Common Pediatric Oncological Diseases

Prof. Abdulrahman Alsultan

Objectives

- To gain knowledge of childhood cancer epidemiology
- To recognize clinical manifestations, diagnostic approach, treatment overview, and prognosis of common childhood cancers.

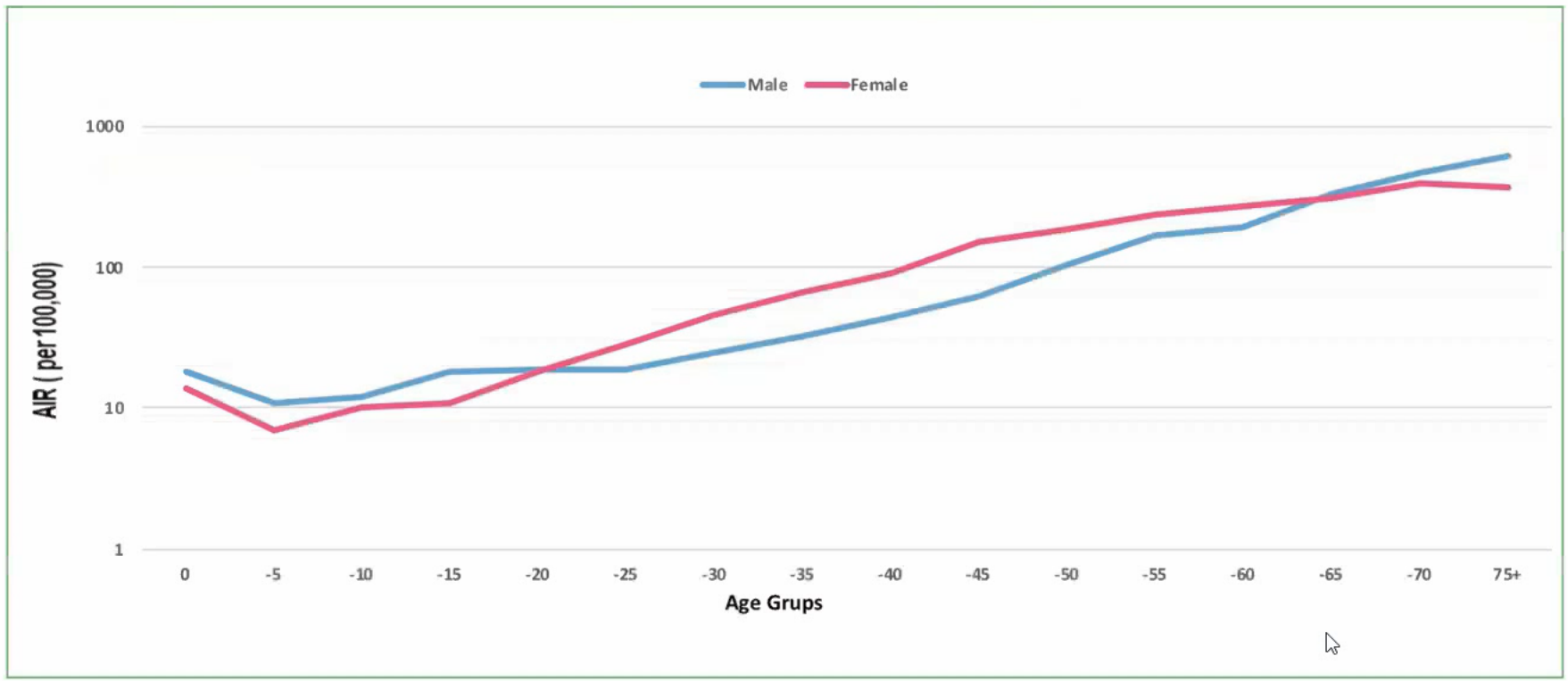
When to suspect childhood cancer

Epidemiology

- Childhood cancer is rare
- Cancer incidence in among US children aged 0-14 years was 16.7/100,000 in 2012-2016 (SEER data)
- Childhood cancer occurs in about 10/100,000 children in Saudi Arabia

Epidemiology- Saudi Arabia

Figure 2.2: Age-Specific Incidence Rate (AIR) for all cancers among Saudis, 2015



National Health Information Center Saudi Cancer Registry

Epidemiology- Saudi Arabia

Table 2.7.3: Top ten cancers reported among Saudi Adults by gender, 2015

Male	5036	%
Colorectal	808	16.0
NHL	437	8.7
Prostate	340	6.7
Lung	323	6.4
Liver	266	5.3
Leukaemia	262	5.2
Hodgkin's lymphoma	226	4.5
Thyroid	224	4.4
Bladder	192	3.8
Stomach	184	3.7

Female	6275	%
Breast	1978	31.5
Thyroid	785	12.5
Colorectal	655	10.4
Corpus Uteri	403	6.4
NHL	303	4.8
Ovary	208	3.3
Leukaemia	185	2.9
Hodgkin's lymphoma	144	2.3
Stomach	131	2.1
Cervix Uteri	102	1.6

National Health Information Center Saudi Cancer Registry

Epidemiology- Saudi Arabia

Table 2.8.2: Top ten cancers among Saudi Children, 2015

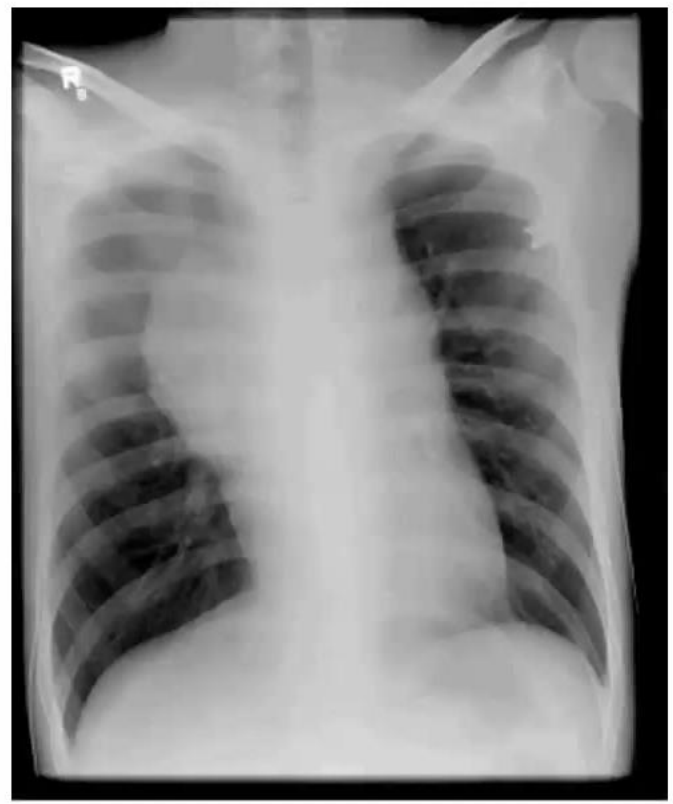
Site	No.	%
Leukaemia	255	35.0
Brain, CNS	89	12.2
NHL	89	12.2
Hodgkin's lymphoma	66	9.1
Kidney	43	5.9
Bone	32	4.4
Adrenal gland	28	3.8
Eye	26	3.6
Connective,Soft tissue	23	3.2
Ovary	12	1.6

Causes of Childhood Cancer

- Unknown in majority of cases.
- Cancer predisposition syndromes:
  - Examples:
    - Down syndrome
    - Neurofibromatosis
    - Fanconi anemia
    - Li-Fraumeni syndrome (germline *P53* mutation)
- Environmental factors:
  - Ionizing radiation
  - Infectious etiology
  - Chemical exposures e.g. pesticides, benzene
- Prior treatment:
  - Chemotherapy (e.g. etoposide or alkylating agents)
  - Radiotherapy

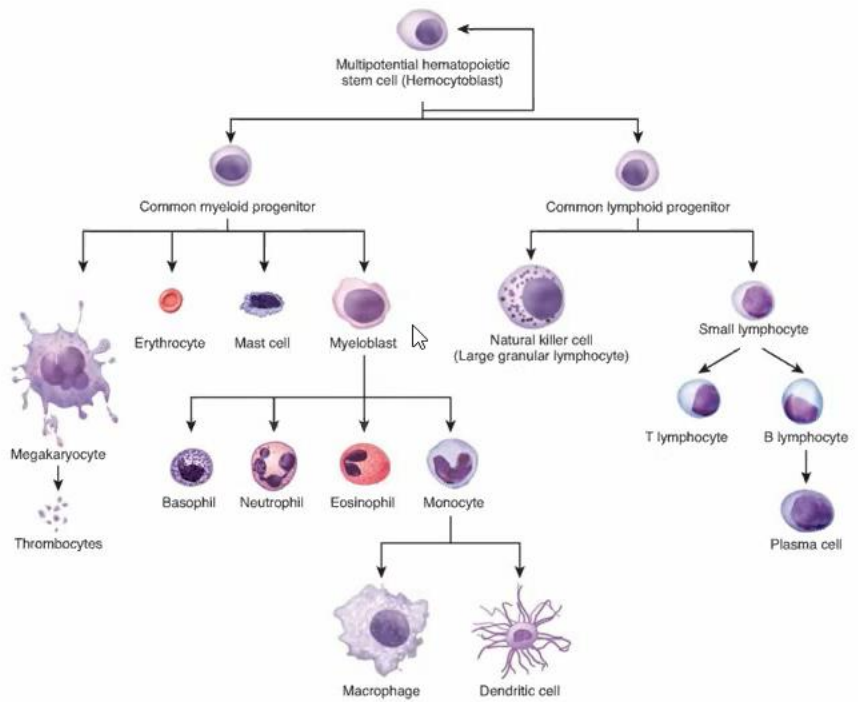
Case

A 5 year old girl presented with a history of cough, shortness of breath, and fever. On exam she is leaning forward and refusing to lay on her back. You also noted swelling of her face, hepatosplenomegaly, and lymphadenopathy. CBC showed WBC 150,000/ul, Hb 7 g/dL, and platelet 20,000/ul with blasts in peripheral blood. Chest X-ray is shown in the figure.



Leukemia

- Types:
  - Acute lymphoblastic leukemia (ALL)
  - Acute myelogenous leukemia (AML)
  - Chronic myelogenous (CML)

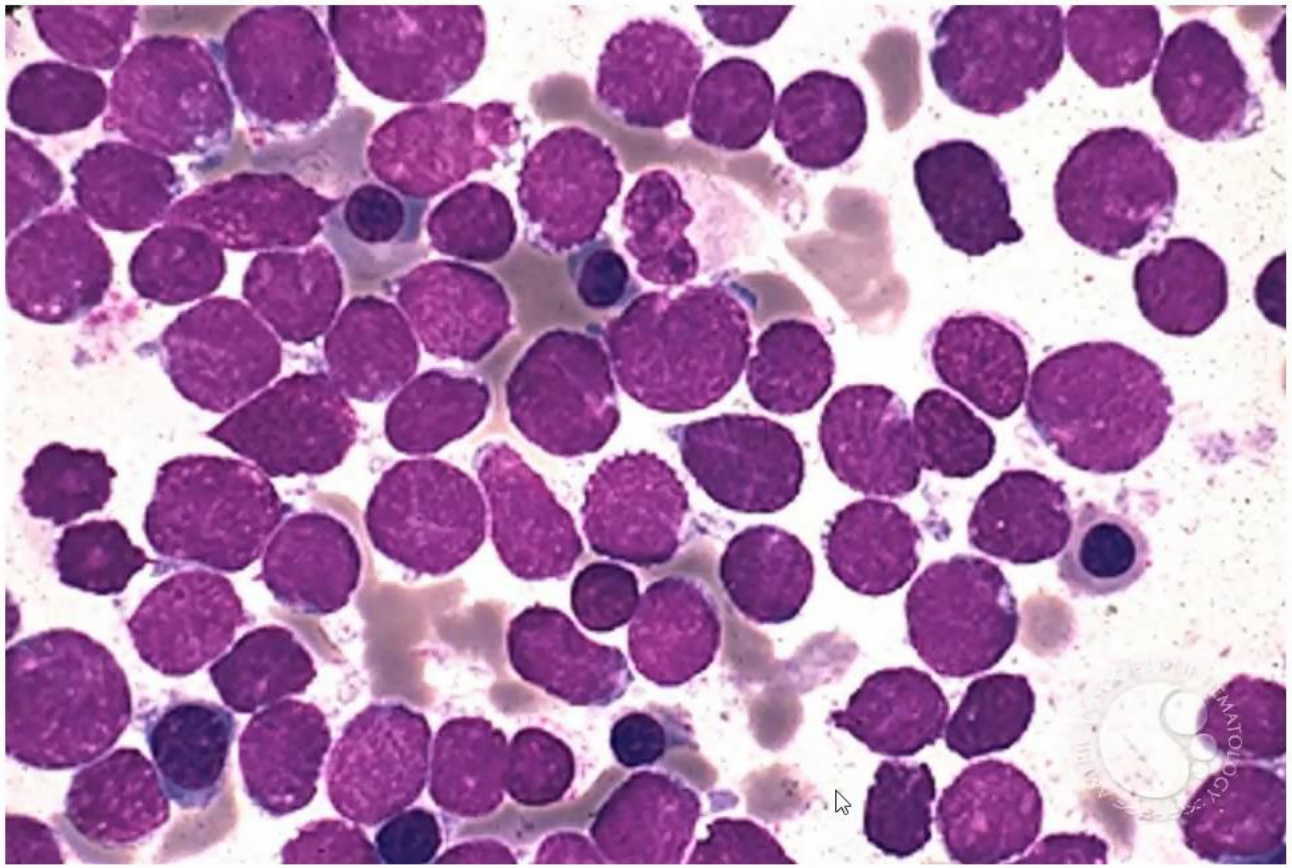


Leukemia

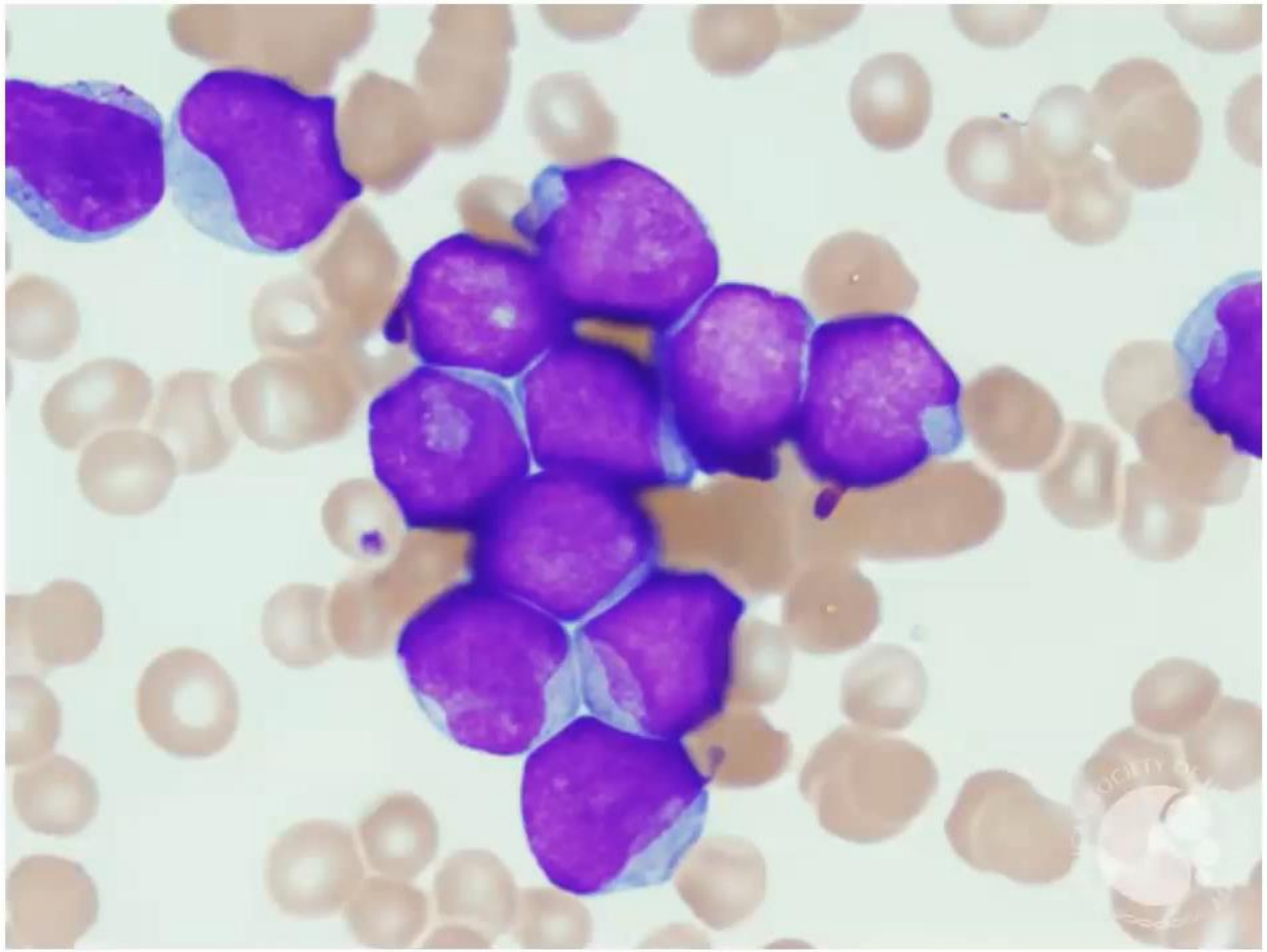
- Symptoms:
  - Lethargy
  - Fever/Infection
  - Bone/Joint pain
  - Bleeding
  - Anorexia
  - Abdominal pain
  - CNS signs
- Signs:
  - Pallor
  - Hepatosplenomegaly
  - Petechiae/Purpura
  - Lymphadenopathy.
  - Testicular involvement

Leukemia

- Workup:
  - CBC and differential
  - LFT, electrolytes (K, Ph), uric acid, LDH
  - CxR
  - Bone marrow study:
    - Morphology
    - Flow cytometry
    - Molecular studies e.g. BCR-ABL
    - Cytogenetics e.g. t (9;22)
  - Lumbar puncture



B-ALL: blasts are generally small with a high nuclear cytoplasmic ratio.



AML: blasts are medium to large in size with increased nuclear:cytoplasmic ratio.

Flow Cytometry

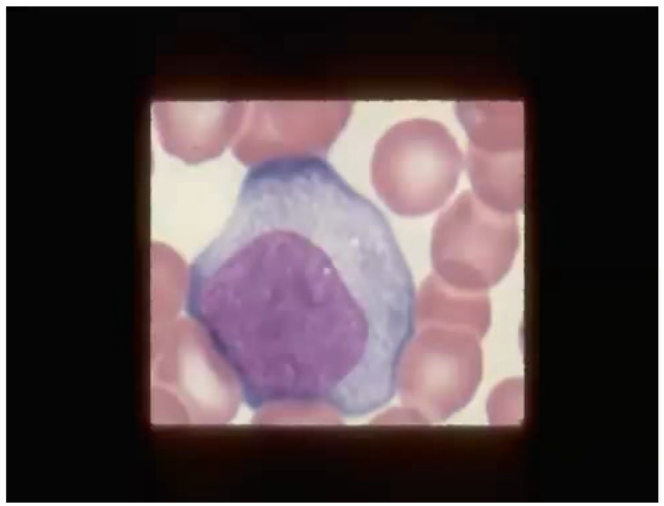
- B-ALL
  - CD10, CD19, CD20, CD22, CD79a, HLA-DR, CD34 & TdT
- T-ALL
  - CD2, CD3, CD5, CD7, CD1a, TdT
- AML
  - CD13, CD15, CD33, CD117, MPO, HLA-DR, CD34

Prognostic Factors in ALL

- NCI Risk Grouping
  - Std Risk: Age 1-9 yr and WBC <50,000/μl
  - High Risk: Age <1 or ≥ 10 yr and/or WBC ≥ 50k
- Immunophenotype
- Cytogenetics
- Response to induction therapy
- CNS disease

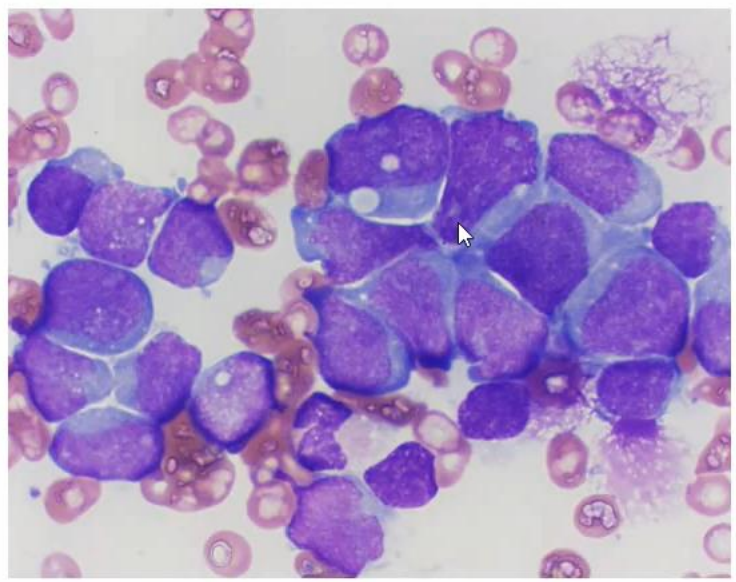
Leukemia

- Differential diagnosis:
  - Non-malignant:
    - Infectious mononucleosis
    - JRA
    - ITP
    - Aplastic anemia
    - Pertusis



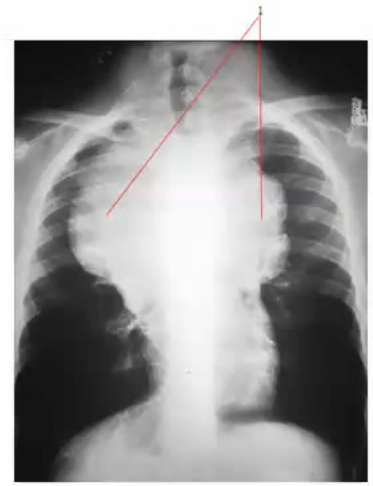
Leukemia

- Differential diagnosis:
  - Malignant:
    - Lymphoma (BM blasts < 20%)
    - Neuroblastoma
    - Rhabdomyosarcoma

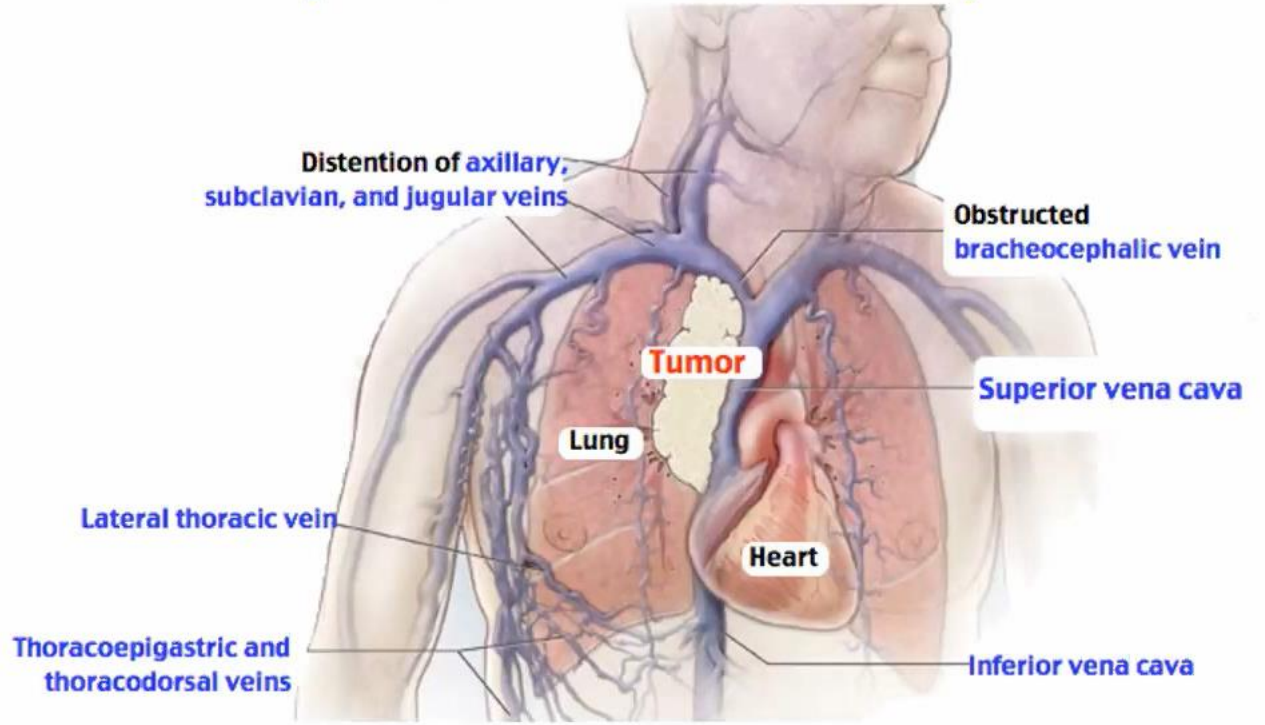


Leukemia

- Treatment:
  - Supportive care:
    - Tumor lysis syndrome
    - Hyperleukocytosis
    - Superior vena cava syndrome
    - Infections
  - **Chemotherapy**
  - Cranial radiation if CNS positive
  - Hematopoietic stem cell transplant (rarely)



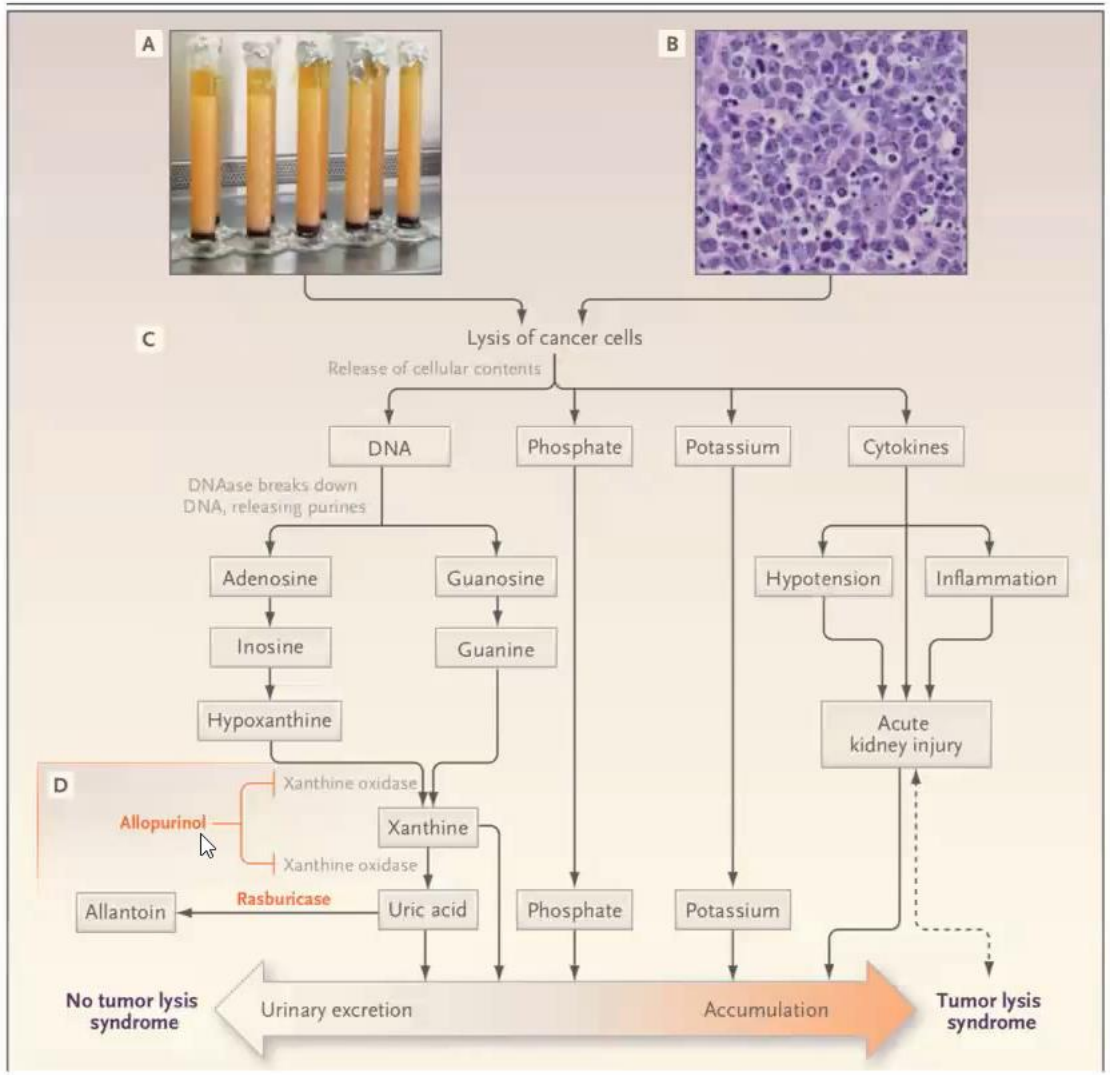
Superior Vena Cava Syndrome



C/F: Cough, dyspnea, orthopnea, dysphagia, wheezing, hoarseness, facial edema, chest pain.

Causes:

- Tumors: T-ALL, NHL, thymoma, teratoma
- Others: TB, thrombosis



N Engl J Med 2011; 364:184

Case

A 10-year-old girl with acute lymphoblastic leukemia presented to emergency department because of history of fever. Vital signs are normal. No evidence of cellulitis or line infections. CBC showed severe neutropenia. Treatment?

Febrile neutropenia:

- High mortality when antibiotics started after blood cultures became positive.
- Narrow spectrum antibiotic coverage results in associated with poor outcomes
- Antibiotics in neutropenic patients should be started at the onset of fever

Treatment:

- Use monotherapy with an antipseudomonal b-lactam, a fourth-generation cephalosporin, or a carbapenem as empirical therapy in pediatric high-risk FN.
- Reserve the addition of a second gram-negative agent or who are clinically unstable, when a resistant infection is suspected, or for centers with a high rate of resistant pathogens.

Indication for adding Vancomycin:

- High dose cytarabine because of risk of Step Viridians.
- Sepsis
- Cellulitis
- Central line infections

Gram-Negative Organisms	No. of strains	β-lactams							Quinolones		Aminoglycosides		Others	
		AMP	CZ	CXM	CAZ	FEP	MEM	TZP	CIP	MXF	AN	GM	NIT	SXT
Acinetobacter baumannii	143	R	R	R	38	32	22	22	32	---	43	48	---	73
Citrobacter freundii[3]	28	R	R	R	---	85	93	---	67	54	100	85	---	39
Enterobacter aerogenes[3]	23	R	R	R	---	84	100	---	92	75	100	80	---	76
Enterobacter cloacae	120	R	R	R	---	80	96	---	93	85	97	96	49	91
Escherichia coli	1119	26	56	58	62	63	100	95	60	52	98	83	98	50
Klebsiella pneumoniae	562	R	61	58	63	65	96	90	76	60	95	82	60	62
Morganella morganii	36	R	R	R	---	80	94	---	60	36	97	69	R	37
Proteus mirabilis	80	48	64	77	---	84	96	---	65	55	87	67	R	32
Pseudomonas aeruginosa	550	R	R	R	75	76	62	77	82	---	94	85	R	R
Salmonella spp.	36	67	---	---	100	100	100	83	46	78	17	---	---	72
Serratia marcescens	52	R	R	R	---	90	96	---	94	88	94	96	R	98
Stenotrophomonas maltophilia	52	R	R	R	24	R	R	R	---	---	---	---	R	87

Note

J Clin Oncol 35:2082-2094

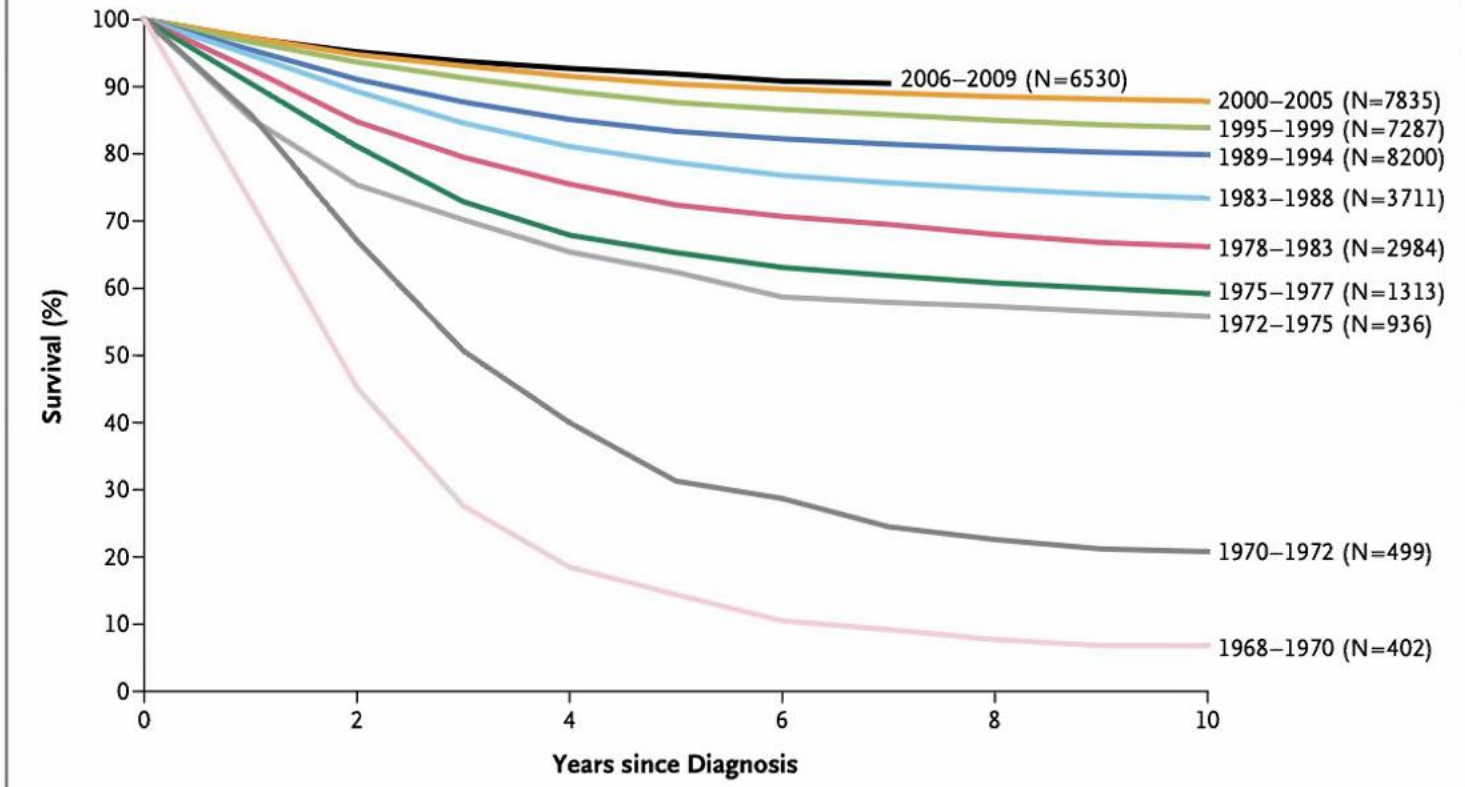


Figure 1. Overall Survival among Children with Acute Lymphoblastic Leukemia (ALL) Who Were Enrolled in Children's Cancer Group and Children's Oncology Group Clinical Trials, 1968–2009.

Brain tumors

Brain tumors in children:

- Second most common childhood cancer
- Low grade gliomas are most common type of brain tumor in children.
- Medulloblastoma is the most common malignant brain tumor in children

Brain tumors

- Clinical presentation:
  - General and non-localizing symptoms

    (e.g. headache, vomiting, behavioral changes, learning problems, weight loss/gain)

  - Increased intracranial pressure

    (e.g. irritability, vomiting, bulging fontanelle, papilledema, parinaud syndrome)

  - Localizing signs

    (depend on tumor location e.g. ataxia)

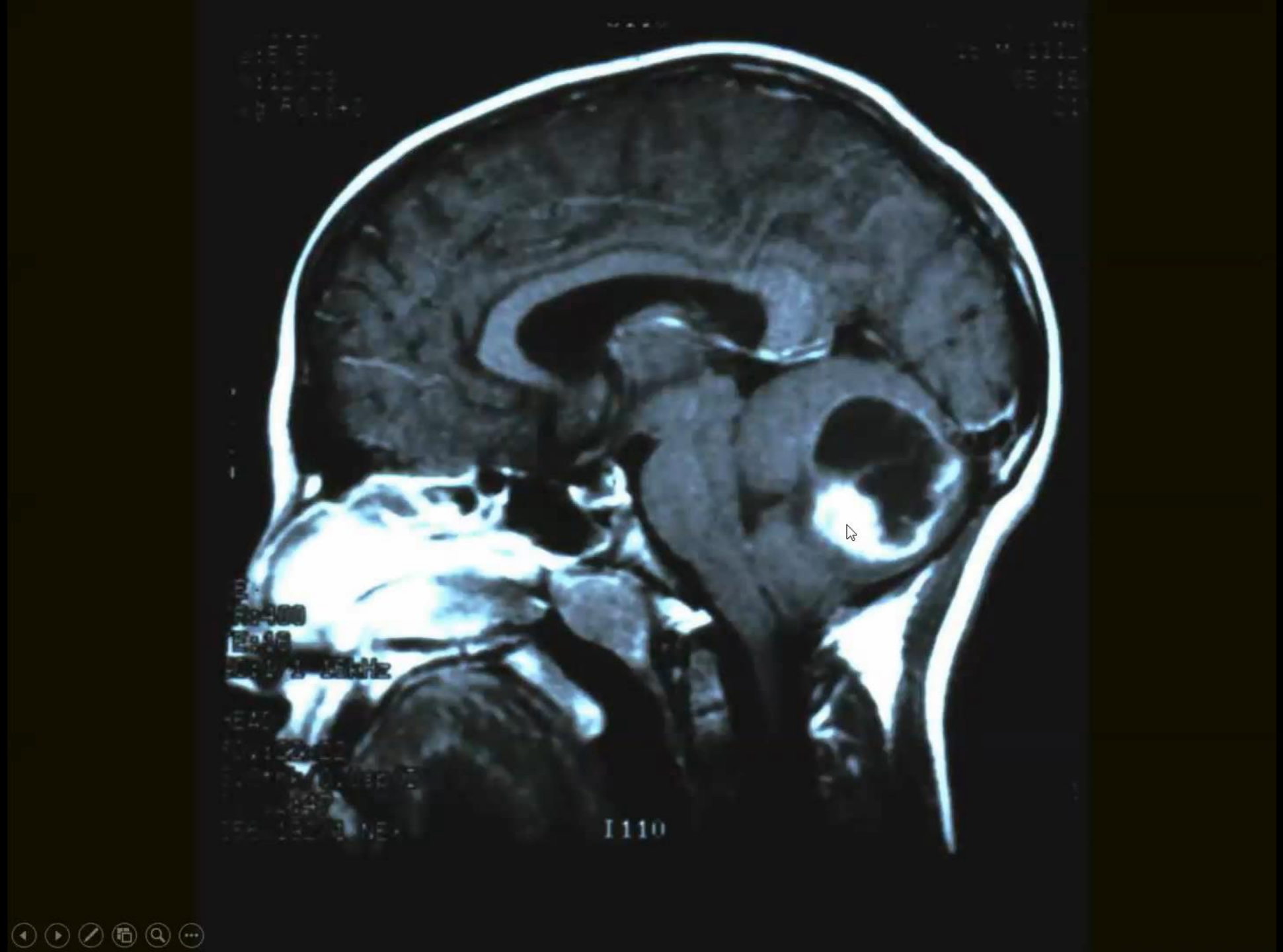
Brain tumors

- Treatment:
  - Surgery
    - Gross total resection if feasible
  - Radiotherapy
  - Chemotherapy

Astrocytoma (Glioma)

- Low grade: good prognosis
  - WHO grade I (juvenile pilocytic astrocytoma)
  - WHO grade II (diffuse fibrillary astrocytoma)

- High grade: v. poor prognosis
  - WHO grade III (anaplastic astrocytoma)
  - WHO grade IV (Glioblastoma multiforme)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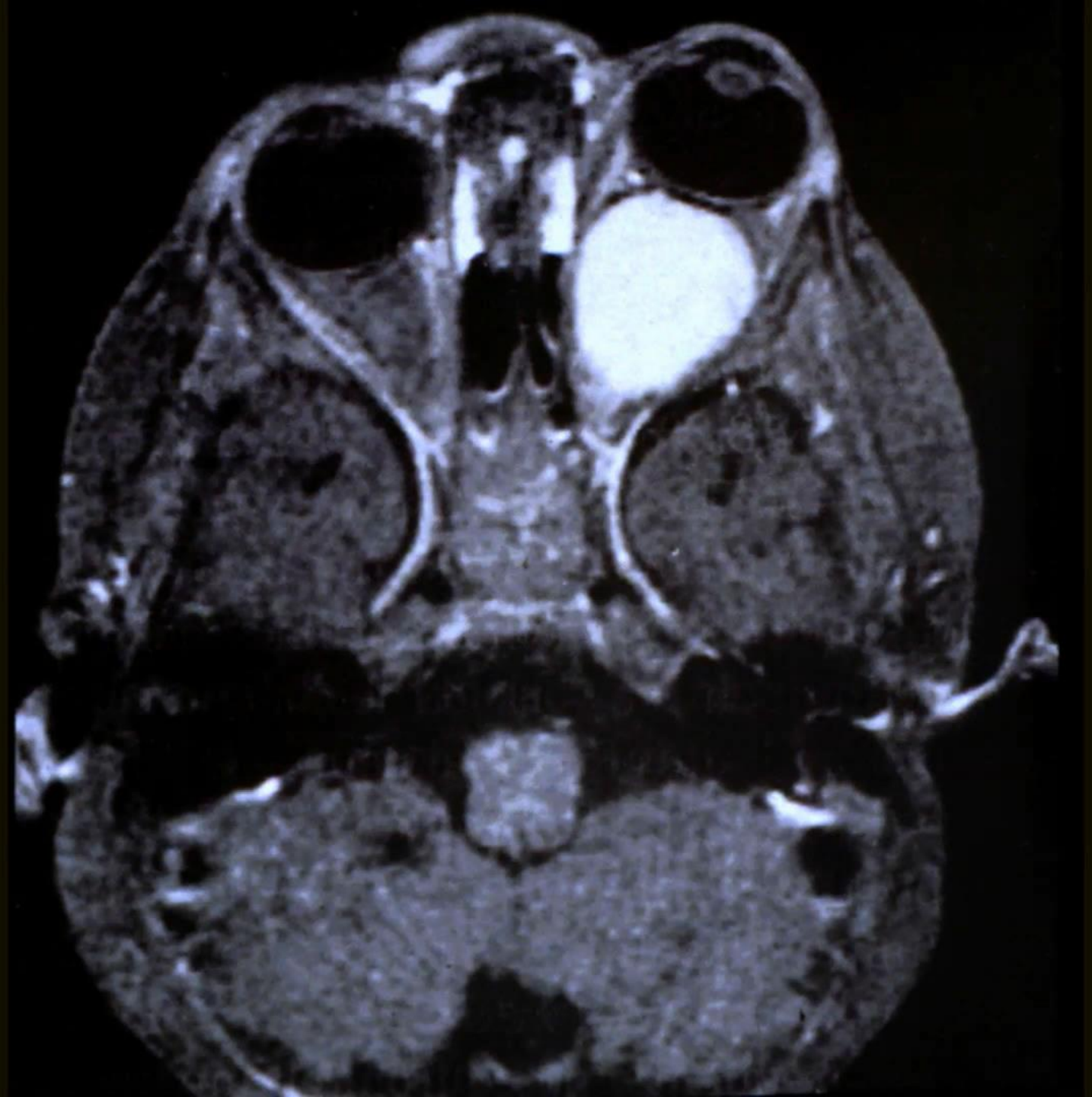
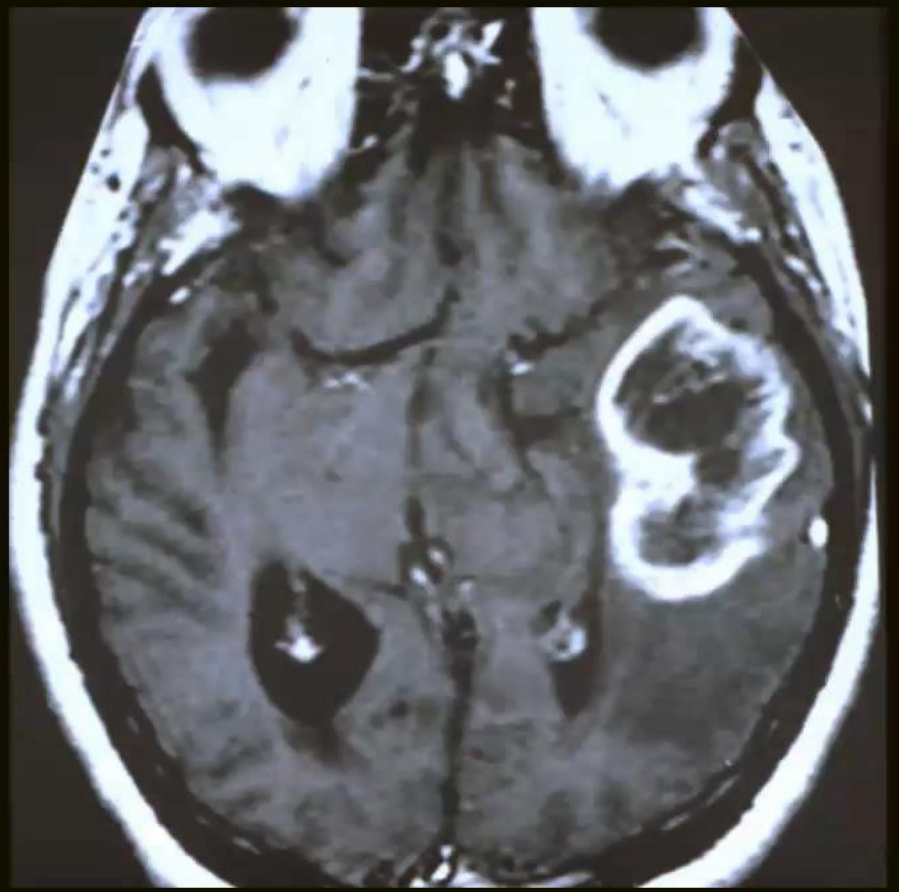
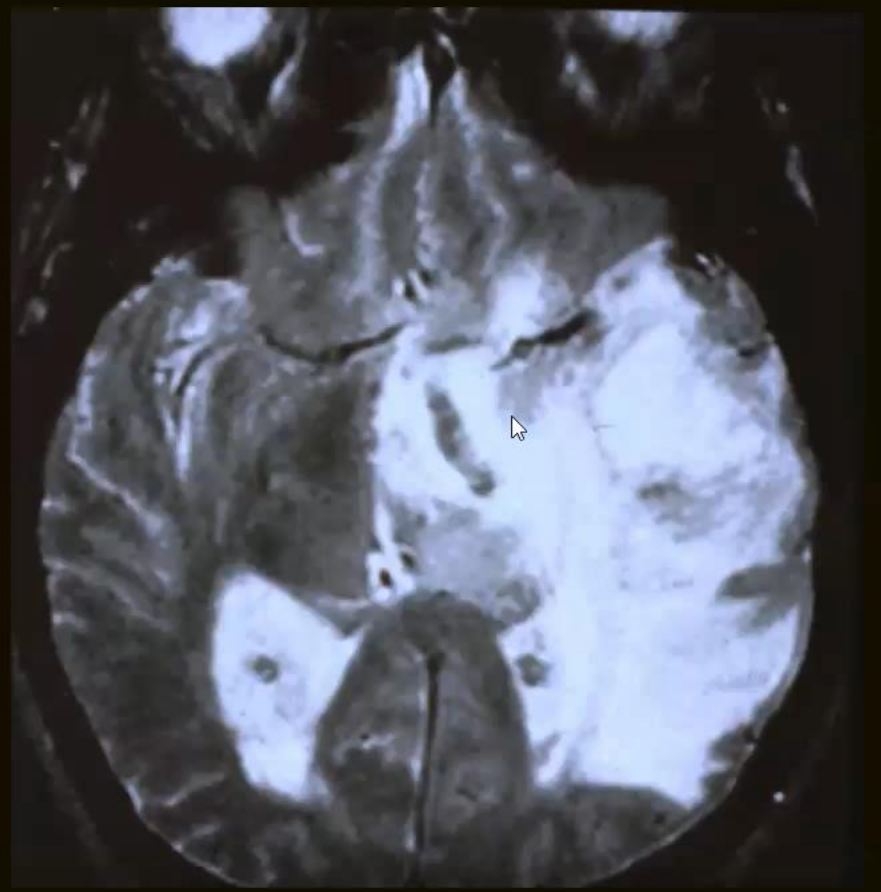
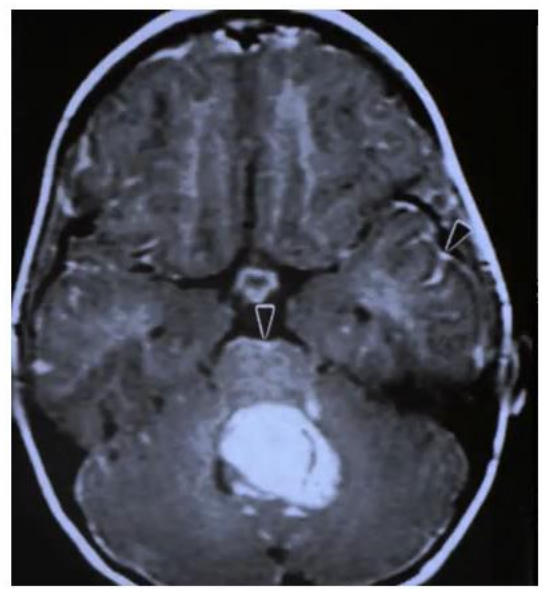






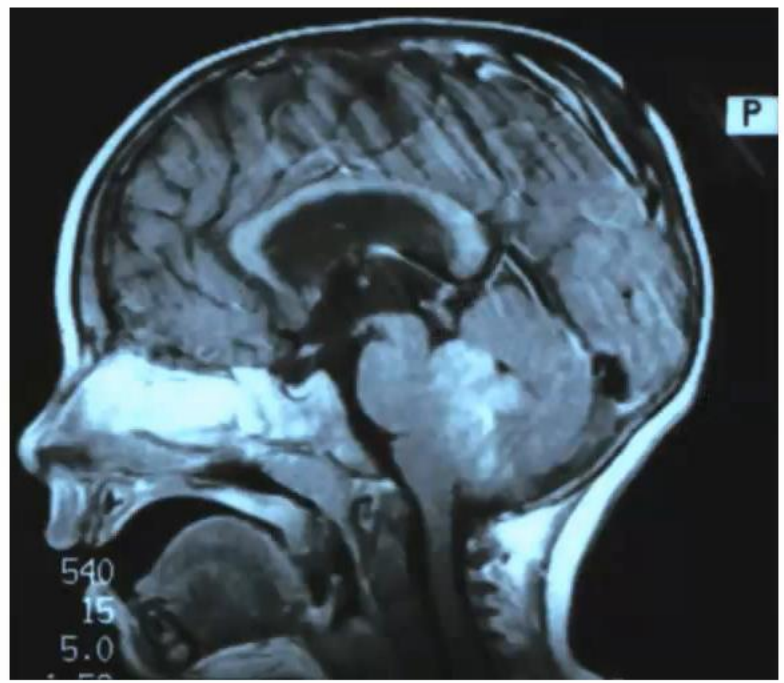
Medulloblastoma

- Location: posterior fossa (PNET)
- Small blue round cell tumor
- Treatment: surgery/radiation/chemotherapy
- Prognosis: 85% survival (non metastatic)
  50% survival (metastatic)



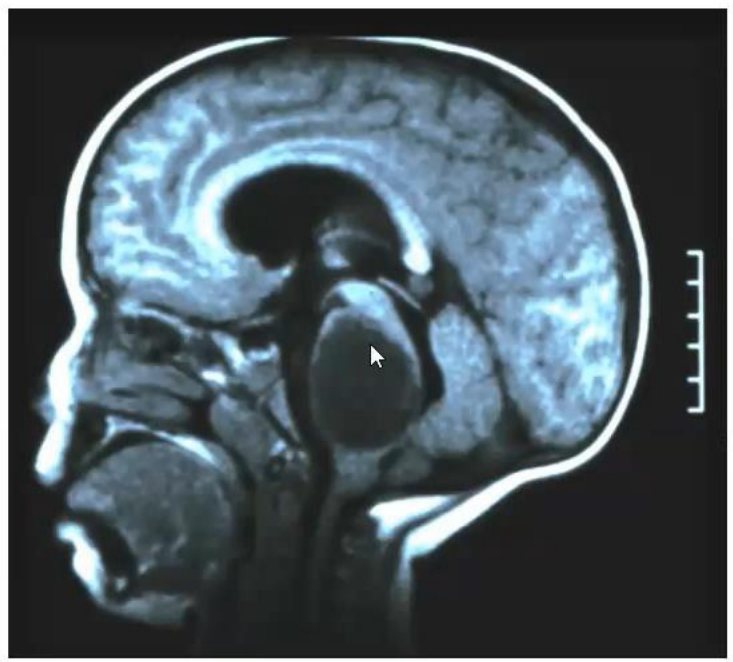
Ependymoma

- Site: ventricular lining
- Treatment: surgery and radiation
- Prognosis: 50-60% if fully resected



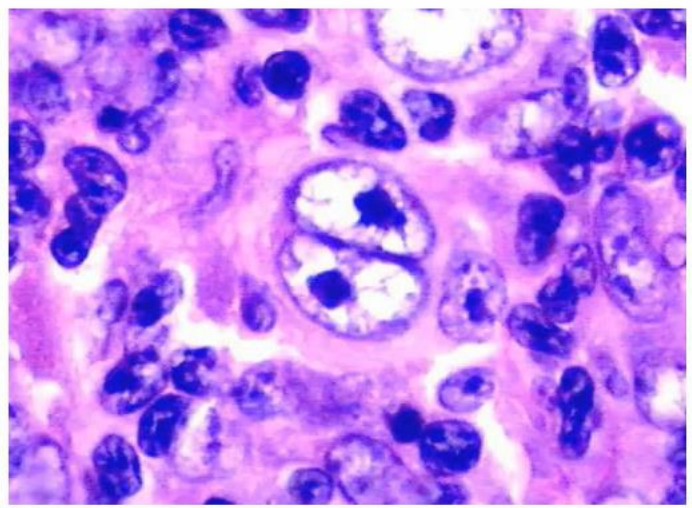
Brain stem glioma

- Highly aggressive tumor
- Treatment: radiation
- Progress in about 12 months



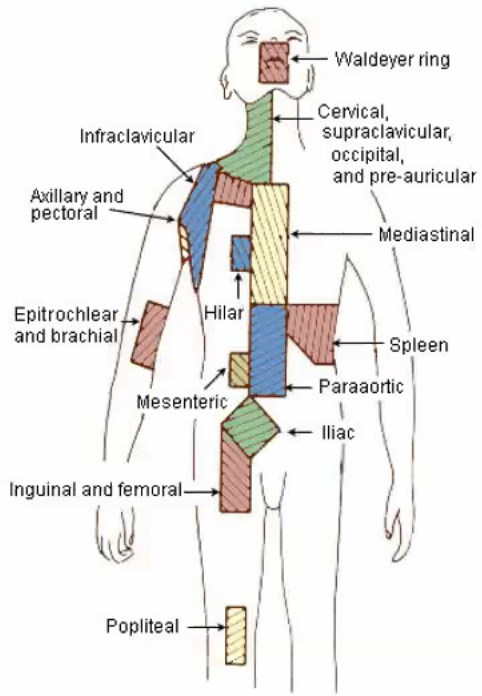
Case

A 10 year old boy presented with right supraclavicular lymphadenopathy. On examination, there is 5 cm non tender lump. Lymph node biopsy showed abnormal cells.



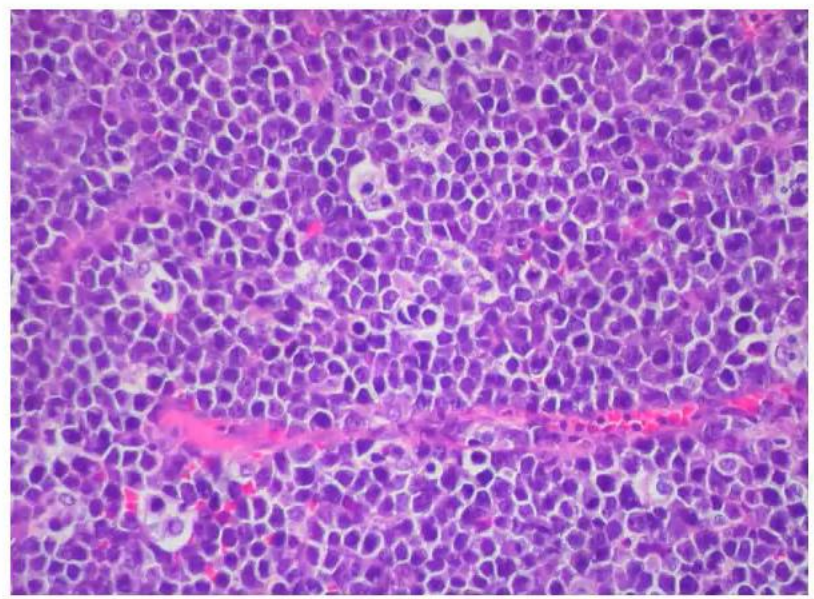
Hodgkin Lymphoma

- Bimodal: 15-34 years and after 50 yr.
  - Rare under the age of 5 years
- Ann Arbor staging
- B symptoms:
  - Fever (>38 C) usually > 3 consecutive days
  - Unexplained weight loss of 10% - preceding 6 months
  - “Drenching” night sweats
- Workup:
  - Labs: CBC, ESR, LDH, uric acid, LFT, Renal
  - Biopsy of the lymph node
  - Bone marrow biopsy (bilateral)
  - CT scan/PET scan
- Treatment:
  - 90-95% of all children can be cured
  - Chemotherapy +/- radiotherapy
  - Aim is to minimize late effects



Case

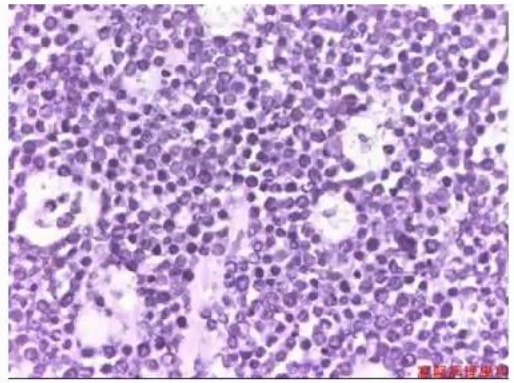
An 8-year-old male presents with a one week history of intermittent abdominal pain, vomiting and gastrointestinal bleeding. Physical examination showed right lower quadrant tenderness. CT demonstrates an ileocecal mass and intussusception. Pathology is shown in the figure.



Burkitt Lymphoma

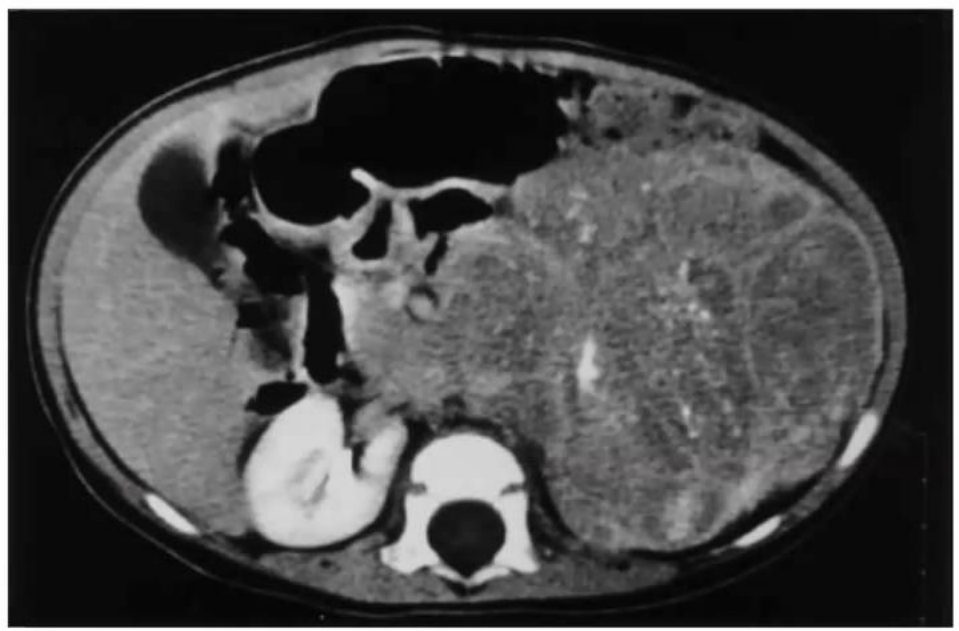
Burkitt lymphoma:

- Mature B-cell
- *C-MYC* +ve
- Abdominal disease most common presentation
- Head & neck second most common site
- Extranodal disease very common
- Almost all Burkitt lymphoma is associated with EBV in endemic Africa
- Very rapidly growing (18-24 hr)
- Treatment: chemotherapy
- Tumor lysis syndrome and SVC syndrome are frequent



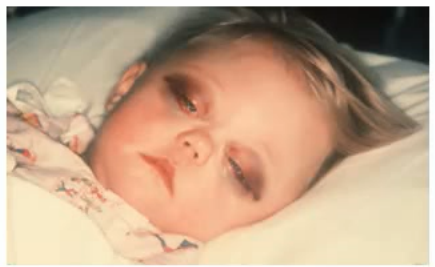
Case

A one year old male infant was discovered by his mother to have abdominal mass. On your assessment, there is abdominal mass that crosses the midline. CT scan showed large calcified mass as shown in the figure. Urine VMA and HVA are high.



Neuroblastoma

- Second most common solid neoplasm in childhood
- Originates from neural crest tissue (sympathetic nerve pathway)
- Median age of diagnosis is 22 months
- Clinical Presentation:
  - Asymptomatic mass (e.g. abdomen or chest)
  - Horner's Syndrome
  - Spinal Cord Compression (medical emergency)
  - "Racoon eyes"
  - Systemic symptoms (hypertension,intractable diarrhea (VIP), opsoclonus/myoclonus)
  - Bone pain
  - Skin lesions
- Work up:
  - Urine catecholamine levels (VMA/HVA)
  - Imaging (CT/MRI, CxR, MIBG)
  - Biopsy: MYCN
- Treatment:
  - Low risk: Surgery +/- chemotherapy
  - Intermediate risk: surgery + chemotherapy
  - High risk: High dose chemo/ autologous stem cell transplant + surgery + radiation+ immunotherapy



Wilms tumor

- Most common primary malignant renal tumor of childhood
- 5-10% of patients have bilateral tumors
- Median age at presentation: Unilateral 44 months Bilateral 31 months
- Clinical features: asymptomatic abdominal mass/hypertension/hematuria/pain
- Associated anomalies:
  - WAGR syndrome (wilms tumor, aniridia, genitourinary malformation, mental retardation)
  - Hemihypertrophy and Beckwith-Wiedemann syndrome
- Workup:
  - CBC, renal and liver function tests
  - CT abdomen and chest
- Treatment:
  - Surgery + chemotherapy +/- radiation

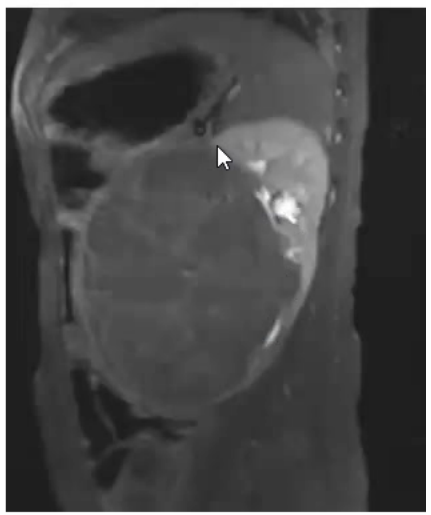
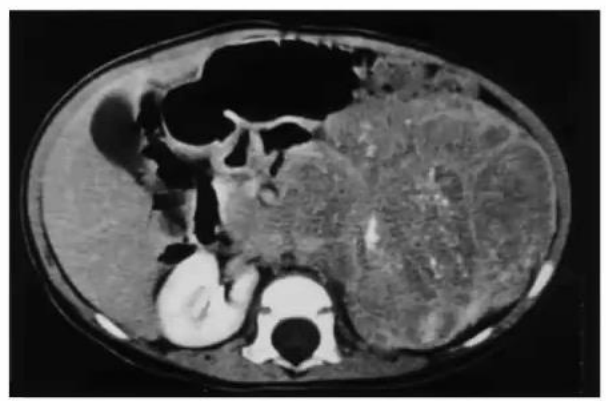
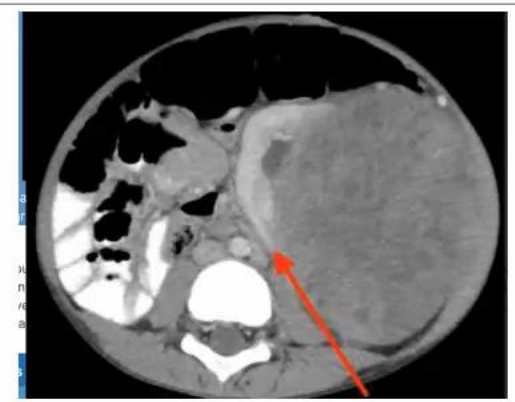


Table 5 Summary of key differences between abdominal neuroblastoma and Wilms tumour

Parameter	Neuroblastoma	Wilms tumour
Age	Younger age group: < 2 years of age commonly	Slightly older age group : peak 3 - 4 years of age
Presentation	Painful abdominal mass	Painless abdominal mass
Calcification	Calcification very common: 80-90%	Calcification uncommon: 10%
Tumour composition	Solid mass lesion, rarely cystic components on US	Often cystic components at US
Tumour margin	Poorly marginated mass that may extend up into chest Adrenal NBL displaces the kidney	Well circumscribed mass - claw sign demonstrating it arises from the kidney
Vessel involvement	Encases vascular structures but does not invade them - elevates the aorta away from the vertebral column	Displaces adjacent structures – invades the vasculature with extension into renal vein/IVC
Metastatic sites	Bone/bone marrow (common)	Lung (common)
	Liver	Liver
	Lung/pleura	Local lymph nodes

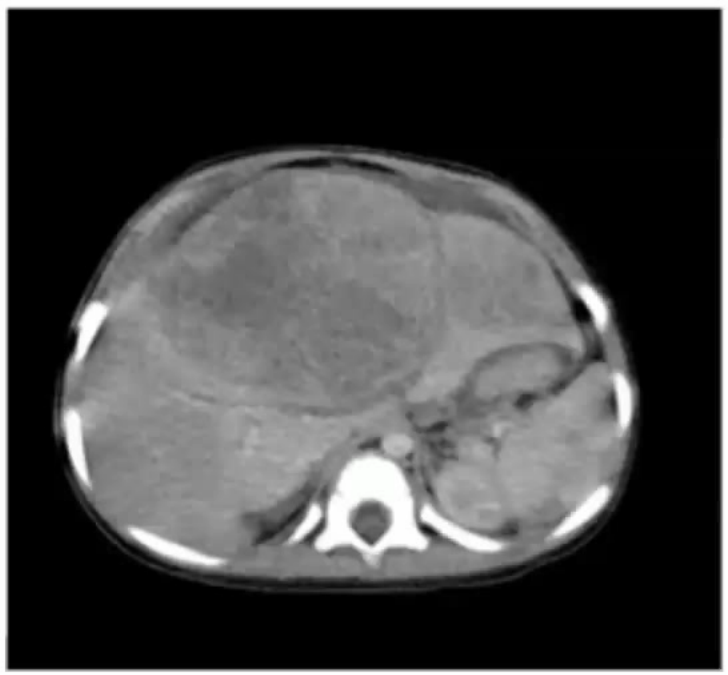




Dumba et al. Cancer Imaging (2015) 15:5

Case

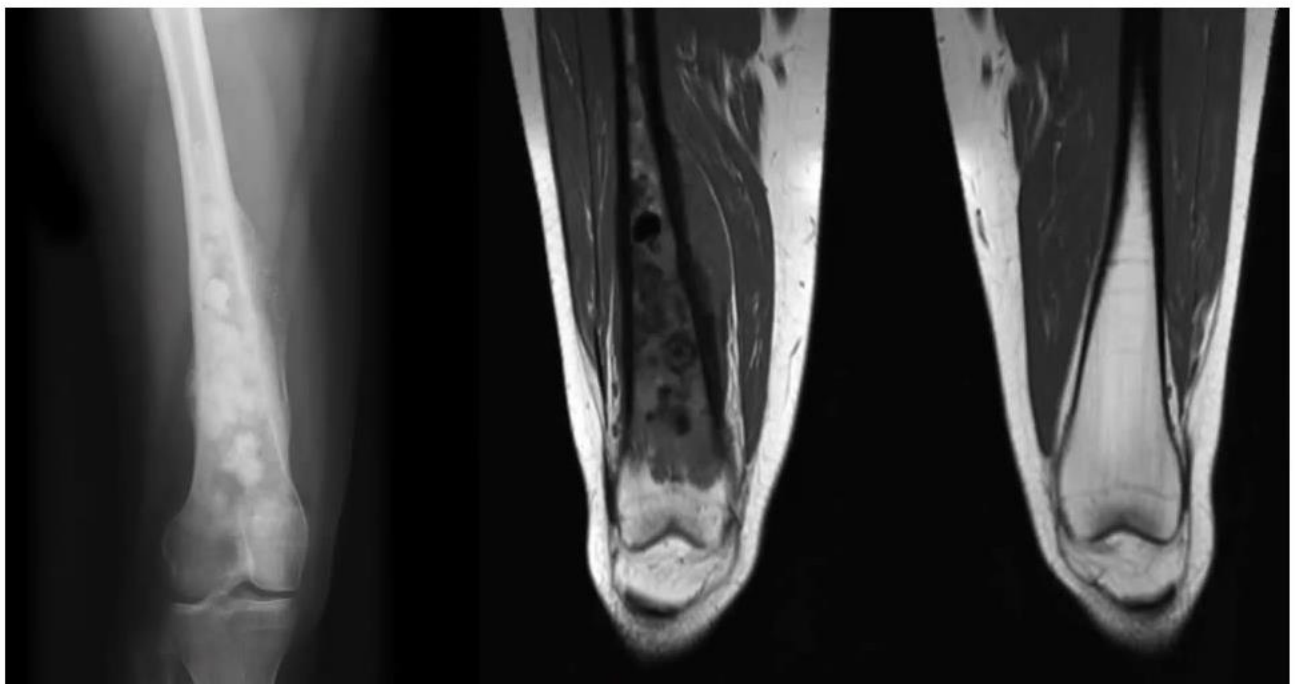
An 18-month-old boy presents with abdominal distension and hepatomegaly. CT scan demonstrates a large heterogeneously enhancing lesion in the liver and ascites. There is increase in serum α-fetoprotein and thrombocytosis.



- Hepatoblastoma is the most common type of hepatic cancer in children.
- A rare pediatric tumor
- Age: usually < 3 years

Case

A 12 year old boy who is previously healthy presented with severe right thigh pain after he sustained minimal trauma. The pain awake him at night and is not responding to over the counter pain medications. Imaging is shown in the figure.



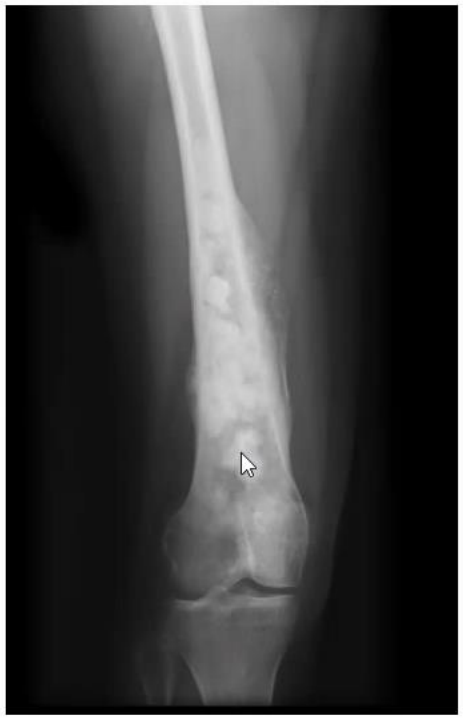


TABLE 1

Characteristics of Various Bone Cancers

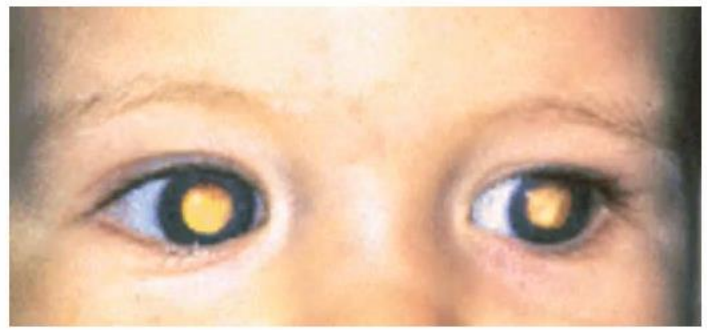
Cancer	Malignant cell origin	Patient demographics[2,3]	Locations (in order of common occurrence)[8]	Sites of metastases
Osteosarcoma	Mesenchymal cells, osteoblasts	Typically five to 25 years of age (median age: 16 years in males, 12 years in females); rare after 60 years of age More common in males and in blacks	Metaphyses of long bones: Distal femur Proximal humerus Proximal tibia Pelvis Skull	Bone, lung
Ewing sarcoma	Unconfirmed; thought to be from primitive stem cells or neural crest cells	Median age: 15 years Slightly more common in males and in whites and Asians	Diaphyses of long bones: Proximal femur Proximal humerus Proximal tibia Pelvis Ribs Scapula	Bone, lung
Chondrosarcoma	Chondrocytes	Typically 40 to 75 years of age Slightly more common in males; no racial predominance	Pelvis Proximal long bones Ribs Scapula Vertebrae	Lungs

Information from references 2, 3, and 8.

Codman triangle: triangular area of new subperiosteal bone that is created when the tumor raises the periosteum away from the bone. Seen in primary bone tumors.

Case

A three month old infant presents with leukocoria and strabismus as shown in the figure.



Retinoblastoma

- **Non-hereditary, unilateral:**
  - 2-3 yrs of age
- **Hereditary, bilateral:**
  - Germline mutation of RB1
  - 6-18 months of age
- **Workup:**
  - Examination under anesthesia
  - MRI orbit and brain
  - Bone scan, BM, and CSF in advanced disease
- **Treatment:**
  - Focal therapy +/- chemotherapy +/- Enucleation