TUMOR LYSIS ALGORITHM

## Pretreatment of Tumor Lysis Patients

1. Baseline labs: Ca, Na, K, CO<sub>2</sub>, uric acid, PO<sub>4</sub>, LDH, SCr, Mg, BUN.
2. Identify individual patient risk factors
3. D/C medications that may contribute to metabolic abnormalities

### High-Risk

1. Daily labs to include basic metabolic panel (BMP), PO<sub>4</sub>, Ca, Mg, LDH, and uric acid (may need to obtain more frequent labs if clinically indicated)
2. Allopurinol 200 - 300mg/m<sup>2</sup>/day beginning 1 - 2 days pre chemotherapy. Adjust doses for renal dysfunction.
3. Hydration: D<sub>5</sub>W + 50 - 150 mEq NaHCO<sub>3</sub>/L at 200 - 250 mL/hour (2 - 3L/m<sup>2</sup>/day)
4. Loop diuretics as needed
5. Rasburicase - see criteria for use

### RASBURICASE CRITERIA FOR USE

Consider use in the following patient populations:

- High grade NHL, including Burkitt's lymphoma, ALL, CML in blast crisis, or high-risk neoplasms with bulky disease.
- LDH greater than 500 units/L.
- Serum uric acid greater than 8.5 mg/dL.
- WBC of 25 - 50 x 10<sup>9</sup>/L.
- Pre-existing renal dysfunction (CrCl < 30 mL/minute).
- Patients with comorbidities including CHF, uncontrolled diabetes, and pulmonary compromise unable to tolerate large fluid volumes.
- Requires Oncology Clinical Pharmacist Approval

### Low Risk

1. Routine Labs as needed
2. Observe for clinical signs and symptoms

Acute Tumor Lysis Syndrome

Transfer to special care unit;  
Treat specific metabolic complications

### Hyperuricemia

- ↑ IVFs and loop diuretic prn
- May need to ↑ allopurinol to 300-400mg/m<sup>2</sup>/d (max 800 mg PO QD)
- Consider acetazolamide for urinary alkalization if fluid overloaded

### Hyperkalemia

- Mild (< 6.5 mEq/L): Kayexelate
- Severe (> 6.5 mEq/L and/or EKG changes): Kayexelate; IV Ca gluconate, aggressive diuresis; dextrose and insulin; sodium bicarbonate

### Hyperphosphatemia

- Phosphate binders
- Restrict dietary phosphate intake to 800 - 1000 mg/day

### Hypocalcemia

- Reserve treatment for symptomatic patients
- IV calcium gluconate for symptomatic patients (i.e., tetany, reverse arrhythmias, etc).

**Rasburicase Orders:** Patient meets the criteria listed above (in middle of flow diagram). Rasburicase 3 mg IV x 1 dose, given 4 - 24 hours prior to initiation of chemotherapy. If after 8 hours, the uric acid is greater than 8.5 mg/dL and the patient meets the criteria listed above again, one repeat dose of rasburicase (3 mg) may be given. This process can continue until the uric acid is less than 8.5 mg/dL. Orders for aggressive hydration (where indicated) should be administered. Uric acid samples require special handling. Samples must be collected into pre-chilled tubes containing heparin anticoagulant and immediately immersed and maintained in an ice water bath. Plasma samples must be assayed within 4 hours of sample collection. Please call the lab and advise them of a pending sample.

# SUPERIOR VENA CAVA (SVC) SYNDROME

## SIGNS/SYMPTOMS OF SVC SYNDROME

- As obstruction of blood flow in SVC develops, venous collaterals form.
  - Collateral veins may arise from the azygos, internal mammary, lateral thoracic, paraspinous, and esophageal venous systems.
  - Rapidity of onset of symptoms depends on the rate at which complete obstruction of the SVC occurs in relation to the recruitment of venous collaterals.
  - Patients with malignant disease may develop signs and symptoms of SVC syndrome within weeks to months because rapidity of tumor growth doesn't allow adequate time for collateral flow to develop.
  - Dyspnea is most common symptom.
  - Patients may complain of facial swelling or head fullness that worsens with bending forward or lying down. Cough, arm edema, cyanosis, and facial plethora occur less often.
  - Most common findings on physical exam are venous distension in the neck and chest wall and facial edema.

## ETIOLOGY OF SVC SYNDROME

- Malignancy accounts for 78 - 85% of SVC syndrome.
  - Nonmalignant conditions account for 15 - 22% (infection and thrombosis).
  - Lung cancer is the most common malignancy associated with SVC syndrome, followed by lymphoma.
  - ~20% of patients with small cell lung cancer will develop SVC syndrome.
  - ~2 - 4% of patients with bronchogenic neoplasms.
  - ~2 - 4% of patients with lymphoma, almost always NHL.

## DIAGNOSIS OF SVC SYNDROME

### Radiographic Studies:

- Chest CT is the preferred imaging modality.
- Contrast-enhanced CT defines the level and extent of venous blockage, maps collateral pathways of venous drainage, and may allow identification of the underlying cause of venous obstruction.
- Bilateral upper extremity venography is superior to CT for defining the site and extent of obstruction and for visualizing collateral pathways, although it doesn't identify the cause of the obstruction unless thrombosis is the sole cause.
- Helical CT with bilateral upper extremity contrast injection appears to combine the diagnostic benefit of CT with the same degree of enhanced vascular detail as digital venography.
- MRI may be useful for patients allergic to contrast dye or in whom venous access cannot be obtained for contrast-enhanced studies.

### Histologic:

- A histologic diagnosis is necessary in order to determine appropriate therapy for the patient with SVC syndrome.

## TREATMENT AND PROGNOSIS

- Treatment is directed at the underlying disease.
- SVC syndrome due to malignant disease has historically been considered a potentially life-threatening medical emergency requiring immediate radiation therapy.
  - This approach is not appropriate for most patients.
    - As the obstruction often develops over weeks prior to clinical presentation, deferring therapy until a full diagnostic workup can be completed usually poses no hazard for most patients.
    - Radiation prior to biopsy may obscure the histologic diagnosis.
    - Exception: patients presenting with stridor, indicative of central airway obstruction or severe laryngeal edema, representing a true medical emergency.
    - Tumors with good prognosis: *NHL*, *germ cell tumors*, and limited-stage *small cell lung cancer* are responsive to chemotherapy +/- radiation.
    - *Non-small cell lung cancer*: SVC obstruction is a strong predictor of poor prognosis.
    - Median survival may be as low as 5 months.
    - Therapy often directed at palliation of symptoms rather than long-term remission.
      - Endovascular stents – may be appropriate for patients where chemotherapy/radiation therapy may not be indicated/effective.
      - Improvement usually occurs within 48 hours of placement.
      - Morbidity following stent insertion is greater if thrombolytics are administered.
- Nonmalignant causes of SVC syndrome:
  - Mediastinal fibrosis: Patients usually develop adequate collateral venous flow, as obstruction is usually slowly progressive.
    - Endovascular stents may be appropriate for patients with rapid onset of symptoms.
    - Benign SVC syndrome – endovascular stents have been successful.
    - Bypass surgery with spiral saphenous vein grafts has also been successful.
    - Catheter-related SVC obstruction – generally due to thrombosis.
    - Thrombolytic therapy has been successful when the clot is 5 days old or less.
    - IV heparin may reduce the risk of progression.
    - Subsequent oral anticoagulant therapy may reduce the risk of thrombosis occurrence or recurrence.

### REFERENCES:

1. Escalante CP, Manzullo E, Weiss M, and Bonin SR. Oncologic emergencies and paraneoplastic syndromes. In: Pazdur R et al, eds. Cancer Management: A Multidisciplinary Approach. 9<sup>th</sup> ed. 2005. CMP Media LLC, Lawrence, KS. pp: 979–1001.
2. [Kvale P, Simoff M, Prakash UBS. Lung Cancer. Palliative Care. \*Chest\* 2003;123\(1 suppl\):284S–311S.](#)
3. [Markman M. Diagnosis and management of superior vena cava syndrome. \*Cleve Clin J Med\* 1999;66:59.](#)
4. [Rowell NP and Gleeson FV. Steroids, radiotherapy, chemotherapy, and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. \*Clin Oncol \(R Coll Radiol\)\* 2002;14:338 – 51.](#)

# SPINAL CORD COMPRESSION

- The strongest prognostic factor for overall survival and ability to ambulate after treatment is pretreatment neurological status, and specifically, motor function.
- Delay in diagnosis and referral can lead to neurological decline.

## CLINICAL SYMPTOMS OF SPINAL CORD COMPRESSION

- Common symptoms include: back pain, motor weakness, sensory changes, bladder dysfunction.
- Back pain is not predictive of SCC.

## RISK FACTORS PREDICTIVE FOR SPINAL CORD COMPRESSION

- Inability to walk;
- Decreased deep tendon reflexes;
- Compression fractures on spine radiographs;
- Presence of bone metastases;
- Bone metastases diagnosed more than 1 year earlier;
- Age less than 60 years.

In a review by [Talcott et al \(Support Care Cancer 1999;7:31–8\)](#), patients with none of these six factors had a 4% risk of SCC compared with a 87% risk in patients with all six factors.

## MALIGNANCIES COMMONLY ASSOCIATED WITH SPINAL CORD COMPRESSION

Breast cancer, lung cancer, and prostate cancer account for approximately 60% of all patients presenting with SCC due to malignancy.

## DIAGNOSIS OF SPINAL CORD COMPRESSION

Whole-spine MRI is the preferred imaging technique for diagnosing SCC.

There are some questions about neurological decline following myelography, although this is not consistently reported.

## CORTICOSTEROIDS WITH SPINAL CORD COMPRESSION

- Some controversy exists regarding the optimal dose of dexamethasone.
- Doses range from 4 - 100 mg bolus, followed by 16 - 96 mg/day in divided doses (q6hr) and tapered over several days.
- High-dose (HD) dexamethasone may be an effective adjunct to radiation in improving post-treatment ambulation but is associated with serious toxicity.
  - At 1 week, 25% of pts treated with HD (100 mg) dexamethasone showed improved neurologic status (more than 1 grade difference in a 5 point score) compared to 8% of pts treated with MD (10 mg) dexamethasone (difference not statistically different).
  - HD dexamethasone associated with high incidence of adverse effects (including psychoses, gastric ulcers requiring surgery, ulcers with hemorrhage, rectal bleeding, GI perforations).
- More high-quality studies are needed to establish the benefits and risks of high-dose vs. moderate-dose dexamethasone.
- Patients who are ambulatory do not need corticosteroids, but should be educated about the symptoms of SCC.

## RADIATION IN THE MANAGEMENT OF SPINAL CORD COMPRESSION

Presence of bony compression is a negative predictive factor for achieving ambulation after RT.

Patients with bony compression, especially those who have mild to moderate paraparesis, who are treated with RT are less likely to recover ambulation compared to paretic patients without bony compression.

For patients without bony compression treated with RT, patients who are ambulatory, ambulatory with assistance, paraparetic, or paraplegic have ambulatory rates of 100%, 94%, 60%, and 11% respectively.

Compared to 92%, 65%, 43%, and 14%, respectively, of patients where bony compression is not excluded who retain or regain ambulation after RT.

RT for patients with subclinical cord compression may preserve neurologic function.

There does not appear to be any clearly superior RT dose/schedule. Doses used include 30 Gy in 10 fractions, 37.5 Gy in 15 fractions, 40 Gy in 20 fractions, 28 Gy in 7 fractions, and split dose of 15 Gy in 3 fractions then 15 Gy in 5 fractions.

Patients who recompress in-field after RT may be reconsidered for irradiation, especially if it has been more than 6 weeks since the completion of the last course of RT.

## SURGERY IN THE MANAGEMENT OF SPINAL CORD COMPRESSION

- Spinal instability is a relative indication for surgery.
- In patients with single site of compression, patients undergoing surgery plus RT may be more likely to retain or maintain ambulatory status longer than patients undergoing RT alone.
- Surgery is associated with significant morbidity:
  - 0 - 13% 30-day postoperative mortality rates;
  - 0 - 54% postoperative complication rates;
  - Overall complication rates are higher for vertebral body resection (10 - 54%) vs. laminectomy (0 - 10%);
  - Surgery should be considered for patients who deteriorate neurologically or who recompress after RT.

Reference: [Loblaw DA et al. Systematic Review of the Diagnosis and Management of Malignant Extradural Spinal Cord Compression: The Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. \*J Clin Oncol\* 2005;23:2028 - 37.](#)