Pediatric Oncologic Emergencies

Chalinee Monsereenusorn, M.D.

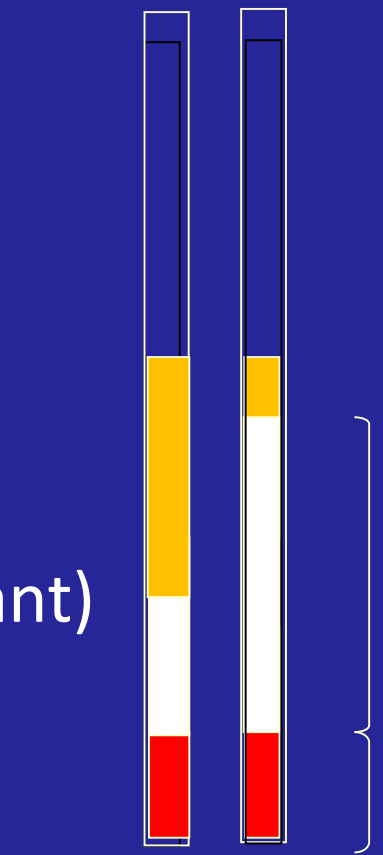
Division of Hematology-Oncology,
Department of Pediatrics, Phramongkutklao Hospital

Outlines

- Metabolic and endocrine emergencies
  - Hyperleukocytosis
  - Tumor lysis syndrome
- Abdominal emergencies
  - Esophagitis
  - Gastric hemorrhage: especially in patients on corticosteroid therapy.
  - Typhlitis
  - Perirectal abscess
  - Hemorrhagic pancreatitis: L-asp
  - Massive hepatic enlargement from tumor: esp infants stage IVS neuroblastoma
- Infectious emergencies
  - Febrile neutropenia
- Structural emergencies
  - Superior mediastinal syndrome(SMS)
  - Superior vena cava (SVC) syndrome
- Neurologic emergencies
  - Spinal cord compression

Hyperleukocytosis

- WBC > 100,000 / mm^3
- AML > ALL
- When
  - ALL : > 300,000 (T cell, infant)
  - AML > 100,000-200,000
  - CML > 600,000



Hyperleukocytosis

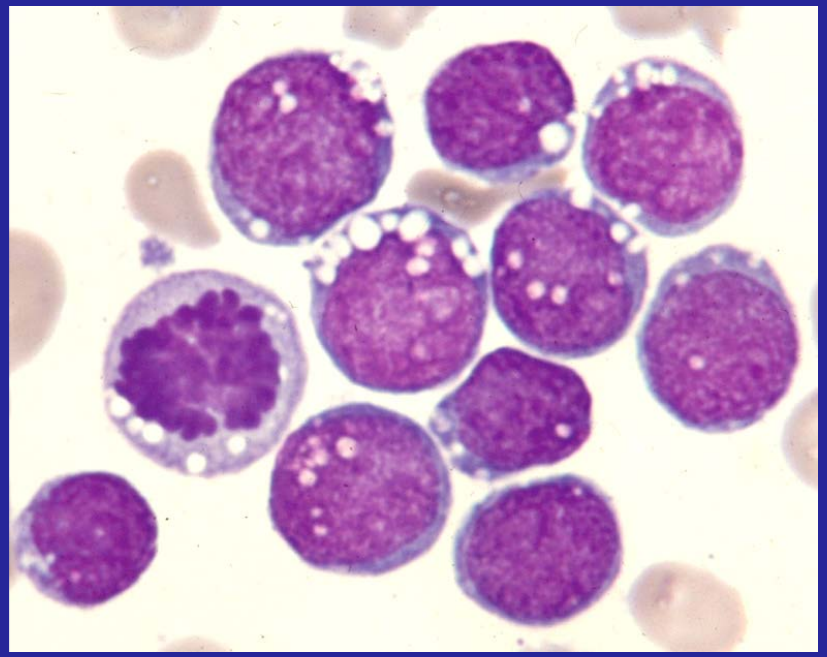
- Adhesive reaction between abnormal endothelium and blast
- Interfere oxygenation of local tissue
- Production of cytokine → tissue hypoxia

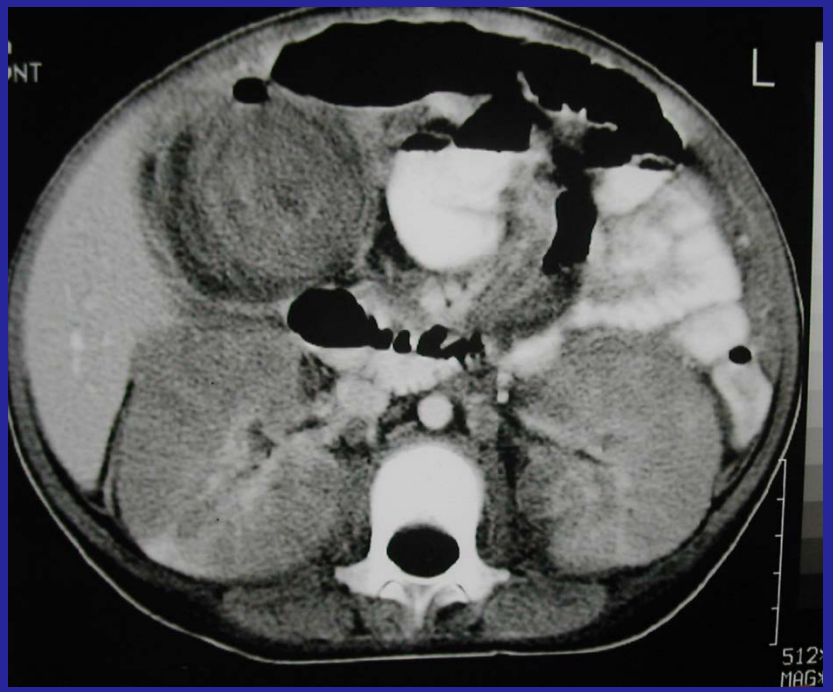
Hyperleukocytosis

- **Increases blood viscosity** → thrombi in microcirculation
- **Respiratory failure**
  - Stasis in pulmonary vasculature
  - Release of intracellular contents → diffuse alveolar damage
- **Hemorrhage**
  - CNS, GI, pulmonary, pericardial
  - Coagulopathy in M3, M4, M5

Hyperleukocytosis

- AML : Hyperviscosity
  - Intracranial hemorrhage
  - Pulmonary hemorrhage
- ALL : TLS




L

Management of Hyperleukocytosis

- Tumor lysis syndrome precaution
- Platelet transfusion, keep Plt > 20,000
- Avoid PRC transfusion
- Exchange transfusion or leukapheresis
- Diuretics : mannitol 0.5-1 gm/kg for oliguria
- Specific treatment : chemotherapy

Leukapheresis

Complication : hypocalcemia

Tumor Lysis Syndrome

- Hyperuricemia
- Hyperkalemia
- Hyperphosphatemia
- Hypocalcemia

Tumor Lysis Syndrome
Clinical features

- **Definition**

  Malignant cell degradation causing
  - Electrolytes abnormalities
  - Renal dysfunction
- **Onset**

  Before therapy or 1-5 days after CMT

High risk

- BL, LL, T-ALL, B-ALL
- Absolute blast ≥100,000/mm^3 in ALL
- Absolute blast ≥50,000/mm^3 in AML
- Massive tumor
- SVC obstruction
- Ascites, pleural effusion
- Palpable kidneys

Elevated uric acid, LDH, serum Cr

Tumor Lysis Syndrome

Common disease associated

- Burkitt's lymphoma
- Acute leukemia esp. ALL (T>B cell)
- Lymphoblastic lymphoma
- Neuroblastoma

Tumor Lysis Syndrome
Pathophysiology

Degradation of malignant cells

- **Release of PO_4, K, uric acid**
  - PO_4^{2-} concentration is 4x in lymphoblasts
  - Calcium phosphate crystal precipitate in microvascular and renal tubules when PO_4^{-2} x Ca^{+2} > 60 mg/dL
  - Secondary hypocalcemia occurs

Tumor Lysis Syndrome
Pathophysiology : Development of hyperuricemia

Tumor nuclei → **Xanthine oxidase**

Purine → Hypoxanthine → Xanthine → Uric acid

- **Symptomatic at uric acid level > 10 mg/dL**
  - Lethargy
  - uric acid calculi
  - seizure, paresthesia
  - nausea vomiting
  - Hematuria
  - Oliguria, anuria

Tumor Lysis Syndrome

Pathophysiology : Inadequate renal function

Inadequate renal function

Oliguria → **Renal failure**

Hyperkalemia
Hyperphosphatemia

Tumor Lysis Syndrome
Evaluation and Monitoring

- Electrolytes — Na, K, Cl, HCO_3 uric a, Ca^{+2}, PO_4^{-2}
- BUN, creatinine — q 4-6 hr
- EKG — widen QRS, peaked T waves
- Urinalysis — pH, sp.gr., I/O q 6-8 hr
- Central lines — for hemodynamic monitoring
- U/S abdomen — obstructive uropathy

Tumor Lysis Syndrome
Management

Preventive intervention

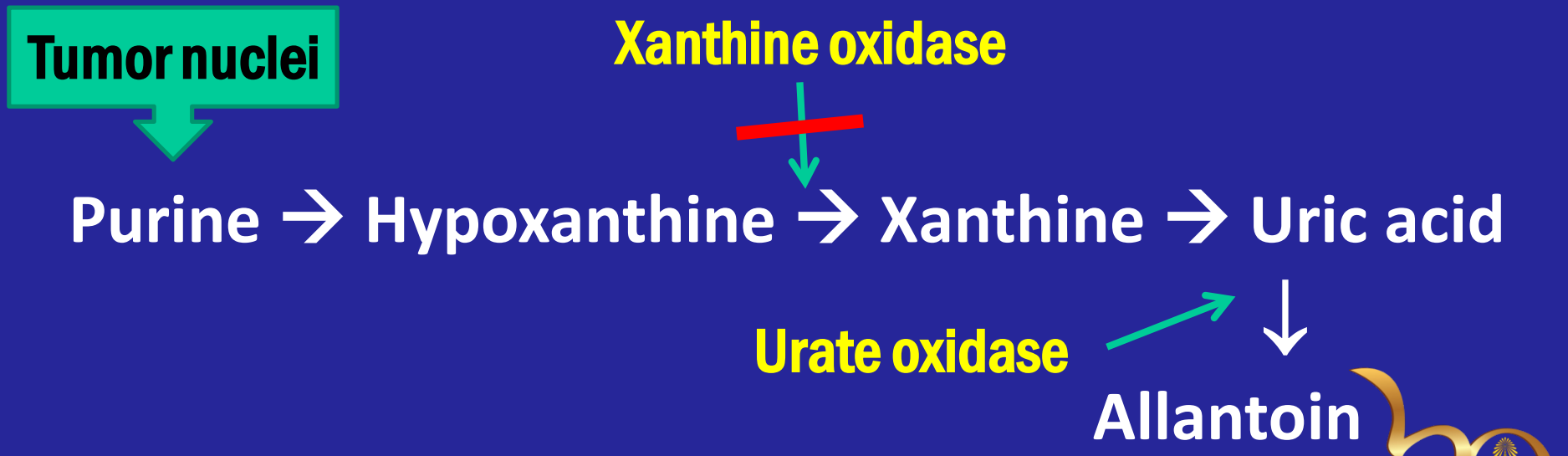
- **Monitoring** : blood chemistry, I&O, BP, BW
- **Hydration**
  - 2-3 x maintenance fluid with 5% D/N/2
  - urine output > 3ml/kg/h (<9 yr) or 90 ml/m^2/hr (older child), may need furosemide or mannitol
  - avoid adding K in IV fluid
- **Alkalinizations** : avoid severe alkalosis
  - Sodium bicarbonate 75-100 mEq/L to keep
    - Urine pH 6.5-7.5 prevent urate nephropathy
    - Sp. gr < 1.010

Tumor Lysis Syndrome
Management

Management & intervention

Uric acid reduction

- Xanthine oxidase inhibitor : Allopurinol
- Urate oxidase : Rasburicase



Tumor Lysis Syndrome
Management

- **HYPERURICEMIA (> 8 mg/dL)**
  - Allopurinol 300 mg/m^2/day PO or 10 MKD bid-tid
  - Rasburicase 0.15-0.2 mg/kg/d IV infusion in 30 min
  - Alkalinization of urine pH from 6.5-7.5
    D5 1/4 NSS + 50-100 mEq/L $NaHCO_3$ at 1.5-2 x maintenance to keep urine > 3ml/kg/hr
- **HYPERPHOSPHATEMIA (> 6.5 mg/dL)**
  - Aluminum hydroxide 50-150 mg/kg/day q 4-6 hrs
  - Calcium carbonate 45-65 MKD qid
  - Keep Ca x PO_4 < 60

Tumor Lysis Syndrome
Management

HYPERKALEMIA (>5.0 mEq/L)

- No K added until tumor lysis is controlled
- Kayexalate 1 gm/kg PO q 6h with 50% sorbitol 50-150 ml
- Calcium gluconate 50 mg/kg IV for arrhythmia (don't give in the same line of $NaHCO_3$)
- $NaHCO_3$ 1-2 mEq/kg
- Glucose (0.5 gm/kg/hr) + Insulin (0.1 u/kg/hr)

Emergency situation

1 unit/kg of RI plus 25% glucose 2 ml/kg IV

Tumor Lysis Syndrome
Management

- **HYPOCALCEMIA (ionized Ca < 1.5 mEq/L)**
  - 10% Ca gluconate 0.5-1 ml/kg slow IV infusion
  - **Indication**
    - Arrhythmia due to hyper K
    - Hypocalcemia with symptoms of neuromuscular irritability (Chvostek or Trousseau sign)

Tumor Lysis Syndrome
Management

Acute Renal Failure

Peritoneal dialysis/ Hemodialysis/ Hemofiltration

- Indication : when failed conservative treatment
  - Hyperkalemia (>7 mg/dL)
  - Volume overload
  - Uremia
  - Symptomatic hypocalcemia
  - Hyperphosphatemia (>10 mg/dL)
  - Hyperuricemia (>10 mg/dL)

ARF from
- Urate
- Hypoxanthine
- $CaPO_4$

Hypercalcemia (>12 mg/dL)

- Osteolytic bone lesion
- Bone mineralization secondary to PTHrP produced by tumor (paraneoplastic syndrome)
- Immobilization
- Defect in renal excretion

Hypercalcemia (>12 mg/dL)

Treatment

- Hydration induced diuresis : NSS 2-3 x M
- Furosemide 1-2 MKDose IV q 6 hrs induced Ca excretion
- Decresed Ca mobilization from bone
  - Bisphosphanate
  - Prednisolone 1.5-2 MKD

Structural emergencies

SVC syndrome

Superior vena cava obstruction

Compression of SVC

SMS syndrome

Superior Mediastinal Syndrome

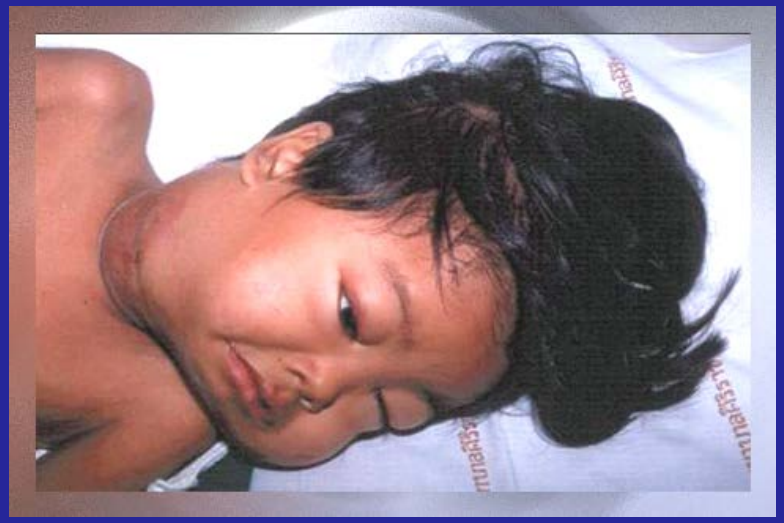
Compression of trachea

Structural emergencies

- Intrinsic cause : Vascular thrombosis
- Extrinsic cause : Malignant anterior mediastinal mass

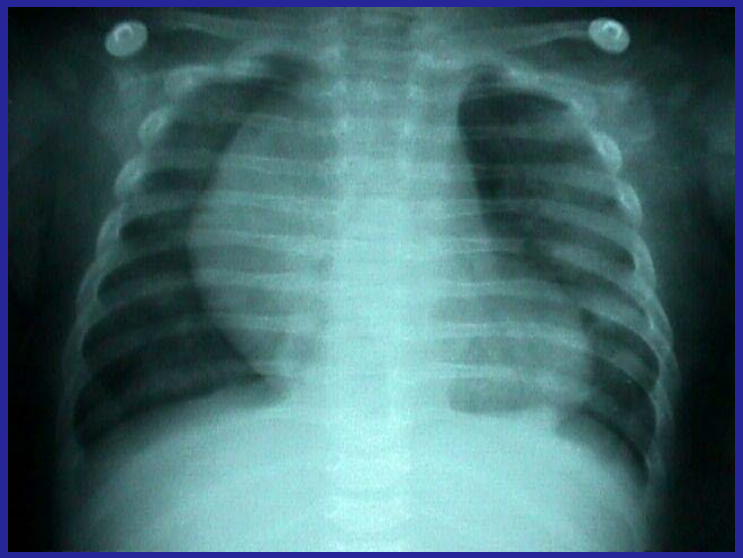
SVC obstruction : Sign & Symptom

- Plethora or facial cyanosis
- Swelling at face, neck, arms and upper chest
- Superficial veins dilatation
- Orthopnea



- Headache, dizziness, fainting, stupor, coma, seizure
- Pulsus paradoxus >> cardiac failure
- Cough , stridor dyspnea, air way obstruction >> respiratory failure

3S which may precipitate Respiratory Arrest



- Supine position
- Stress
- Sedation

Evaluation & Investigations

- History and physical examination
- CBC & BM aspiration
- Imaging study: CXR (PA, lat.), CT scan
- Tumor markers
- Thoracocenthesis and cytology
  - Lymph node biopsy under local anesthesia
  - Fine needle biopsy : CT guide

Tumor Markers

- LDH : Lymphoma
- NSE : neuroblastoma, Ewing's sarcoma, PNET
- AFP, βHCG : germ cell tumors

Tumor Markers

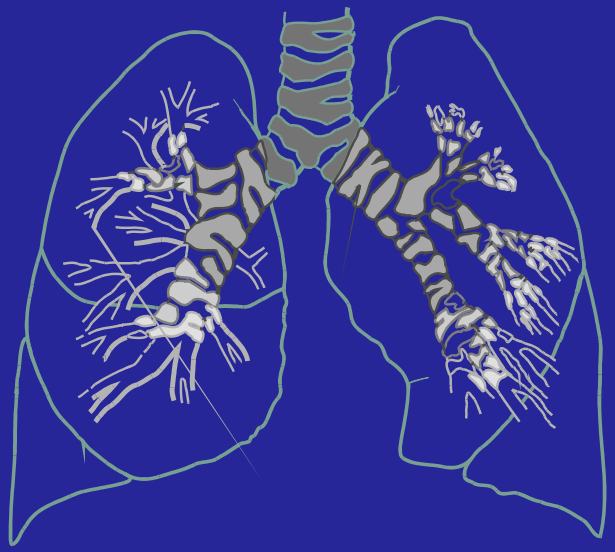
Symptoms	Tumor markers				
	LDH	NSE	βhCG	AFP	VMA
Mediastinal masses	✓	✓	✓	✓	
Abdominal mass RUQ	✓	✓		✓	✓
Abdominal mass LUQ	✓	✓			✓
Pelvic mass	✓		✓	✓	
Testicular mass			✓	✓	
CNS (Pineal) tumor		✓	✓	✓	

Thoracic masses

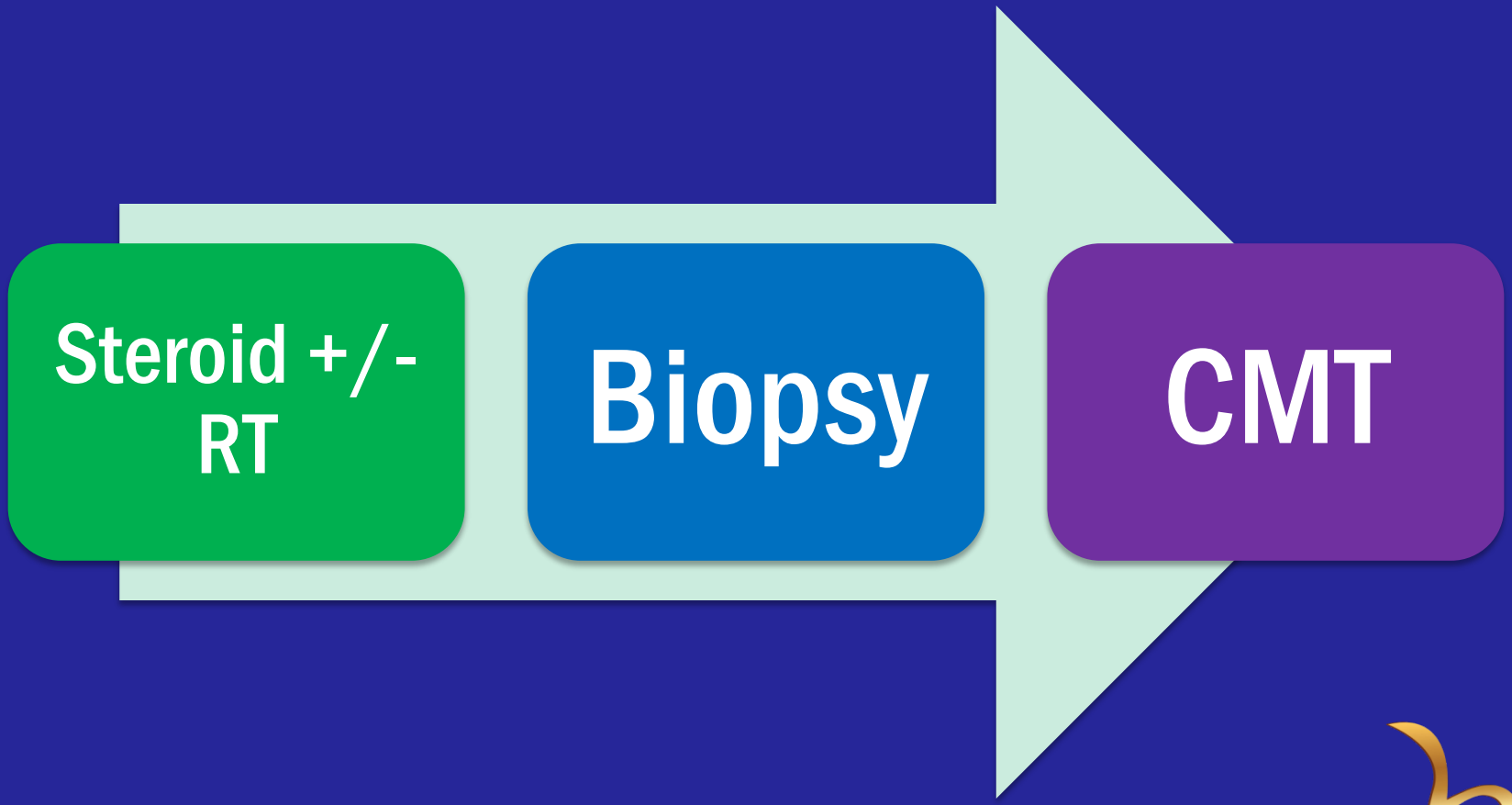
	Non-malignant	Malignant
Anterior	Thymus Angioma,lipoma Thyroid mass	Lymphoma (HL, T cell NHL) Thymoma Teratoma, germ cell tumors
Middle	Infections: TB Hernia, cardiac or Bronchogenic cysts	Lymphoma, metastatic tumor
Posterior	Thoracic meningocele, Enterogenous cyst,	Neurogenic tumors: neuroblastoma, ganglioneuroma, neurilemmoma, EWS, Rhabdo, pheochromocytoma,

Thoracenthesis and cytology

- Chemistry
  - protein, sugar, LDH
- Cytology
  - hematology, pathology
- Infectious
  - bacteriology, gram stain, AFB, culture etc.



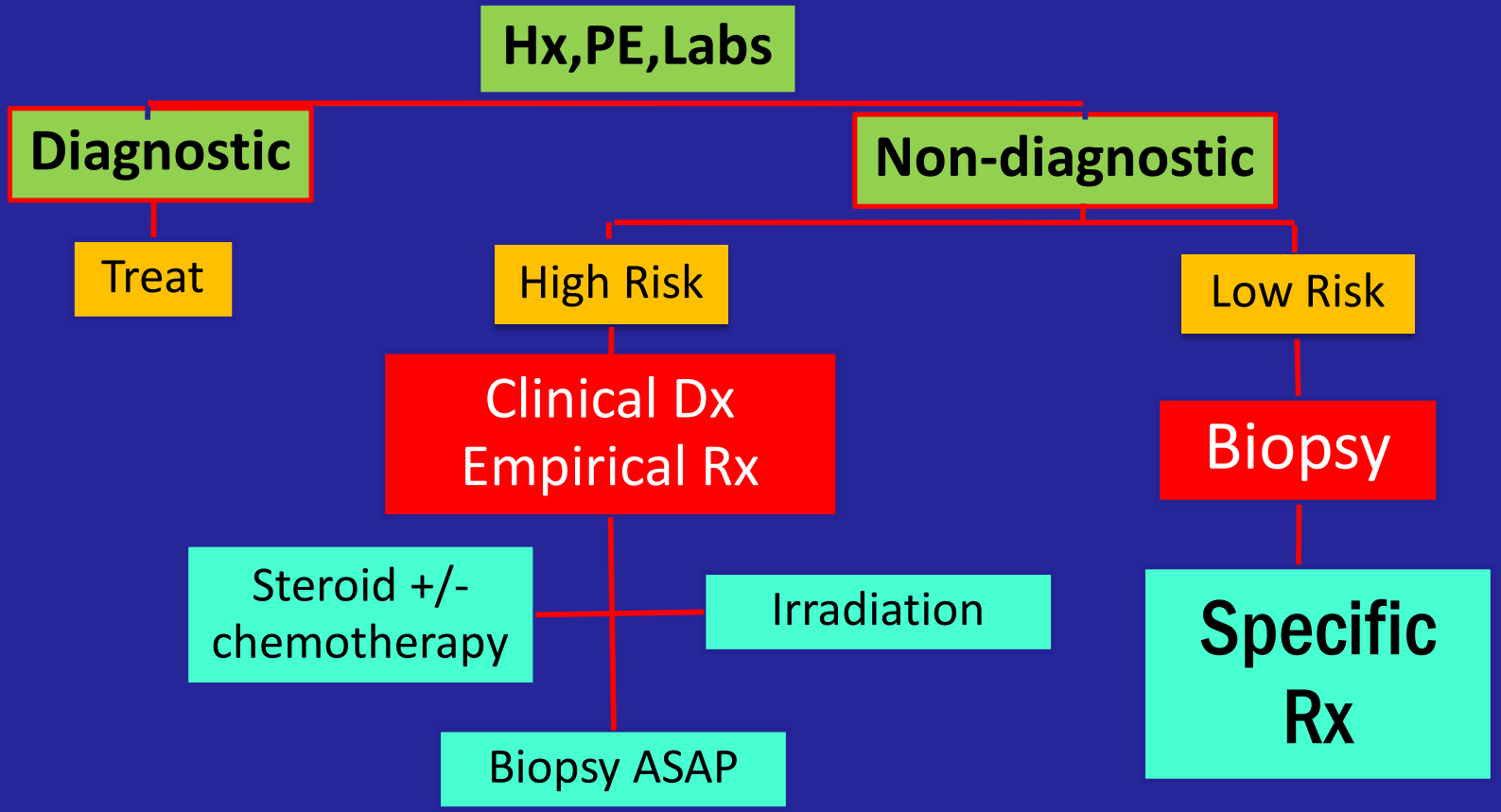
Emergency treatment of SVC Obstruction



Treatment of SVC Syndrome

- Steroid
  - Prednisolone 40 mg/m^2/day divided q 6 hr
  - Methylprednisolone
  - Dexamethasone
- Radiation *if emergency service available*
- Biopsy ASAP
- Chemotherapy
  - Lymphoma: Prednisolone +CTX, VCR, ADR
  - Neuroblastoma: CDDP+CTX

Therapeutic Approach to SVC Obstruction



Febrile Neutropenia

- Temp > 38.5˚ C once or 38.3˚ C > 4 hrs.
- Neutrophil < 500 / cu mm
- ANC: absolute neutrophil count

  = (%N +%band) x WBC

Febrile Neutropenia : Evaluation

- History
  - Sign & symptoms, pain, diarrhea, skin rash,
  - Exposure to persons with infection
  - Date of last chemotherapy
- Physical Exam
  - Thoroughly
  - Oral, perianal
  - Skin & puncture sites :IV, LP, BM
  - Sinuses

Febrile Neutropenia : Management

- Admit
- Complete PE
- Appropriate culture : Bacterial
- Lab evaluation : CBC, LFT, RFT,
- Radiographic evaluation, if pulmonary symptoms present
- Broad spectrum antibiotics
- Add on therapy

Febrile Neutropenia

- Broad spectrum antibiotics
  - Aminoglycoside + semisynthetic penicillin
  - Ceftazidime + aminoglycosides
  - Imipenem + Amikin
- Guideline for febrile neutropenia

Febrile Neutropenia

Add on therapy

- skin infection : anti-staphylococcus
- Vancomycin : central line, fever with chill and peritonitis
- Metronidazole : GI, diarrhea, typhlitis, perianal abscess
- Oral ulcer : anti fungus, acyclovir, metronidazole
- Antifungal : if febrile persisted > 10 days on broad spectrum antibiotics and still neutropenia

Abdominal Emergencies

- Esophagitis
- Gastric hemorrhage:especially in patients on corticosteroid therapy.
- Typhlitis
- Perirectal abscess
- Hemorrhagic pancreatitis : L-asparaginase
- Massive hepatic enlargement from tumor.esp. infants stage IVS neuroblastoma

Typhlitis

- Neutropenia, leukemia and in stem cell transplant recipient
- Bacterial or fungal invasion of the mucosa and can quickly progress inflammation, infarction causes peritonitis perforation and septic shock
- Pseudomonas species, E.coli,other GNB, S. aureus, α-hemolytic Streptococcus, Clostridium, Aspergillus, and Candida.

Typhlitis
Diagnosis

.

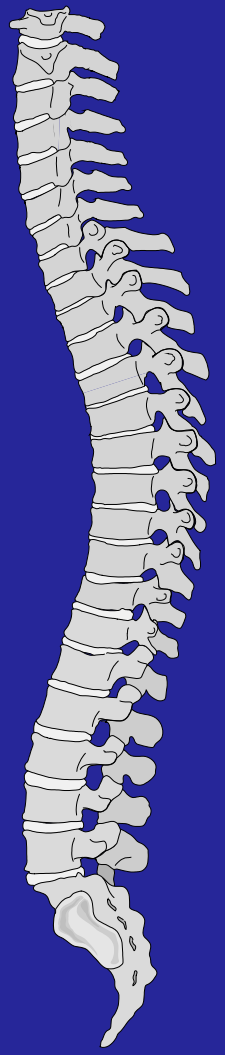
- Clinically : RUQ pain, neutropenia
- Serial abdominal
- Pneumatosis intestinalis,free air bowel wall thickening
- U/S: thickening of the bowel wall in the region of the Cecum
- CT : definite Dx : thickening Of the caecal wall
- BE: mucosal irregularity,rigidity,loss of haustral markings and occasional fistula formation

Treatment

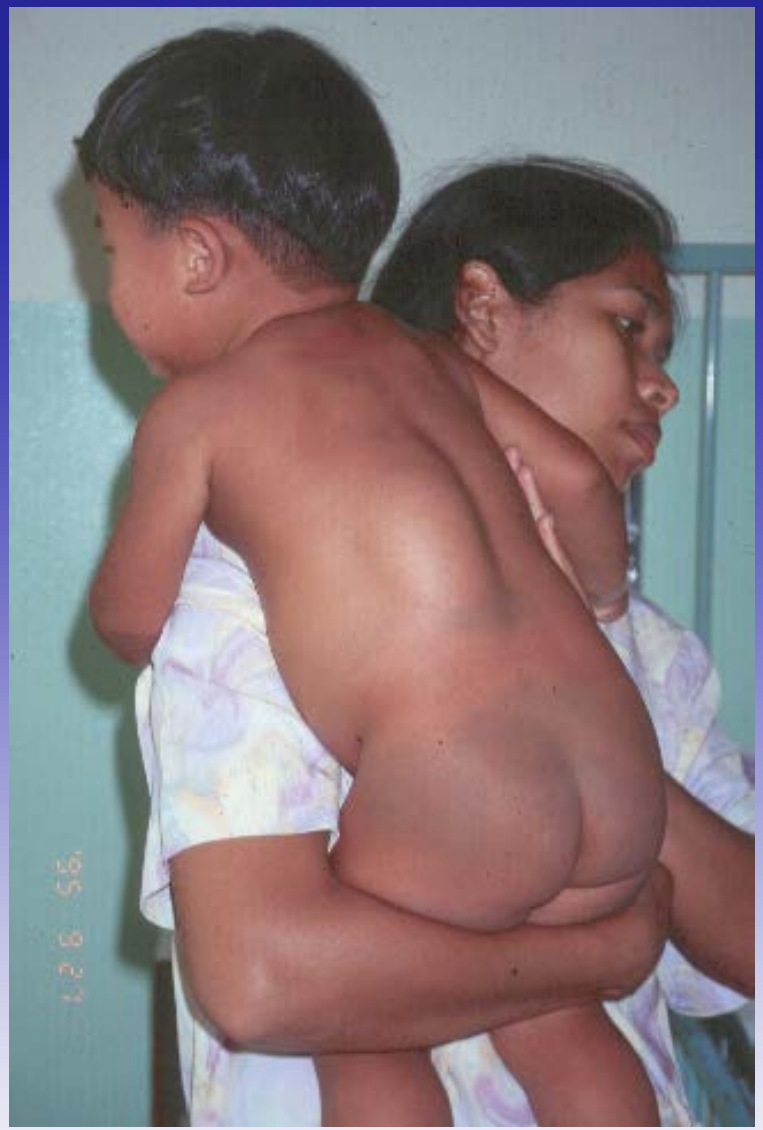
- NPO
- Nasogastric tube suctioning
- Broad-spectrum antibiotics (anaerobic and Gram-negative coverage)
- Intravenous fluid and electrolytes
- Packed red cell and platelet transfusions, as indicated
- Vasopressors, as needed (hypotension is associated with a poor outcome)

Indications for surgical intervention:

- Persistent GI bleeding despite resolution of neutropenia and thrombocytopenia
- Evidence of free air in the abdomen on abdominal radiograph
- Uncontrolled sepsis from bowel infarction.



SPINAL CORD COMPRESSION



PNET

Tumor with Spinal cord compression

- Primary spinal cord tumors
- Paravertebral in origin
  - Neuroblastoma
  - Ewing's sarcoma family: PNET, Extraosseous EWS
- Drop Metastasis from CNS
  - Medulloblastoma
  - CNS Germ cell tumors
  - Retinoblastoma
- Bone (vertebral) metastasis
  - Lymphoma (may be primary at vertebra)
  - Rhabdomyosarcoma or other soft tissue sarcomas

Investigations

- Spine X-ray
- MRI spine
- Lumbar Puncture
- Others

Treatment

Emergency

- Dexamethasone 1-2 mg/kg loading dose (max 10 mg) and then 0.5 mg/kg/dose q 6 hr
- Laminectomy and fixation for osteoporosis and vertebral collapsed

Treatment

- Surgery
  - Decompressive Laminectomy
    - unknown Dx., acute, tumor resisted to chemotherapy
- Chemotherapy
  - Lymphoma, Leukemia, neuroblastoma, Germ cell tumors
- Radiation
  - After chemotherapy and surgery


THANK YOU