Oncology Emergencies

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Objectives:

- Recognize and Initiate Early Treatment for Onc Emergencies:
  - Neutropenic Fever
  - TLS
  - Hypercalcemia
  - SVC Syndrome
  - Cord Compression

Neutropenic Fever

Definition:

One time oral temperature of >38.3 (100.9 F) or a sustained temperature of >38 (100.4) for greater than one hour in a patient who has an ANC of 0.5 or less, or an ANC expected to decrease to 0.5 within 48 hours.

Neutropenic Fever

Who is at Risk:

Solid Tumor patients can develop neutropenia approximately one week after cytotoxic chemotherapy, and neutropenia can last less than 7 days (5-30% of these patients will have febrile neutropenia)

Heme malignancy patients/Hematopoeitic Stem Cell Patients will have prolonged neutropenia that can last 14 days at more (80% of these patients will have febrile neutropenia)

Neutropenic Fever

Neutrophils are essential for attacking bacteria and fungal hyphae

Cytotoxic chemotherapy causes cell damage to GI tract

Neutropenic Fever

Evaluation:

Obtain blood cultures (one from arm, one set from central catheter)

Urine culture

Respiratory viral culture/COVID test

Detailed History and Physical examination:

- chemo regimen, underlying disease, co morbidities
- current antibiotics, prior infections
- sick contacts
- examine the skin, mouth, catheter site, lungs/sinuses, abdomen, peri-rectal area
- Imaging (symptom directed)

Neutropenic Fever

Risk Assessment:

MASCC Score:

Low risk- 21 or greater, can consider outpatient management

Heme Malignancy/Hematopoietic Stem Cell patients: admit

Neutropenic Fever

Scores 21 or greater, low risk of complications

MASCC item	Interpretation (points)
Age	Below 60 (2) 60 or above (0)
At onset of fever	Outpatient (3) Inpatient (0)
Symptoms	None or Mild (5) Moderate (3) Severe or Moribund (0)
Blood Pressure	Systolic BP >90 mmHg (5) Systolic BP ≤90 mmHg (0)
Active COPD	Active chronic bronchitis, emphysema, decrease in forced expiratory volumes, and need for oxygen and corticosteroids therapy with or without bronchodilators. If COPD absent 4 points, if present 0 points.
Solid tumor	Absent (0) Present (2)
Previous fungal infection in patient with a hematologic malignancy	Absent (0) Present (2)
Dehydration requiring parental fluids	Absent (4) Present (0)

Neutropenic Fever

Treatment

Immediate (within one hour of presentation) broad spectrum antibiotics with coverage against pseudomonas

Admit for further treatment if high risk. Inpatient team will manage escalation/de-escalation antibiotics based on response to therapy, culture results

If low risk and remains outpatient:

Daily evaluation

Can continue IV antibiotics or use oral antibiotics (Levofloxacin, augmentin with Cipro/levo/moxifloxacin).

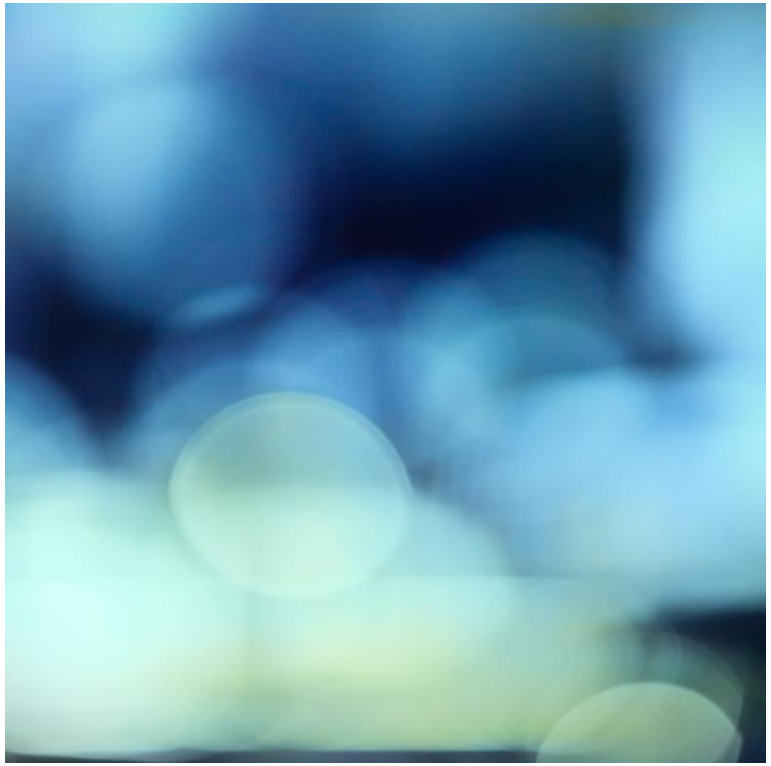
Tumor Lysis Syndrome

Definition:

Intracellular release of material in lysing cells that can lead to hyperuricemia, hyperkalemia, hyperphosphatemia

Acute tumor lysis syndrome- formation of emboli as a result of nuclear and cytoplasmic debris that results in mechanical obstruction of capillary beds

Spontaneous tumor lysis- cells are rapidly destroyed and lyse spontaneously without chemotherapy



Tumor Lysis Syndrome

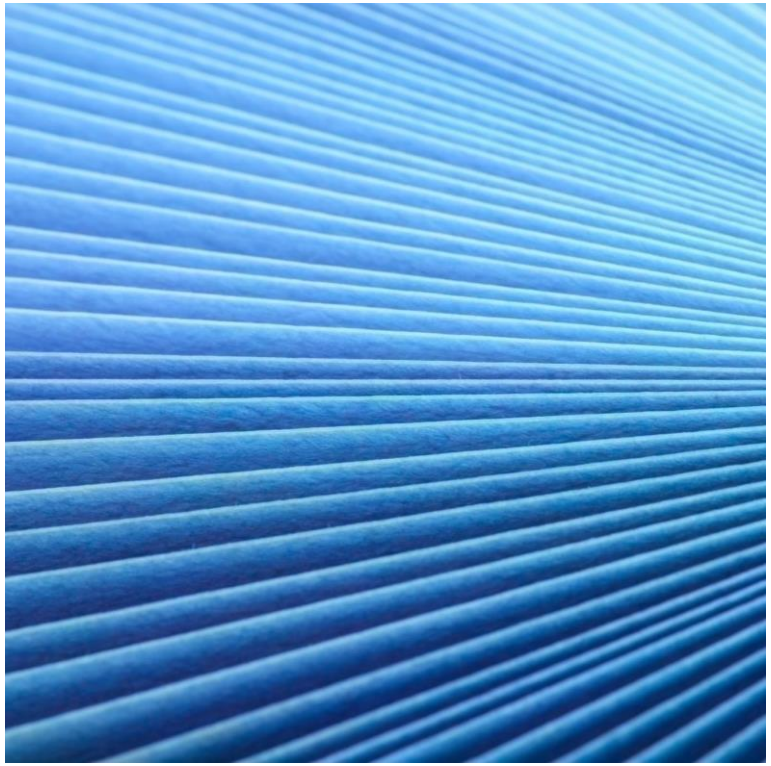
Who is at risk:

Hematologic Malignancies, especially with proliferative type disease (high grade lymphomas, leukemias), bulky disease, highly sensitive to cytotoxic chemotherapy, large areas of tumor necrosis

CART cell therapy: cytokine release syndrome (CRS) can lead to TLS

Tumor Lysis Syndrome

- Cell destruction leads to increased hyperuricemia, hyperkalemia, hyperphosphatemia, secondary hypocalcemia, acute kidney injury
- Arrythmias from elevated potassium, low calcium
- Renal Failure from elevated uric acid, elevated phosphate
- The electrolyte imbalances can lead to multiple organ dysfunction;
- Cardiac arrest, QTc prolongation, muscle tetany, CNS toxicity with seizures, death



Tumor Lysis Syndrome

Two or more criteria that occur 3 days prior to or within 7 days following chemotherapy:

- Serum uric acid level >= 8 mg/dl or a 25% increase from baseline
- Serum potassium level >= 6 mmol/L, or a 25% increase from baseline
- Serum phosphate level >=6.5 mg/dL in children or >=4.5 mg/dL in adults, or 25% increase baseline
- Serum calcium level <7 mg/dL or a 25% decrease from baseline

Or

- Two of the above and serum creatinine >= 1.5 x ULN, or the development of cardiac arrythmia or sudden death, or seizures

Tumor Lysis Syndrome

Prevention is the Goal!

- Assess risk for TLS before starting chemotherapy
- Allopurinol before starting chemotherapy
- Hydration
- TLS labs:
  - every 4-6 hours if high risk
  - every 8-12 if medium risk
  - daily if low risk

TABLE 2 Symptoms associated with low, intermediate, and high risk of tumor lysis syndrome[3,10]

Low Risk (<1% Chance)	Intermediate Risk (1%-5% Chance)	High Risk (>5% Chance)
Acute myeloid lymphoma (AML) with white blood cell (WBC) count <25 000/microL and serum LDH level <2X upper limit of normal (ULN)	Adult T-cell lymphoma/leukemia, diffuse large B-cell lymphoma, peripheral T-cell lymphoma, transformed lymphoma, or mantle cell lymphoma with an ULN serum LDH level above ULN that does not have a bulky disease	All Burkitt leukemia, stage III or IV Burkitt lymphoma or early stage Burkitt lymphoma with serum LDH level ≥2X ULN
Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with a WBC count ≤50 000/microL and not treated with fludarabine/rituximab or venetoclax	Stage III or IV childhood anaplastic large cell lymphoma with serum LDH level <2X ULN	ALL with WBC count ≥100 000 per microL and/or serum LDH level ≥2X ULN
Multiple myeloma and chronic myelogenous leukemia (CML)	Stage III or IV childhood diffuse large B-cell lymphoma with serum LDH level ≥2X ULN	AML with WBC count ≥100 000 per microL
Other types of adult non-Hodgkin lymphomas that do not meet the high risk or intermediate risk thresholds. Normal limit serum LDH level is required in this case.	Early stage Burkitt lymphoma with serum LDH level <2X ULN	Stage III or IV lymphoblastic lymphoma or early stage lymphoblastic lymphoma with serum LDH level ≥2X ULN
Other solid tumors in the body	Acute lymphoblastic leukemia (ALL) with WBC <100 000/microL and serum LDH level <2X ULN	CLL treated with venetoclax and lymph nodes ≥10 cm or lymph nodes ≥5 cm and absolute lymphocyte count ≥25 × 109/L, and an elevated level of serum uric
	AML with WBC 25 000 to 100 000/microL or AML with WBC < 25 000/microL and LDH ≥2X ULN	Adult T-cell lymphoma/leukemia, diffuse large B-cell lymphoma, peripheral T-cell lymphoma, transformed lymphoma, or mantle cell lymphoma with serum LDH level above the ULN and a bulky tumor mass
	Early stage lymphoblastic lymphoma with serum LDH level <2X ULN	Stage III or IV childhood diffuse large B-cell lymphoma with serum LDH level ≥2X ULN
	CLL/SLL treated with fludarabine, rituximab, or lenalidomide, or venetoclax with lymph nodes ≥5 cm or an absolute lymphocyte count ≥25 × 109/L, and/or those with a high WBC count (≥50 000/microL)	
	Rare bulky solid tumors that are highly sensitive to chemotherapy (such as neuroblastoma, germ cell cancer, and small cell lung cancer)	

Tumor Lysis Syndrome

Treatment:

- requires hospital admission

-Rasburicase, which degrades uric acid into allantoin (which is water soluble)

-Vigorous hydration

-Hemodialysis

Hypercalcemia

Definition:

Mild hypercalcemia: serum Ca 10.4-11.9 mg/dL

Moderate: serum Ca 12-13.9 mg/dL

Severe: serum Ca >= 14 mg/dL

Symptoms usually reflect level of serum calcium and rate of change

Hypercalcemia

Who is at Risk:

Can occur in up to 30% patients with malignancy but most common in lung cancer, multiple myeloma, renal cell carcinoma, breast, colorectal cancers.

Hypercalcemia

Humoral Cause: production of parathyroid hormone-related protein is most common cause (80% of cases, especially squamous cell carcinomas, colon cancers, renal cell, bladder, breast, endometrial, and ovarian cancers)

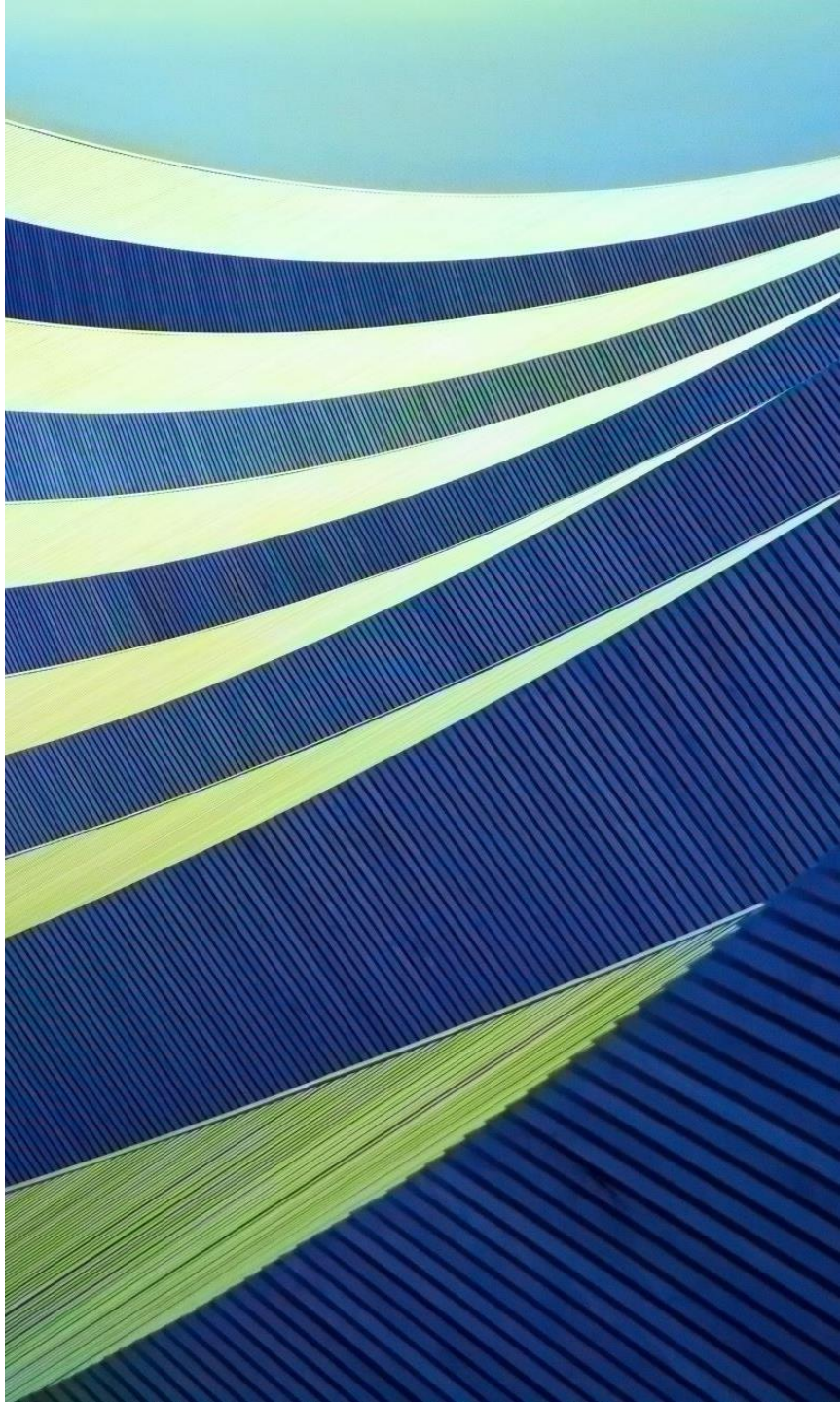
Bone Invasion with local osteolysis by cytokines (20% of cases, especially myeloma, metastatic breast cancer, less commonly in lymphoma)

Extrarenal production of Vitamin D (1% of cases, especially Hodgkin/NHL)

Rare Causes – immobilization, medications (including Vitamin D intoxication)

Hypercalcemia

- Evaluation:
- Calcium
- Albumin
- Creatinine
- Phosphorous
- PTH
- PTHrP
- 25 (OH)D level
- 1, 25 (OH)2D level



Hypercalcemia

Treatment

-treat the underlying malignancy

-determine severity of hypercalcemia, usually admit if severe

-review medications and stop/limit meds that contribute to calcium such as calcium, vitamin D, thiazide diuretics, lithium

Increase Calciuresis: Give 1-2 Liter NS as bolus, then 150-300 cc/hr until volume replete

Hypercalcemia

Reduce Bone Resorption

- IV bisphosphonates (within 48 hours) especially after hydration: zometa 4 mg IV x 1 (consider holding if Cr >4.5)
- Calcitonin 4-8 IU/kg subcut q 6 -12 hours
- Denosumab 60 mg subuct x 1 (may repeat in7 days if no response)

Hypercalcemia

Reduce Intestional Absorption of Calcium

- Glucocorticoids can be used, especially if hypcalcemia due to excess extra-renal (1,25) OH2 D especially seen with lymphoma and myeloma

Hydrocortisone 200-400 mg/day for 3-4 days, then can add prednisone 10-40 mg/day for 7-10 days

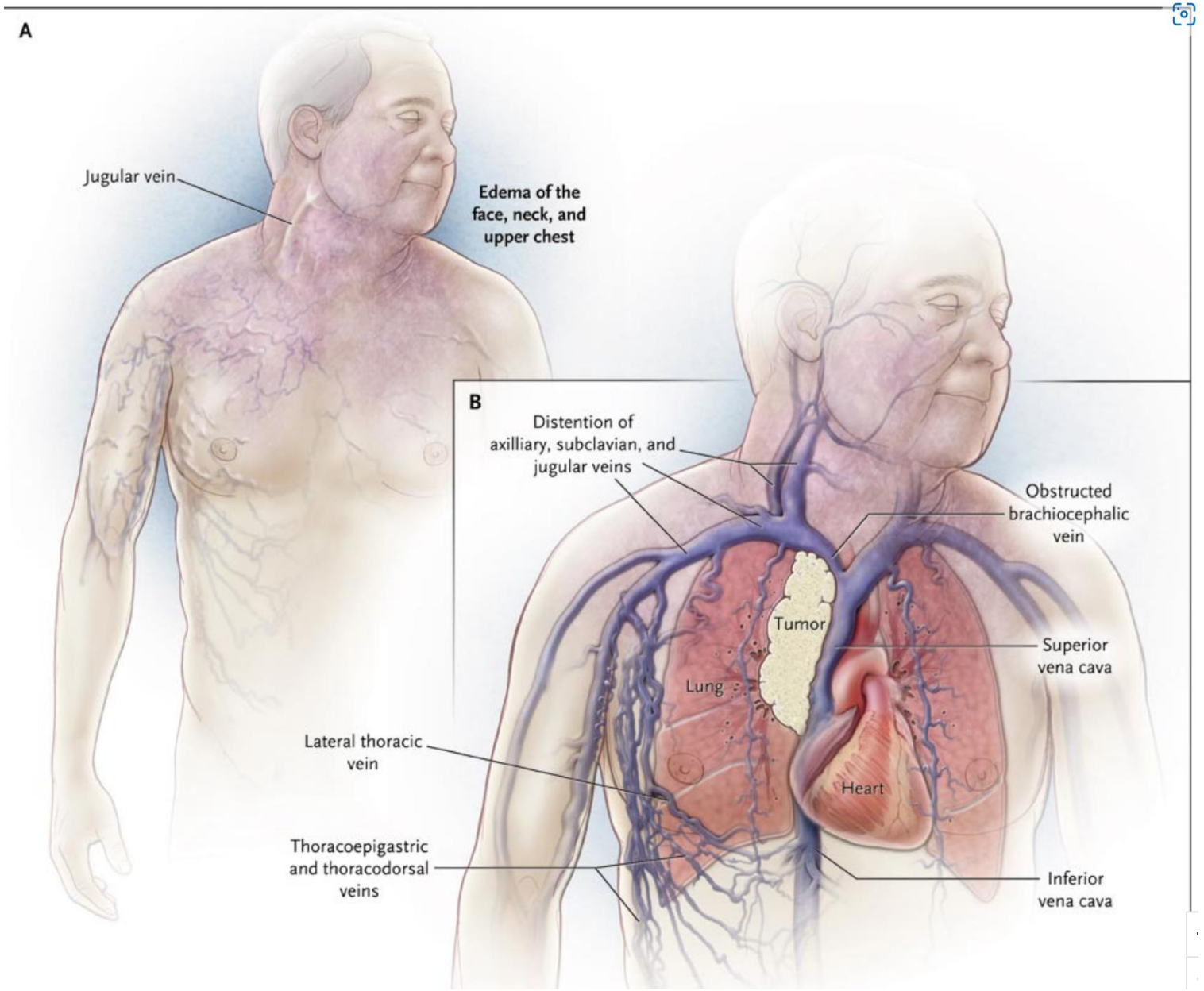
Superior Vena Cava Syndrome

Definition:

Compression of the superior vena cava where it enters the right atrium. Extrinsic compression from a mass, intrinsic compression from cancer or thrombus.

Most commonly from lung cancer, but any cancer can cause this (lymphoma, metastatic mediastinal tumors or lymph nodes) as well as catheters

Superior Vena Cava Syndrome



Superior Vena Cava Syndrome

Treatment:

Intravascular Stenting

Treatment of the Underlying Problem: chemo, radiation, steroids

Cord Compression

Definition:

Spinal Cord Compression caused by malignant tumor compressing the dural sac.

Can lead to progressive neurologic decline, paralysis

Cord Compression

Majority of patients have primary lung, prostate, breast cancer. But can also occur with myeloma, lymphoma

Results from the hematogenous spread of malignant cells to the vertebral body; the vertebral mass enlarges and compresses the adjacent epidural venous plexus, spinal artery, thecal sac, and spinal cord.

Myeloma can present with soft tissue extension from lytic bone lesions and lymphoma presents with sclerotic bone disease and soft tissue growth into the epidural space.

Metastatic bone lesions can cause compression fractures with bony fragments compromising the spinal cord.

Spinal Cord Compression

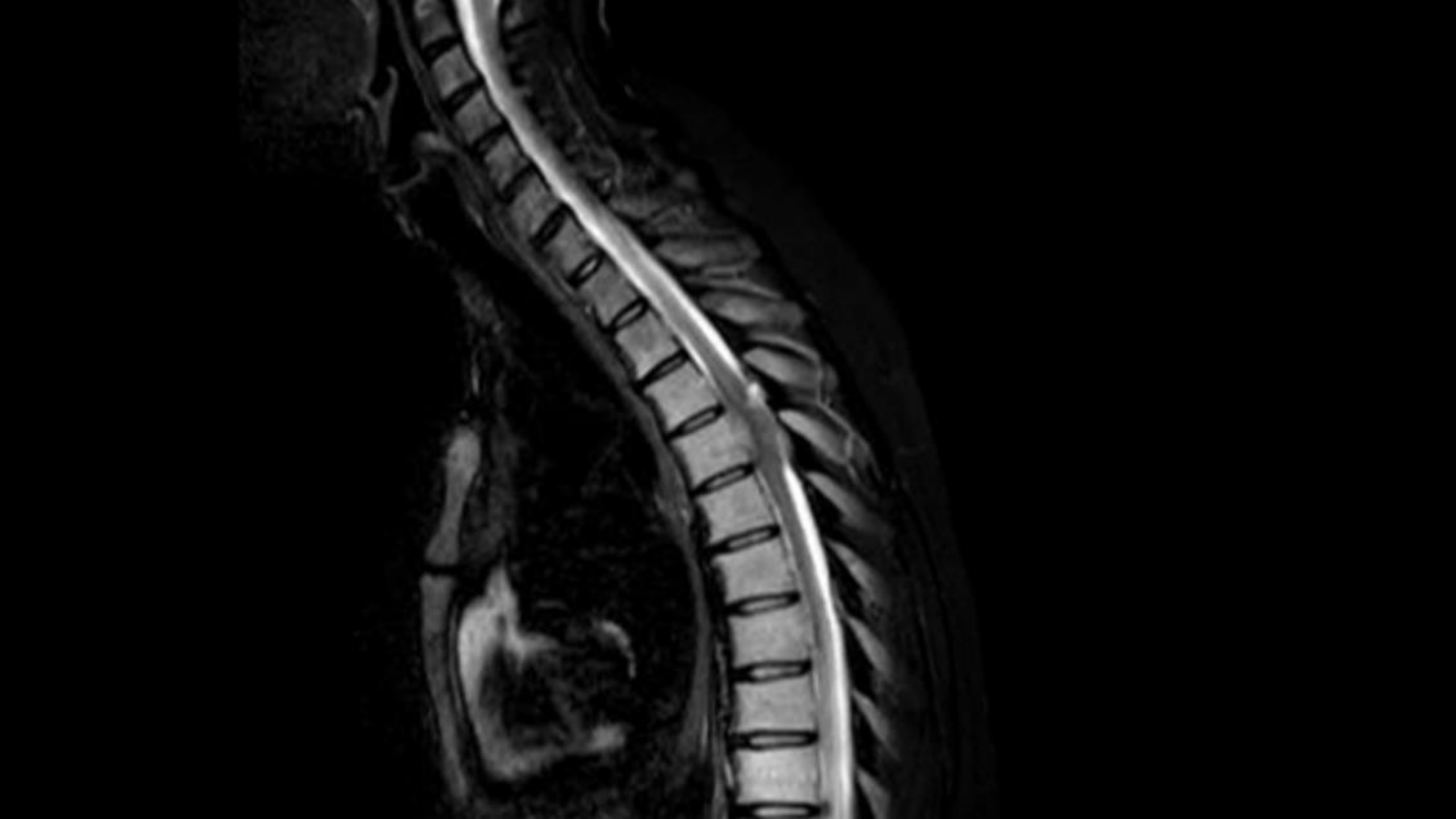
Evaluation:

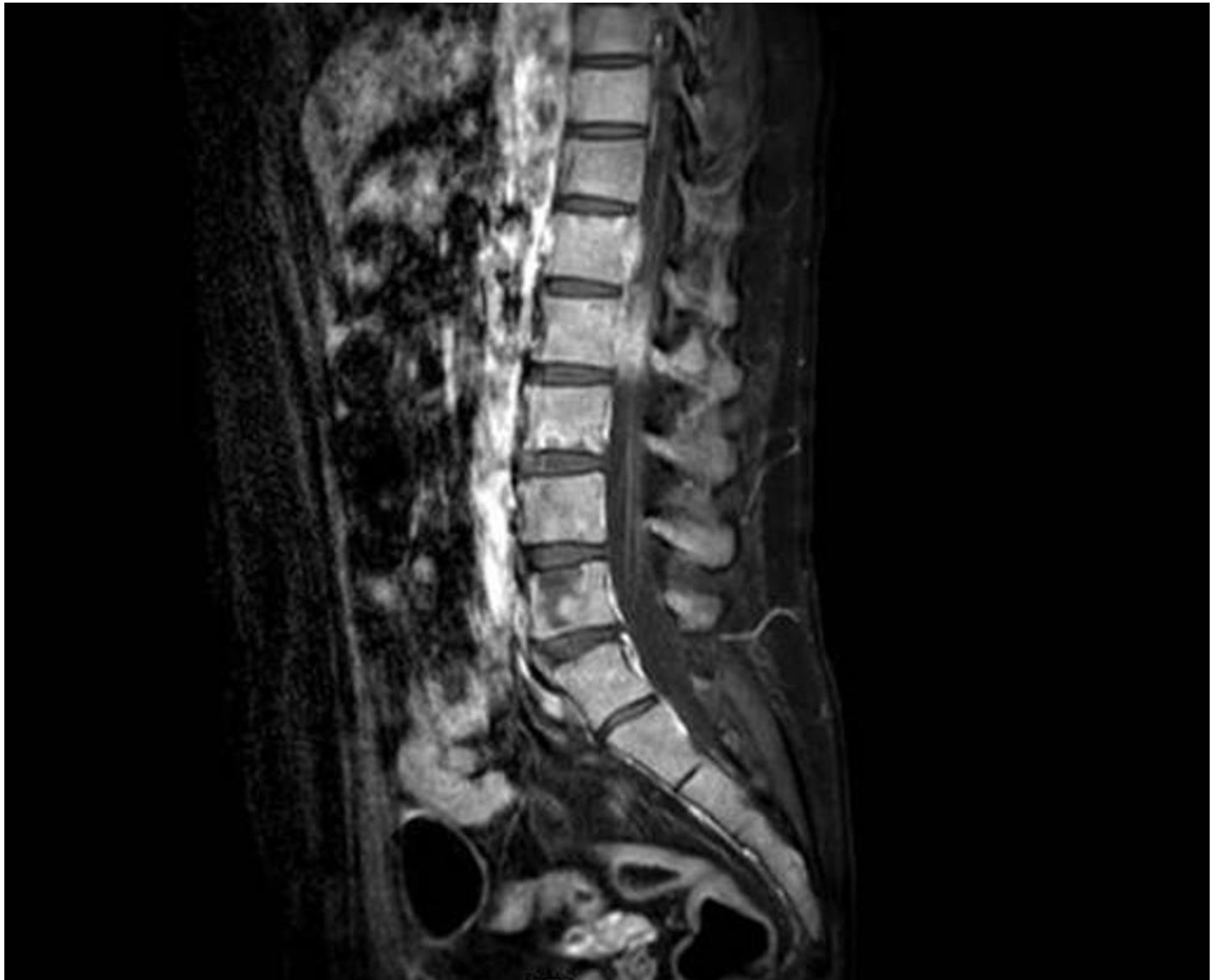
History of back pain (typically described as constant, aching, worse at night and early morning, exacerbated by coughing/valsalva, lying flat) motor weakness, sensory deficits, bowel or bladder dysfunction

MRI of entire spine

Spinal Cord Compression

- grade 1a=epidural impingement without deformation of thecal sac
- grade 1b= deformation of thecal sac, without spinal cord abutment
- grade 1c=deformation of thecal sac, with spinal cord abutment, no cord compression
- grade 2=spinal cord compression, with CSF visible around the cord
- grade 3=spinal cord compression, with no CSF visible around the cord





Spinal Cord Compression

Treatment:

Dexamethasone 10 mg IV x 1 then 4-6 mg IV every 6 hours, can taper over two weeks after completion of radiation therapy

Surgery/Radiation: Will need review by both services to determine if surgery is best intervention (takes into account spinal instability, neuro deficits, and prognosis). Radiation takes into account prior treatment, radiosensitivity, prognosis

Other Onc Emergencies

Hyperviscosity syndrome: Myeloma, Waldenstrom's macroglobulinemia, leukemia

Immune Checkpoint Inhibitor AEs: pneumonitis, gastritis, hypophysitis, DKA

Hyponatremia secondary to SIADH

Malignant Pericardial Effusion

Severe GI complications (SBO/obstipation/severe diarrhea)

Resources

Lawton, Andrew et al; Assessment and Management of Patients with Metastatic Spinal Cord Compression: A Multidisciplinary Review; J Clin Oncol 2018; 37:61-71

Rahman, Benjamin et al: Current Understanding of tumor lysis Syndrome; Hematological Oncology. 2019; 37: 537-547

Goldner, Whitney; Cancer-Related Hypercalcemia; J Oncol Pract; 2016; 12(5): 426-432

Wilson, Lynn D et al; Clinical Practice: Superior Vena Cava Syndrome with malignant causes; N Engl J Med. 2007 May 3; 356 (18): 1862-9

Zimmer, Andrea J et al; Optimal Management of Neutropenic Fever in Patients with Cancer; J Oncol Pract. 2019; 15: 19-24

Higdon, Mark L et al: Oncologic Emergenices: Recognition and Iniital Management; American Family Physician; 2018 June 1: 97 (11): 742-748.


Thank you for your time