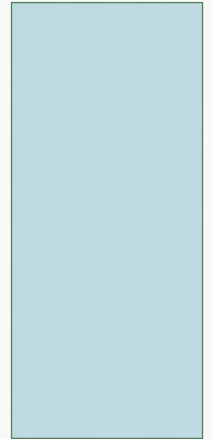


HEMATOLOGIC & ONCOLOGIC EMERGENCIES

MEG KELLEY MS, FNP-BC, OCN



COURSE OBJECTIVES

At the conclusion of this presentation, participants should be able to:

1. Define hematological and oncologic (heme-onc) emergencies
2. Recognize lab and clinical presentations of heme-onc emergencies
3. Review initial work up including basic labs and imaging for patients with concern of heme-onc emergencies



CBC Abnormalities

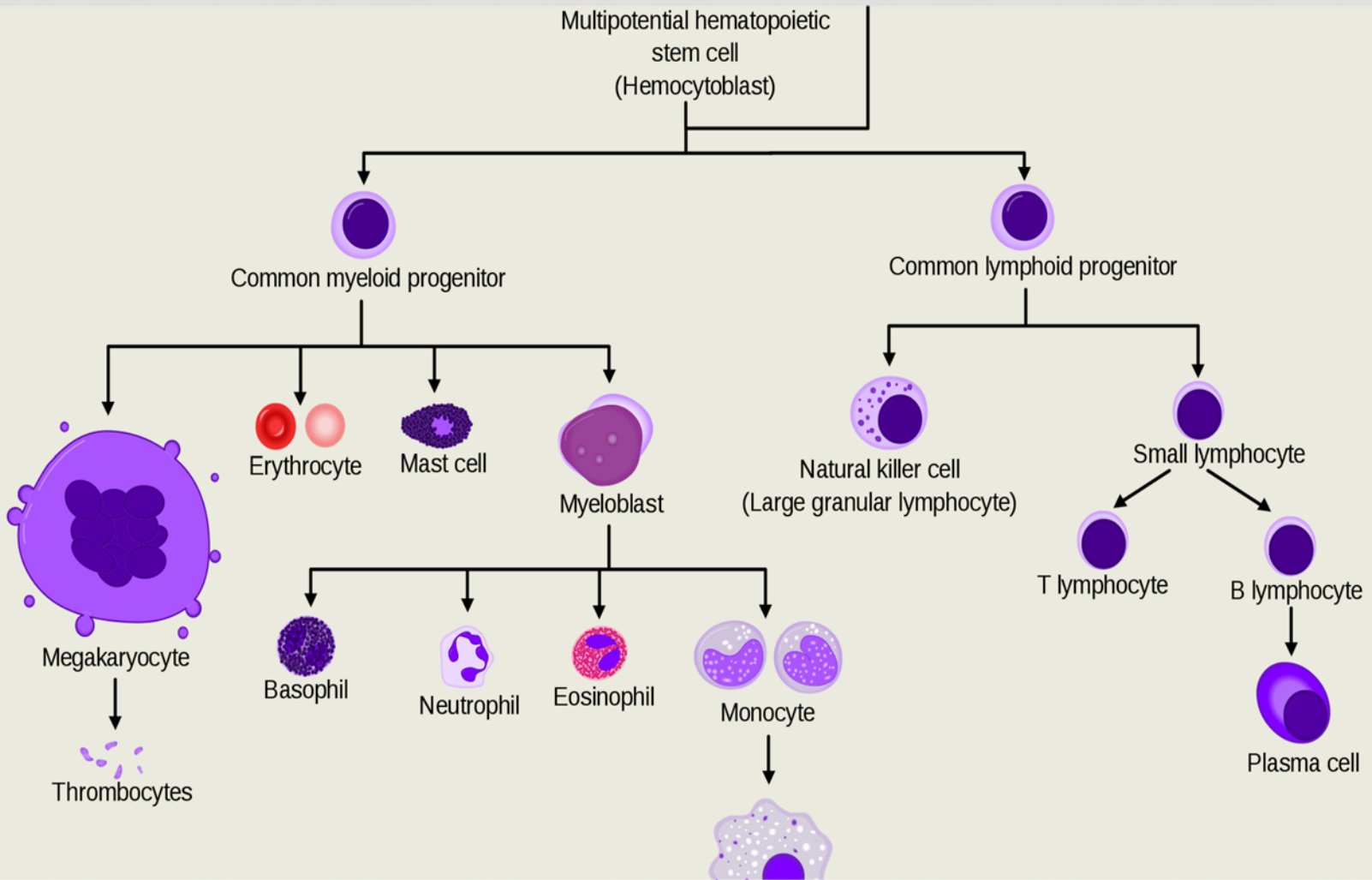
- Leukopenia/Leukocytosis
- Febrile neutropenia
- Hyperleukocytosis/Leukostasis
- Thrombocytopenia
- DIC, TTP/aHUS

Metabolic Abnormalities

- Tumor lysis syndrome
- Hypercalcemia

Compressive/ Obstructive Syndromes

- SVC syndrome
- Spinal cord compression



HEMATOPOIETIC STEM CELL DIFFERENTIATION

LEUKOPENIA/NEUTROPENIA

Definition: Low white blood cells

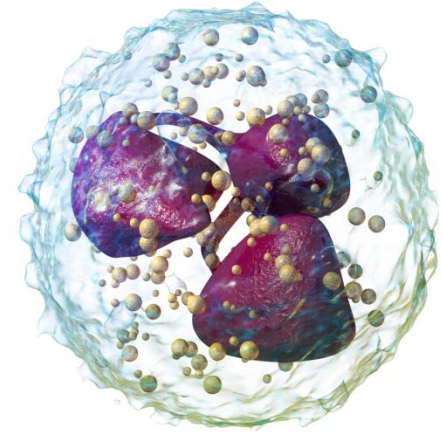
- Neutropenia is ANC < 1500 (1.0×10^9)
- Severe neutropenia is ANC < 500 (0.5×10^9)

Implications: Increased risk of infection

- Particularly risk of fungal or bacterial infections if prolonged neutropenia

Differentials:

- Inherited and acquired conditions
- Micronutrient deficiencies
- Autoimmune disorders, splenomegaly
- Drug-induced neutropenia
- Neutropenia with infectious diseases
 - Acute or chronic bacterial infections, viral or parasitic infections, i.e. HIV, hepatitis, sepsis



Neutrophil

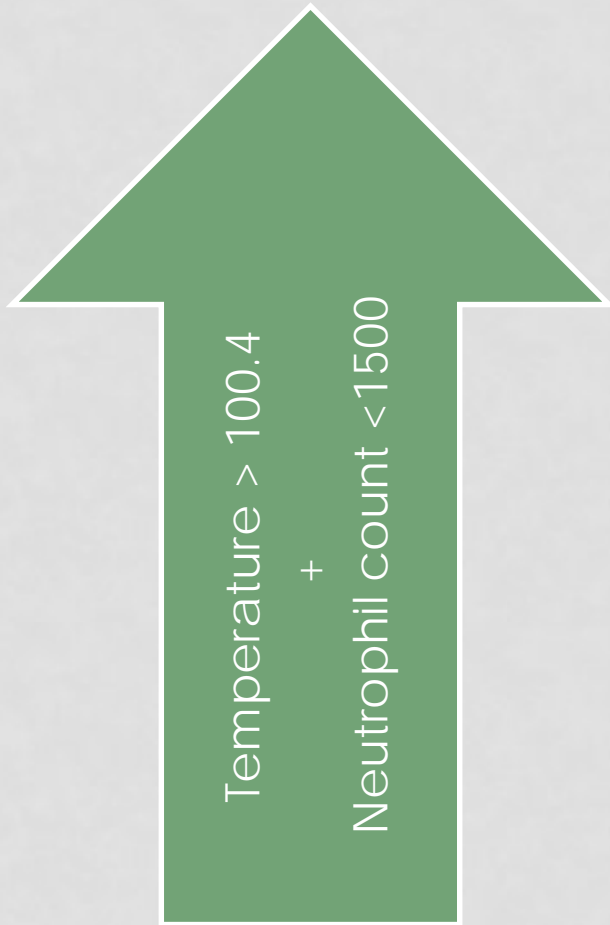
LEUKOPENIA/NEUTROPENIA WORK UP

Chronicity: Acute vs chronic?
Obtain baseline labs if possible

Patient history: Recent travel
Diet
ETOH use
GI/malabsorption issues
Chemical exposures
Recent infections
Review of medications

Labs: Peripheral smear
CBC **with differential**
Liver function test
Consider micronutrients, ANA, rheumatoid factor
Screening for infectious diseases
May need bone marrow evaluation (especially if other cell lines affected or no clinical explanation)

NEUTROPENIC FEVER



Prompt evaluation is imperative!

- Pan culture
- Start broad spectrum antibiotics
 - Infectious Disease recommends monotherapy with antipseudomonal beta-lactam agent
 - cefepime 2g IV q8h
 - meropenem 1g IV q8h
 - piperacillin-tazobactam 4.5g IV q6h
 - Vancomycin should be added if concern for catheter infection, skin/soft tissue infection, mucositis, pneumonia
- Management of sepsis if criteria met
- In patients with history of prolonged neutropenia, consider work up and coverage for fungal infections

HYPERLEUKOCYTOSIS/LEUKOSTASIS

Definition

- Leukocytosis: WBC count > 100,000

Implications

- WBC plugs microvascular and can cause respiratory or neurological distress
- Increased blood viscosity
 - Blasts more rigid and impede blood flow
- Typically seen with acute leukemia or CML in blast crisis
 - **not typically with chronic lymphocytic leukemia (CLL)

Clinical Presentation

- Typically related to respiratory or neurological compromise
 - Dyspnea, hypoxia
 - Visual changes, headache, dizziness, tinnitus, gait instability, confusion, somnolence
 - ~80% are febrile

HYPERLEUKOCYTOSIS WORK UP

Labs

- CBC with diff
- Peripheral smear
- Complete metabolic panel
- Uric acid
- Phosphorus
- Coags
- Peripheral blood flow cytometry

Physical exam

- Neurologic changes
- respiratory compromise
- Fever/hemodynamic instability

Clinical History

- Recent infections
- Exposures
- Family history

HYPERLEUKOCYTOSIS/LEUKOSTASIS

Management

- Stat heme-onc consult
- Stabilize patient and reduce WBC count
 - Hydrea
 - WBC depletion by apheresis
- Obtain diagnosis and start appropriate treatment ASAP
- Monitor for tumor lysis syndrome

CASE STUDY

- 46 year old healthy male. Presented to urgent care with malaise. Viral URI 2 weeks prior to presentation. Treated with antibiotics/steroids with no improvement
- Subjective: c/o nausea, vomiting, abdominal pain, + weight loss, night sweats, subjective fevers
- Physical exam: enlarged cervical nodes, + gum swelling, CV RRR, Resp: even, unlabored on room air with O2 sats in upper 90s, A&O, no neurologic deficits
- Work up:
 - CBC revealed WBC 136,000 with blasts – primarily monocytes, hgb 12.4, plt 379,000
 - CMP Normal electrolytes except phos low at 1.2, creatinine 1.19, uric acid 5.0. LFTs normal, Bilirubin 0.4
 - LDH markedly elevated at 1700

CASE STUDY CONTINUED

- Interventions:
 - Hydrea
 - No leukopheresis - rationale
 - Monitor TLS
 - Bone marrow biopsy
 - Confirmed AML with monocytic features
 - Ultimately started chemotherapy within 48 hours
- Spiked fever within 12 hours of admission
 - Management?

THROMBOCYTOPENIA

Definition: low platelet count

- mild (platelet count 100,000 to 150,000/microL)
- moderate (50,000 to 99,000/microL)
- severe (<50,000/microL)

Implications:

- Increased risk of bleeding (or thrombosis)

Differentials:

- Drug induced
- Thrombotic microangiopathies
- Heparin induced
- Disseminated intravascular coagulation
- Bone marrow disorders
- Increased consumption due to sepsis

Work up:

- CBC, peripheral smear, coags, eval liver/spleen

If anemia associated, check hemolysis labs (LDH, haptoglobin, retic)

THROMBOTIC MICROANGIOPATHY:
THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) / ATYPICAL
HEMOLYTIC UREMIC SYNDROME (AHUS)

Classic pentad:

Thrombocytopenia

Hemolytic anemia

Neurological symptoms

Renal involvement

Fever

TTP/AHUS

Classic presentation:

- *Hemolysis, *thrombocytopenia, fever, neurologic symptoms, renal dysfunction

TTP:

- Severe deficiency of ADAMTS13 (activity <10%) but treatment initiated before testing results (can take several days)

aHUS:

- Complement mediated: Typically degree of renal failure is more profound

Work up:

- CBC, peripheral smear, haptoglobin, retic count, LDH, fractionated bilirubin, direct coombs, coags, B12, CMP, ADAMTS 13, shiga toxin if diarrhea is present

Treatment:

- Mortality from untreated TTP is high (>90%) so if clinical suspicion is high, start urgent plasma exchange
- Mortality decreased to <20% with prompt PLEX

TTP/AHUS

- Don't wait on ADAMTS13 but must collect prior to apheresis!
 - If apheresis not available at your facility, transfer the patient urgently
- If aHUS, anti-complement mediated treatment available
- **Differentiating between the types of TMA can be sorted out later!



DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

Inappropriate, accelerated and systemic activation of coagulation cascade

- Causes thrombosis and hemorrhage
- Can be acute, life threatening or a chronic/subclinical process

Pathophysiology

- Sudden exposure of blood to procoagulants initiates coagulation cascade
- Platelets and clotting factors are consumed quickly so bleeding occurs
- Simultaneous thrombus formation in venous system can cause ischemia and organ failure

Causes of DIC

- Sepsis, malignancy, trauma, obstetrical complications and intravascular hemolysis (i.e., ABO incompatible transfusion)

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

Work up

- CBC, PT, PTT, fibrinogen, ddimer
- Trend serially (every 8-12 hours with acute DIC)

Clinical Manifestations

- Can have bleeding (oozing to severe bleeding), thromboembolism, renal or liver dysfunction, respiratory or neuro dysfunction
- Usually see petechiae, ecchymosis, oozing from wounds/lines or mucosa

Treatment

- **Identify and treat underlying cause**
- Support with blood products
- Monitor hemodynamic status
- Additional medications available for management

DIC



Prothrombin time
DDimer



Platelet count
Fibrinogen

PICTURES PETECHIAE, PURPURA



BLOOD PRODUCT REPLACEMENT GUIDE

Blood components: Indications and dosing in adults

Component (volume)	Contents	Indications and dose
Whole blood (1 unit = 500 mL)	RBCs, platelets, plasma	Rarely required. May be appropriate when massive bleeding requires transfusion of more than 5 to 7 units of RBCs (increasingly used in early trauma management).
RBCs in additive solution (1 unit = 350 mL)	RBCs	Anemia, bleeding. The increase in hemoglobin from 1 unit of RBCs will be approximately 1 g/dL; the increase in hematocrit will be approximately 3 percentage points.
FFP or other plasma product* (1 unit = 200 to 300 mL)	All soluble plasma proteins and clotting factors	Bleeding or expected bleeding (eg, emergency surgery) in individuals with deficiencies of multiple coagulation factors (eg, DIC, liver disease, massive transfusion, anticoagulation with warfarin or warfarin overdose if not corrected by vitamin K and/or PCC, depending on the clinical setting); therapeutic plasma exchange in TTP. FFP may be used to manage bleeding in individuals with isolated factor deficiencies (most often factor V) if a factor concentrate or recombinant factor is not available. In the rare event that FFP is used to replace a clotting factor, the dose is 10 to 20 mg/kg. This dose will raise the level of any factor, including fibrinogen, by close to 30%, which is typically sufficient for hemostasis.
Cryoprecipitate, also called "cryo" (1 unit = 10 to 20 mL)	Fibrinogen; factors VIII and XIII; VWF	Bleeding or expected bleeding with low fibrinogen: The increase in plasma fibrinogen from 1 unit of Cryoprecipitate per 10 kg body weight will be approximately 50 mg/dL. Bleeding or expected bleeding in individuals with deficiencies of factor XIII or factor VIII (hemophilia A) if a recombinant product or factor concentrate is unavailable. Bleeding or expected bleeding in individuals with VWD if DDAVP (desmopressin) is ineffective and recombinant VWF or a VWF concentrate is unavailable. Cryoprecipitate is generally provided in pools containing 5 units, and most patients receive one to two pools.
Platelets (derived from whole blood or apheresis) (1 unit of apheresis platelets or a 5 to 6 unit pool of platelets from whole blood = 200 to 300 mL)	Platelets	The platelet count increase from 5 to 6 units of whole blood-derived platelets or 1 unit of apheresis platelets will be approximately 30,000/microL in an average-sized adult.

Refer to UpToDate topics on these products and on specific conditions for details of use. Frozen blood products (FFP, Cryoprecipitate) take 10 to 30 minutes to thaw. It may take the same amount of time to perform an uncomplicated crossmatch.

Reference: UpToDate

<https://www.uptodate.com/contents/image?imageKey=HEME%2F53854&source=autocomplete&index=0~1&search=blood%20component>



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TUMOR LYSIS SYNDROME

Tumor lysis syndrome

- Massive cell lysis with release of intracellular contents into systemic circulation
- Most often occurs once cytotoxic treatment (i.e. chemotherapy)
- Typically seen with aggressive lymphoma/leukemias
- Increased risk with high proliferative rate, large tumor burden/bulky disease

Etiology

- Due to rapid breakdown and overwhelming release of intracellular content into blood from cell lysis

Work up

- CBC, CMP, phosphorus, uric acid, LDH, magnesium

Prevention/treatment

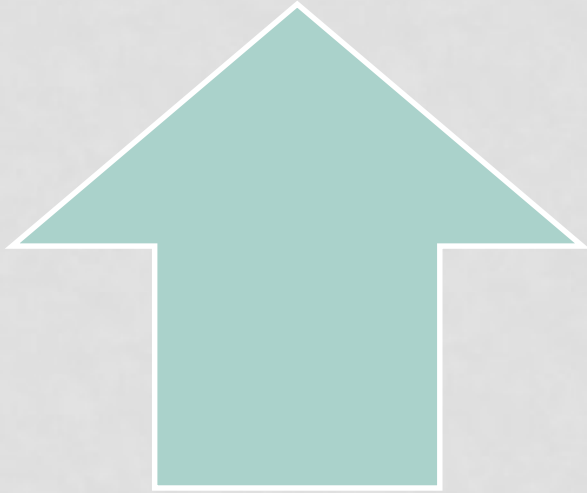
- Allopurinol
- Rasburicase
- Aggressive hydration
- Frequent lab monitoring

Complications

- Renal failure, arrhythmias, death



TUMOR LYSIS SYNDROME: LAB ABNORMALITIES



Hyperkalemia
Hyperuricemia
Hyperphosphatemia



Hypocalcemia

HYPERCALCEMIA

Elevated blood calcium levels

- Classic definition calcium > 10.5 but usually do not see symptoms until serum levels > 12

Serum calcium is bound to protein (esp albumin)

- If albumin level is low or high, must correct
 - $(4 - \text{serum albumin}) \times 0.8 + \text{serum calcium level}$

Etiology:

- Caused by pathologic destruction of bone from malignant cell activity
- Occasionally may be stimulated by parathyroid hormone (PTH) or prostaglandin

Types of cancer associated

- breast cancer (esp with bone mets), head and neck cancers, renal cancer, multiple myeloma, lymphoma, and lung (esp small cell) cancer
 - Often seen with bony mets but not always (10-15% do not have bony involvement)

HYPERCALCEMIA

Symptoms

- nausea, vomiting, constipation, anorexia, altered mental status, renal failure

Work up

- Serum calcium levels, albumin, phosphorus, ionized calcium

Treatment

- Aggressive hydration +/- diuresis (250-500ml/hr)
- Bisphosphonate therapy (can take 2-3 days to see impact)
- Calcitonin (for max 2-3 days)



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SUPERIOR VENA CAVA SYNDROME

Definition

- Obstruction of blood flow through the SVC

Etiology

- Can be caused by direct invasion of tumor into the SVC, or by external compression of the SVC by an adjacent pathologic process involving the right lung, lymph nodes, and other mediastinal structures, leading to stagnation of flow and thrombosis
- Most often caused by lung cancer but can be from lymphoma, mediastinal tumors or catheters

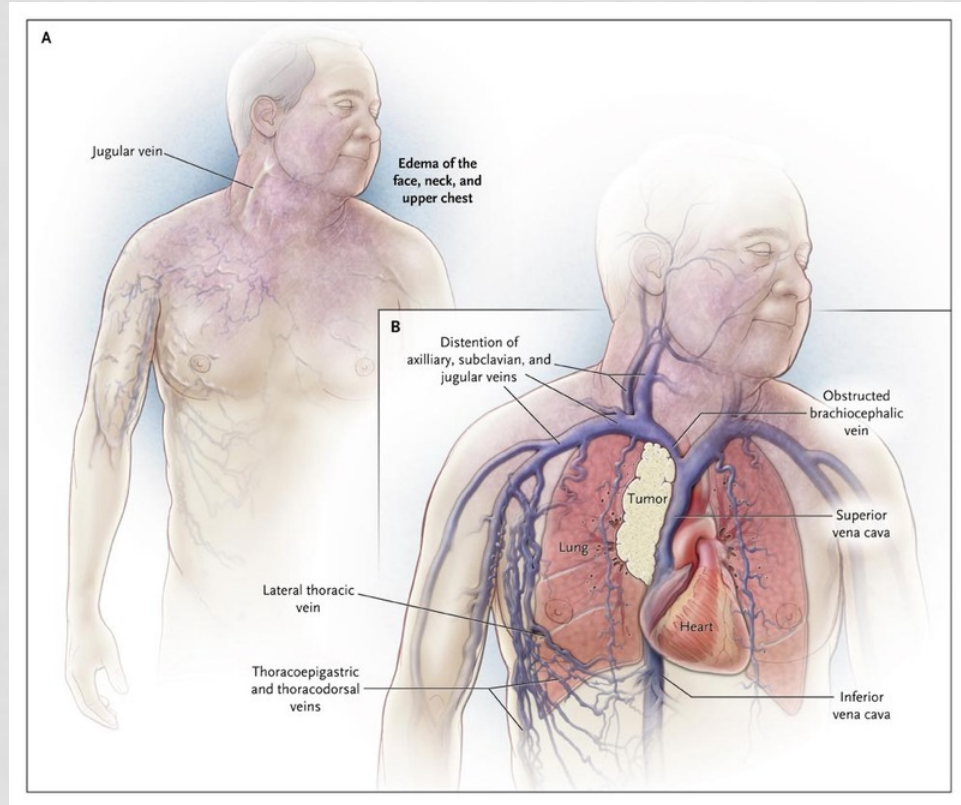
Symptoms:

- Swelling of neck, face, upper extremities, JVD and distention of superficial veins in chest wall
- Dyspnea, cough

Diagnostic work up:

- Xray, CT can confirm
- Treat underlying problem, i.e. cancer with chemotherapy or radiation
- Can utilize diuretics, steroids, elevating head of bed, thrombolytics (if clot present)

SUPERIOR VENA CAVA SYNDROME



<https://www.nejm.org/doi/full/10.1056/NEJMcp067190>

SPINAL CORD COMPRESSION

Definition

- External compression of spinal cord (thecal sac)

Implication

- Can cause permanent damage if not treated urgently (sometimes even if it is treated urgently)

- 70% involve thoracic spine
- Typically seen with renal, prostate, breast, lung cancers and multiple myeloma

Symptoms:

- **New back pain, pain with percussion of vertebral bodies**
- Later signs: loss of bladder/bowel control, paraplegia, loss of sensory function, cauda equina syndrome

Work up

- MRI to evaluate spinal column

Treatment

- Stat neurosurgery consult
- Stat radiation oncology consult (if nonsurgical)
- 10mg loading dose of dexamethasone followed by dexamethasone 4mg q 6 hours

SPINAL CORD COMPRESSION



QUESTIONS?



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