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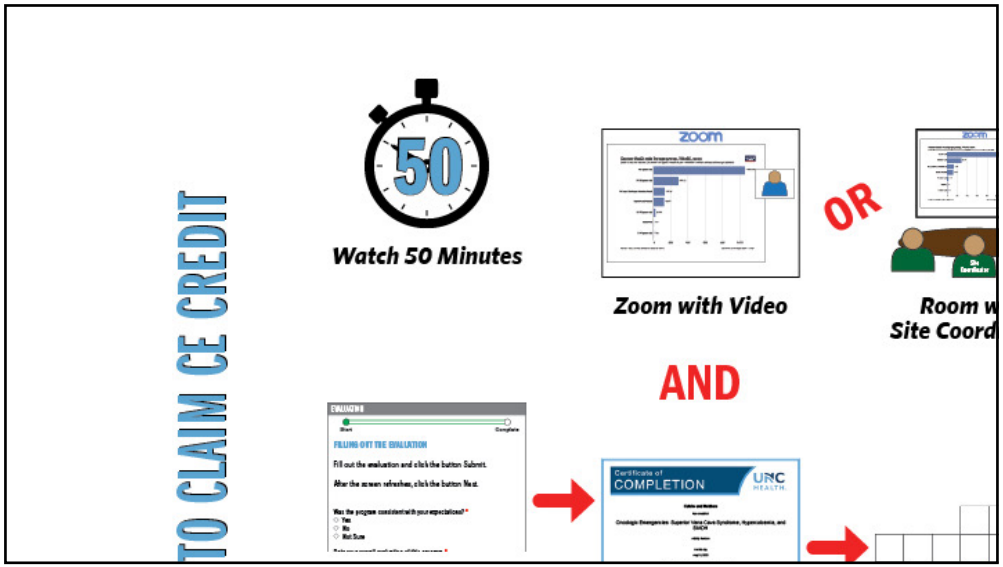
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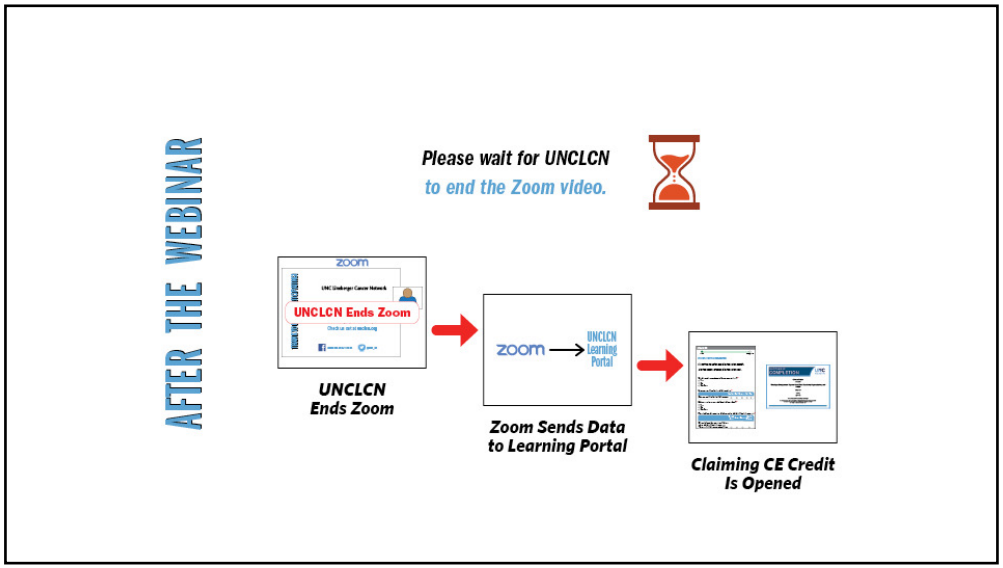
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Allison Phillips,
MPAP, MHPE, PA-C

Allison Phillips, MPAP, MHPE, PA-C, is a physician assistant working for the UNC Breast Cancer group with Dr. Lisa Carey.

She has over nine years of clinical experience and an interest and passion for public health and improving clinical education.

Prior to joining the UNC Oncology team, she worked as a provider in a local health department for nearly eight years, specializing in Women's and Children's health.

Allison is also adjunct faculty in the Physician Assistant Program at Campbell University.

She has a particular interest in providing equitable healthcare to patients from underserved communities and improving health literacy.

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An oncologic emergency is an acute health problem caused by the cancer or its treatment and requires immediate treatment.

(A) True 0%

(B) False 0%

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Oncologic Emergencies:
Hypercalcemia, SIADH, and Superior Vena Cava Syndrome

Allison Phillips, MPAP, MHPE, PA-C
Clinical Assistant Professor
UNC School of Medicine Physician Assistant Program

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Learning Objectives

1. Recognize the common presentation, causes, and management of superior vena cava syndrome.
2. Discuss the presentation, risk factors, and management of hypercalcemia in patients with cancer.
3. Review the presentation, causes, and management of SIADH as it relates to patients undergoing cancer treatment.

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All of the following are TRUE of oncologic emergencies EXCEPT:

Can be caused by structural, metabolic, or hematologic factors related to cancer or the cancer treatment 0%

Can be the presenting symptom in patients with previously undiagnosed malignancy 0%

Only present in patients with advanced stage cancer 0%

Important for all clinicians treating cancer patients to be aware of 0%

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What is an Oncologic Emergency?

- Any acute, potentially life-threatening event either directly or indirectly related to a patient's cancer or treatment of the cancer
- Can be the presenting symptom for an undiagnosed neoplasm
- Classified as metabolic, hematologic, structural, or treatment related

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Metabolic Oncologic Emergencies

- Tumor Lysis Syndrome
- Hypercalcemia of Malignancy
- Syndrome of Inappropriate Anti-diuretic Hormone (SIADH)

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Hematologic Oncologic Emergencies

- Febrile Neutropenia
- Hyperviscosity Syndrome

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Structural Oncologic Emergencies

- Malignant Spinal Cord Compression
- Superior Vena Cava Syndrome
- Malignant Pericardial Effusion

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Treatment Related Oncologic Emergencies

- Extravasation
- Immunotherapy
- Hypersensitivity Reactions

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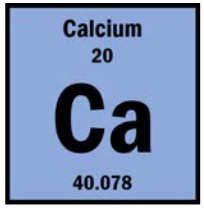
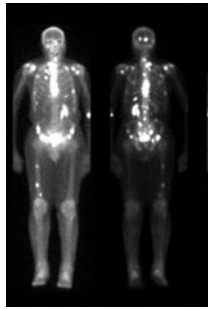
Hypercalcemia of Malignancy





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Case 1

LH is a 61-year-old female recently diagnosed with recurrent breast cancer with metastatic lesions in her pelvis and spine. She presents for routine follow up with her oncologist and reports that she has been feeling "awful" for the past week with severe stomach pain, constipation, frequent urination, and body aches "like I have the flu".

Vitals are stable and she is afebrile.

CBC: mild anemia (Hgb 11.1)

CMP: Sodium 141, Potassium 3.4, Calcium 12.0

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Hypercalcemia of Malignancy

- Defined as serum calcium > 10.5 mg per dL
- Occurs in 10-30% of patients with cancer
- Most common in breast cancer and myeloma but also seen with SCC of the head & neck, lungs, kidney, and cervix

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Causes of Hypercalcemia of Malignancy

- Excessive secretion of parathyroid hormone-related protein
- Release of osteoclasts from bone metastasis
- Excessive production of 1,25-dihydroxy Vitamin D (calcitriol)

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Excessive secretion of parathyroid hormone-related protein

- Accounts for 80% of all cases of hypercalcemia in cancer patients
- PTHrP enhances renal tubular reabsorption of calcium while also increasing urinary excretion of phosphorus
- Does NOT increase production of 1,25 Vitamin D, therefore does not increase intestinal absorption of calcium

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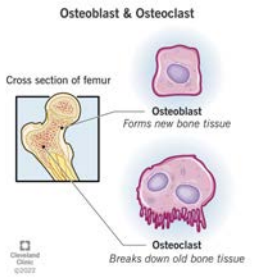
Osteolytic Hypercalcemia

- ~20% of all cases of hypercalcemia in cancer patients
- Associated with extensive bone metastasis/skeletal tumors
- Previously thought to be caused by destruction of the bone, but now believed to be related to release of cytokines which cause excessive osteoclast activation



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Excessive production of 1,25-dihydroxy Vitamin D (calcitriol)

- Less than 1% of all cases of malignant hypercalcemia
- Extrarenal production of 1, 25-dihydroxy Vitamin D
- Most common in Hodgkin's and Non-Hodgkin's Lymphoma

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Presentation of Hypercalcemia

- Painful bones
- Renal stones
- Abdominal groans
- Sitting on the throne (polyuria, constipation)
- & Psychiatric overtones.

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Correcting for Hypoalbuminemia

- Total serum calcium is ~ 40% albumin bound, which means serum calcium can be UNDER estimated in the patient with low albumin
- **Corrected Calcium mg/dL = 0.8 x (Normal Albumin (4.0)- Patient's Albumin)+ Serum Calcium**

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Additional Lab Work-Up

	Humoral Hypercalcemia	Osteolytic hypercalcemia	1,25(OH)D – mediated hypercalcemia
Calcium	↑	↑	↑
Phosphorus	↓	↑	↑
PTH	↓	↓	↓
25(OH)D	↔	↔	↔
1.25(OH)2D	↔	↔	↑
PTHrP	↑	↓	↓

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Treatment of Hypercalcemia of Malignancy

- **Treatment of the underlying malignancy is the primary goal**
- **Discontinue contributing medications**
  - *Vitamin D, Calcium, Lithium, Thiazide diuretics*

- **Patients are often hypovolemic**
  - 1 to 2 L of isotonic saline as an initial bolus; maintenance fluids of 150 to 300 mL/h for the next 2 to 3 days or until they are volume replete.

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Treatment of Hypercalcemia of Malignancy

- **Bisphosphonates=First Line Therapy**
  - *Should be given ASAP upon diagnosis (within 48 hours)*
  - *Zoledronic acid > pamidronate*
  - *Induce osteoclast apoptosis & prevent apoptosis of osteoblasts*
  - *Reduce osteoclastic bone resorption*
  - *Associated with nephrotoxicity to dose reduction may be warranted*
- **Denosumab**
  - *Reduces osteoclast activity and bone resorption*
  - *More effective than bisphosphonates in prevention of hypercalcemia of malignancy*
  - *Can also be used to treat if refractory to bisphosphonates*

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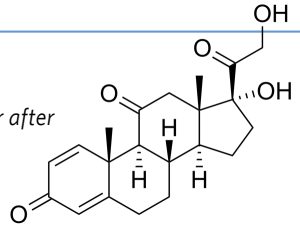
Treatment of Hypercalcemia of Malignancy



- **Calcitonin**
  - *More rapid lowering of calcium; tachyphylaxis can occur after 48 hours*
- **Glucocorticoids**
  - *Inhibit osteoclastic bone resorption by decreasing cytokines*
  - *Also have direct tumorolytic effects; can make calcitonin more effective*

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Prognosis of Hypercalcemia of Malignancy

- Even with treatment, approximately 50% of cancer patients presenting with hypercalcemia will die within 30 days
- Believed to be related to this most often occurring in advanced stage cancer

- DOI: 10.1200/JGO.2016.006890 *Journal of Global Oncology* 3 no. 6 (2017) 728-733. Published online March 15, 2017.

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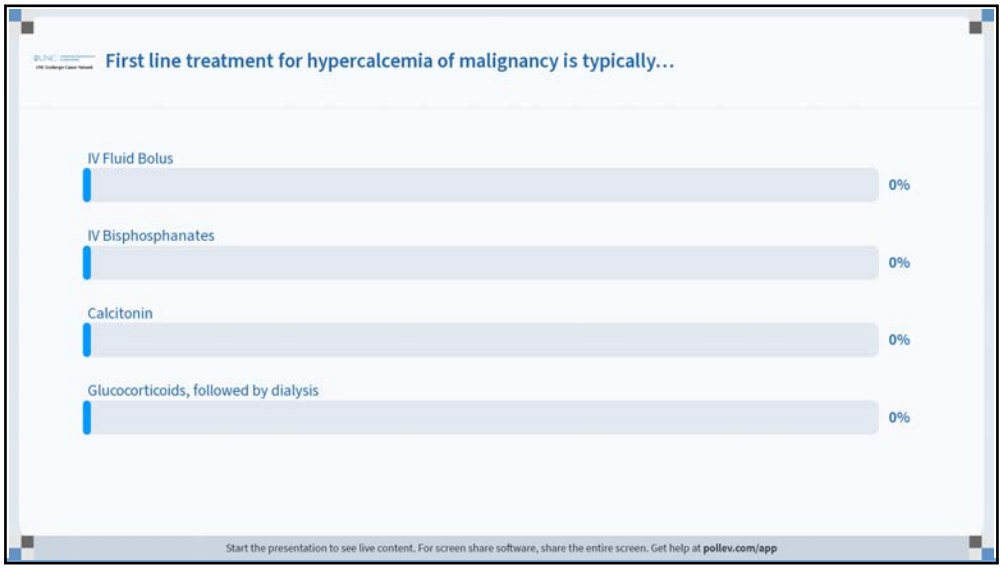

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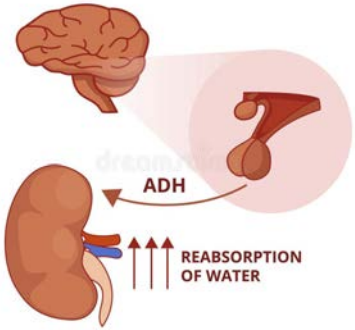
SIADH



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Case 2

MJ is a 75-year-old male who has been undergoing treatment for lung cancer for the past 6 months. He presents to the emergency room where his wife reports he has been groggy and complaining of nausea and a headache for the past 3 days. She brings him today because he appeared confused and could not remember her name or what day it was.

HR: 57 BP: 90/66

CMP: Sodium 118

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SIADH--Syndrome of Inappropriate Antidiuretic Hormone

- ADH is usually released by the pituitary gland in response to high sodium levels
- Neuroendocrine tumor cells can cause the body to secrete too much antidiuretic hormone, causing kidneys to retain fluid, leading to hyponatremia
- Certain cancer therapies, like platinum chemotherapy and methotrexate can also cause excessive ADH secretion

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SIADH Incidence

- ~70% of all cases of SIADH are associated with malignancy
- The majority of these cases are linked to Small Cell Carcinoma of the Lung
- Can also be seen with lymphoma, Ewing's sarcoma, mesothelioma, or SCC of the head and neck

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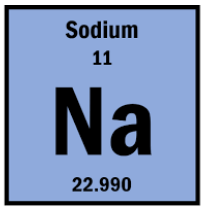
Diagnosing SIADH

- Normal Sodium Range is 135-145 mEq/L
- Hyponatremia <135 mEq/L
- Severe Hyponatremia <125 mEq/L



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Presentation of SIADH

- **Symptoms of Hyponatremia**
  - *Fatigue*
  - *Nausea/Vomiting*
  - *Headache*
  - *Shaking*
  - *Confusion*
  - *Muscle Cramps*

- Rapid drop in sodium can lead to bradycardia, hypotension, seizures, coma

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Treatment of SIADH

- **Depends on**
  - *Underlying cause*
  - *Symptomatic*
  - *Acute (<48 hour onset) or chronic*
  - *Urine osmolality and creatinine clearance*
- **Goal: Raise serum sodium by 0.5-1 mEq/hr but not more than 10-12 mEq in the first 24 hours**

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Avoid Overly Rapid Correction

- Central pontine myelinolysis (CPM)
- Also known as osmotic demyelination syndrome
- Neurological disorder that can occur after too rapid medical correction of sodium deficiency resulting in decreased sensation, motor functioning, coordination

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Treatment of Acute SIADH (<48 hours onset)

- Water restriction
- 3% hypertonic saline
- Loop diuretics with hypertonic saline
- Vasopressin-2 receptor antagonists

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Treatment of Chronic SIADH (Asymptomatic)

- Fluid restriction
- Vasopressin-2 receptor antagonists
- Consider loop diuretics with increased salt intake, urea, mannitol, and demeclocycline

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Which of the following types of malignancy is most highly associated with SIADH?

Small Cell Carcinoma of the Lung	0%
Renal Cell Carcinoma	0%
Triple Negative Breast Cancer	0%
Ewings Sarcoma	0%

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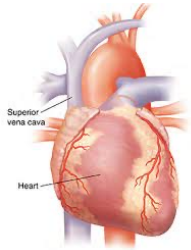

Superior Vena Cava Syndrome

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Case 3

AK is a 56-year-old female who presents to the ED with new onset of headache, blurry vision, and cough. You notice on physical exam that her face appears swollen and the veins of the right side of her neck are distended, but nonpulsatile. She has a port in place in her upper right chest as she is currently undergoing treatment for non-Hodgkins lymphoma.

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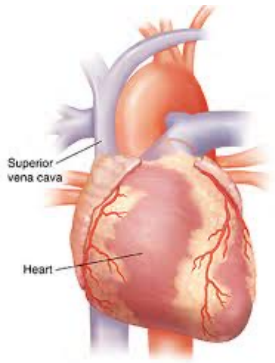
Superior Vena Cava Syndrome

- Collection of clinical signs and symptoms that are the result of partial or complete obstruction of blood flowing through the SVC
- Usually secondary to malignancy (ie-tumor infiltrating the vessel wall or thrombus)
- ~50% associated with non-small cell lung cancers; ~35% associated with small cell lung cancer/lymphomas
- Can also be associated with pacemakers and ports



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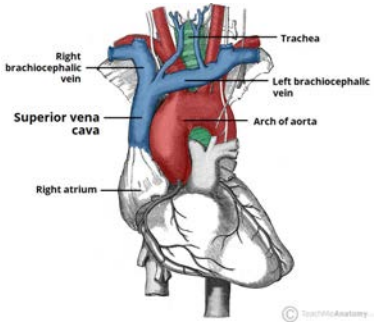
Superior Vena Cava Anatomy

- Formed by the junction of the left and right brachiocephalic veins
- Responsible for blood return from the head, neck, upper extremities, and torso back to the right atrium



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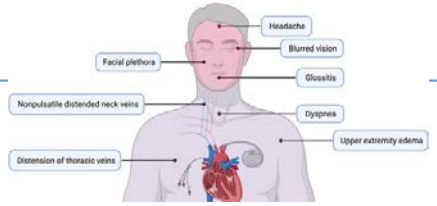
Presentation of SVC Syndrome



- Swelling of the neck and face
- Headache/blurry vision
- Distended veins of the neck and/or chest wall (nonpulsatile)
- Cough
- Dyspnea/orthopnea
- Dysphagia
- Upper extremity swelling
- Conjunctival erythema without infectious exudate

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Grading SVC Syndrome

- 0 Asymptomatic: SVC on imaging without symptoms
- 1 Mild: edema of head or neck
- 2 Moderate: edema in head or neck with functional impairment
- 3 Severe: mild or moderate cerebral edema/laryngeal edema, or diminished cardiac reserve
- 4 Life-threatening: significant cerebral edema, laryngeal edema, hemodynamic compromise
- 5 Fatal: death

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Diagnosing SVC

- **Largely based on H&P**
- **Imaging:**
  - *Ultrasound of the jugular, subclavian, and brachiocephalic veins*
  - *Chest CT and/or MRI with the presence of collateral vessels is associated with a diagnostic sensitivity of 96%*

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Management of SVC

- **Step One: Elevate the patient's head to decrease venous pressure**
- Further management is determined by the underlying disease and cause of SVC Syndrome
  - *Anticoagulation*
  - *Diuretics and corticosteroids*
  - *Removal of Port*
  - *Chemo, surgerical removal and/or radiation for the obstructing tumor*
  - *Thromboplasty*
  - *Open surgical repair of SVC with grafting*

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Kishi Score for SVC Syndrome Severity

Clinical signs	Weighting
Neurological signs	
Awareness disorders, coma	4
Visual disorders, headache, vertigo, memory disorders	3
Mental disorders	2
Malaise	1
Thoracic/pharyngeal-laryngeal signs	
Orthopnoea, laryngeal oedema	3
Stridor, dysphagia, dyspnoea	2
Coughing, pleuresy	1
Facial signs	
Lip oedema, nasal obstruction, epistaxis	2
Facial oedema	1
Vessel dilation (neck, face, arms)	1

Score of 4 or higher indicates a need for stent placement

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What should be the first step in management of a patient presenting with SVC Syndrome?

Anticoagulation with IV Heparin 0%

Administration of vaspressors 0%

Palliative Radiation to the invading tumor 0%

Elevation of the patient's head 0%

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Summary

- Oncologic emergencies are common among cancer patients
- Treatment should be initiated ASAP and largely focuses on the underlying cause

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Questions/Comments?

Nobody has responded yet.

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THANK YOU!

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12:00 PM

Caring for Older Adults with Acute Leukemia in North Carolina: Updates for 2023
Daniel Richardson, MD, MA, MSc

PATIENT CENTERED CARE

October 11
12:00 PM

Role of Specialty Pharmacy
Sonali Acharya, PharmD

ADVANCED PRACTICE PROVIDER

October 18
4:00 PM

CRS and ICANS: Pathophysiology and Management
Bejal Kikani, MSN, FNP-BC, WHNP-BC

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