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.

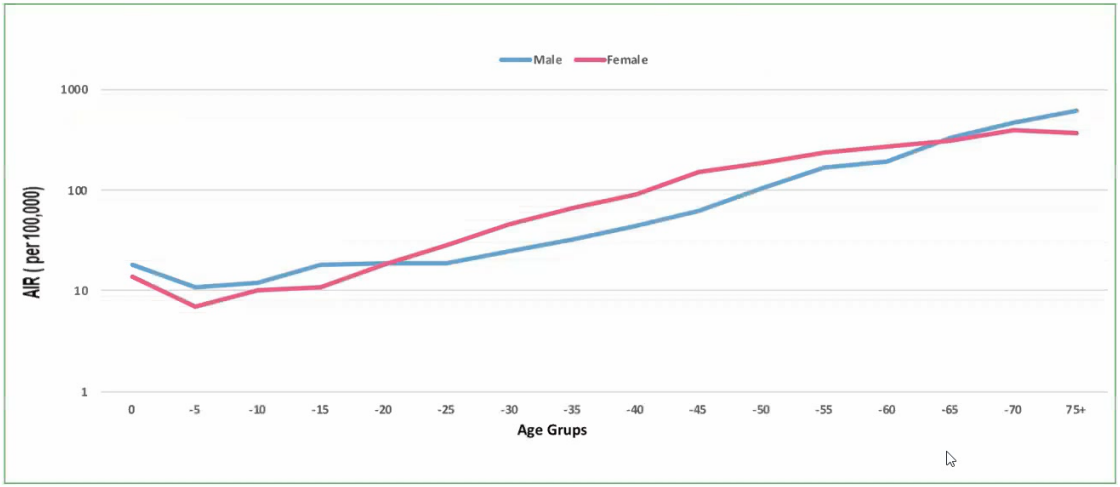
When to suspect childhood cancer

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 Or 1 in every 10,000.

Epidemiology- Saudi Arabia

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



Up to the ages 14-15 age specific incidence rate is around 10 per 100,000 and as the persons ages the risk of cancer goes up all the way to more then hundred around the age of 40.

Epidemiology- Saudi Arabia

There is a big difference between the pattern or type cancer that we see in adults compared to pediatrics:

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 The most common childhood cancer	255	35.0
Brain, CNS	89	12.2
NHL	89	12.2
Hodgkin's lymphoma	66	9.1
Kidney Wilms' tumor	43	5.9
Bone Ewing's sarcoma or osteosarcoma	32	4.4
Adrenal gland Neuroblastoma	28	3.8
Eye Retinoblastoma	26	3.6
Connective,Soft tissue Rhabdomyosarcoma	23	3.2
Ovary germ cell tumor	12	1.6

So the pattern of cancer is different depending on the age

National Health Information Center Saudi Cancer Registry

Causes of Childhood Cancer

The most common question the parents will ask when we diagnose the child with cancer is why?
It's a reasonable and an important question but unfortunately in 90% of the cases we don't know.

- Unknown in majority of cases.
- Cancer predisposition syndromes: Explains about 5-10%
  - Examples:
    - Down syndrome
    - Neurofibromatosis
    - Fanconi anemia
    - Li-Fraumeni syndrome (germline *P53* mutation)
- Environmental factors: Depending on the region or area the child is living in
  - Ionizing radiation
  - Infectious etiology EBV Epstein-Barr virus
  - Chemical exposures e.g. pesticides, benzene
- Prior treatment:
  - Chemotherapy (e.g. etoposide or alkylating agents)
  - Radiotherapy e.g. Children who receive chest radiotherapy for Hodgkin lymphoma are at increase risk of breast cancer in adulthood.

Patient receiving etoposide or alkylating agents like cyclophosphamide or any phosphamides are at risk of secondary cancer such as acute myeloid leukemia.

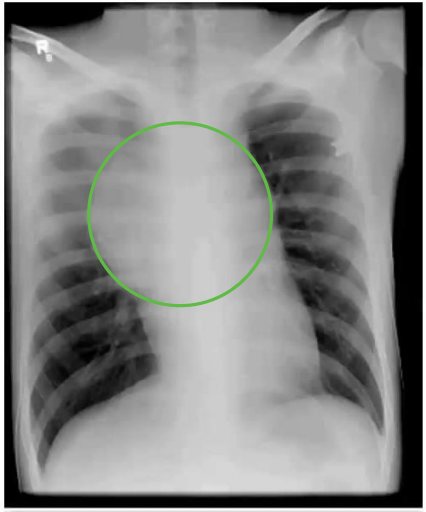
Case

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.

Here we see widening of the mediastinum

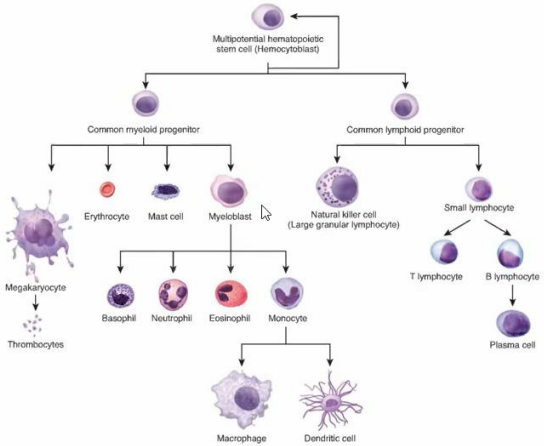
Ddx: lymphoma or leukemia.

Diagnosis: leukemia; because of the high WBC count and presence of blast in peripheral blood.



Leukemia

- Types:
  - Acute lymphoblastic leukemia (ALL) Number 1 in children
  - Acute myelogenous leukemia (AML) Number 2, but it's less frequent than ALL
  - Chronic myelogenous (CML) Rarely seen in children, mostly in adults.



Leukemia

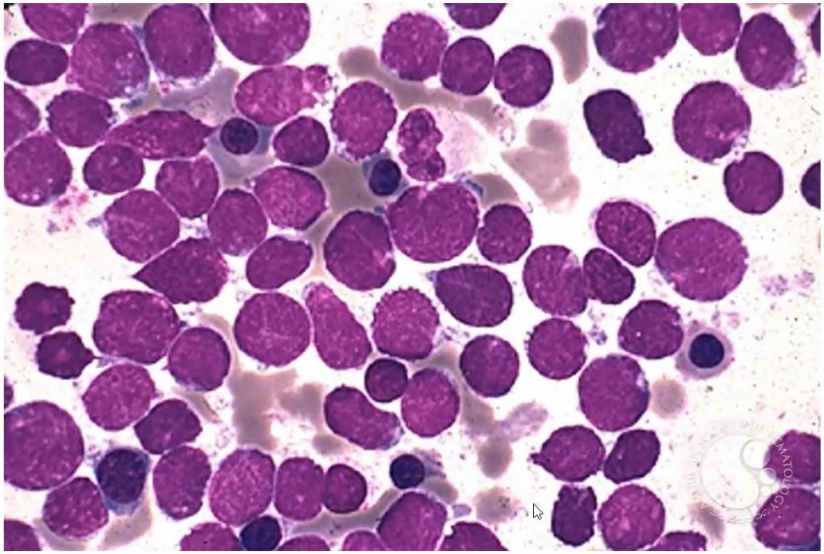
- Symptoms:
  - Lethargy
  - Fever/Infection
  - Bone/Joint pain
  - Bleeding
  - Anorexia
  - Abdominal pain
  - CNS signs If there is leukemia in the CNS
- Signs: Because of the bone marrow infiltration
  - Pallor
  - Hepatosplenomegaly
  - Petechiae/Purpura
  - Lymphadenopathy.
  - Testicular involvement

Symptoms can over lap with many other symptoms from different diseases, like disease in infection or rheumatology.

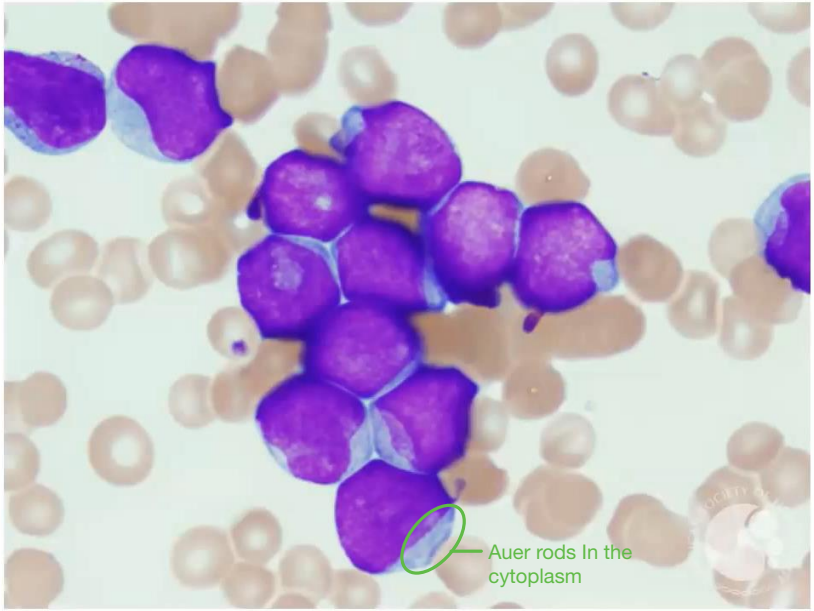
Leukemia

- Workup:
  - CBC and differential + peripheral blood smear is essential
  - LFT, electrolytes (K, Ph), uric acid, LDH Are important because of the risk of tumor lysis syndrome.
  - CxR We always do CXR for any new leukemia mainly to check for any mediastinal mass (because they will probably go for sedation or anesthesia so we need to make sure there is no mediastinal mass before they proceed)
  - Bone marrow study: **Gold stander**
    - Morphology
    - Flow cytometry To define the antigen on the surface of the leukemia cells.
    - Molecular studies e.g. BCR-ABL
    - Cytogenetics e.g. t (9;22)

    To further characterize the risk stratification of the leukemia
  - Lumbar puncture To check if there is CSF involvement.



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 Has the T cell marker
  - CD2, CD3, CD5, CD7, CD1a, TdT
- AML Has the myeloid marker
  - CD13, CD15, CD33, CD117, MPO, HLA-DR, CD34

Myeloperoxidase (MPO)

Prognostic Factors in ALL

- NCI Risk Grouping
  - Standard risk
    Std Risk: Age 1-9 yr and WBC* <50,000/μl
  - High Risk: Age <1 or ≥ 10 yr and/or WBC* ≥ 50k
- Immunophenotype B cells is better than T, and T is better then the myeloid.
- Cytogenetics The presence of Philadelphia translocation is a high risk feature and there are other cytogenetic features that help in the prognosis.
- Response to induction therapy Response at the end of the month to induction therapy which will be mainly of steroids and chemotherapy, we repeat the bone marrow and decide weather the patient responded will or not
- CNS disease is a poor prognostic factor.

*Initial WBC

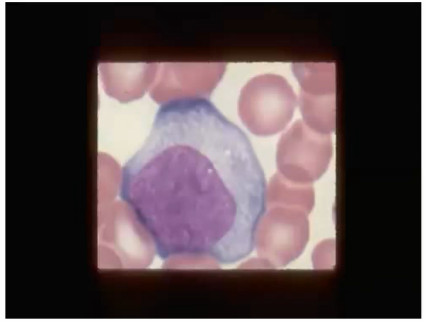
Leukemia

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

In infectious mononucleosis there is atypical lymphocytes that can mimic Leukemia and can mistakenly be labeled as leukemia

Usually In Immune thrombocytopenic purpura there is no hepatosplenomegaly or lymphadenopathy.

Juvenile rheumatoid arthritis: in these cases we do bone marrow biopsy because bone and joint pain can be common presentation of leukemia.

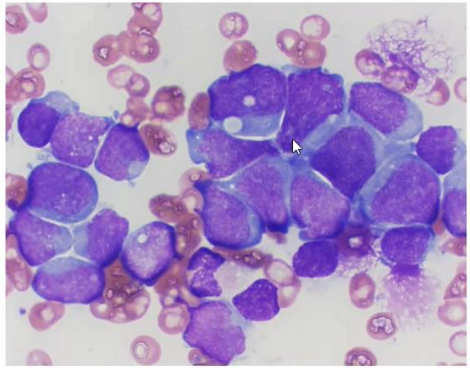


In pertussis they can have very high WBC count especially in infancy and can be confused with leukemia.

Leukemia

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

Neuroblastoma and rhabdmyosarcoma can infiltrate the bone morrow and mistakenly labeled as leukemia cells

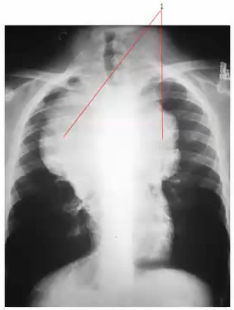


Leukemia

The most important thing is the emergency management. Will be discussed later

- Treatment:
  - Supportive care:
    - Tumor lysis syndrome
    - Hyperleukocytosis
    - Superior vena cava syndrome
    - Infections
  - **Chemotherapy** Is the main treatment
  - Cranial radiation if CNS positive Rarely used
  - Hematopoietic stem cell transplant (rarely) Reserve transplant for relapse cases

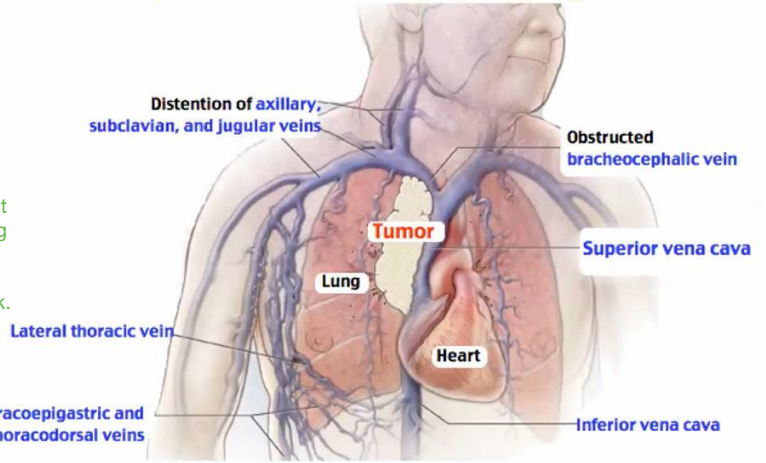
-Now there are more Immune therapy options



Mediastinal mass

Superior Vena Cava Syndrome

The case we dissed initially we call it superior vena cava syndrome because you saw the mediastinal mass pushing on the superior vena cava (in the CXR we saw earlier there is widening of the mediastinum and tumor pushing on the superior vena cava) causing congestion of the face and upper limb vessels and it also cause SOB, the child will be leaning forward to relive the pressure effect on the airway and the vessel, so you shouldn't force them to lay on their back.



Venous flow to the heart is reduced because of the compression if the mass so it's contraindicated to intubation them. because when you sedate them you may decrease venous return to the heart and the patient will collapse and die so we try our best to avoid anesthesia , and try to diagnose them as quickly as possible so we can start to rapidly to reduce the mass effect in the chest.

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

Causes:

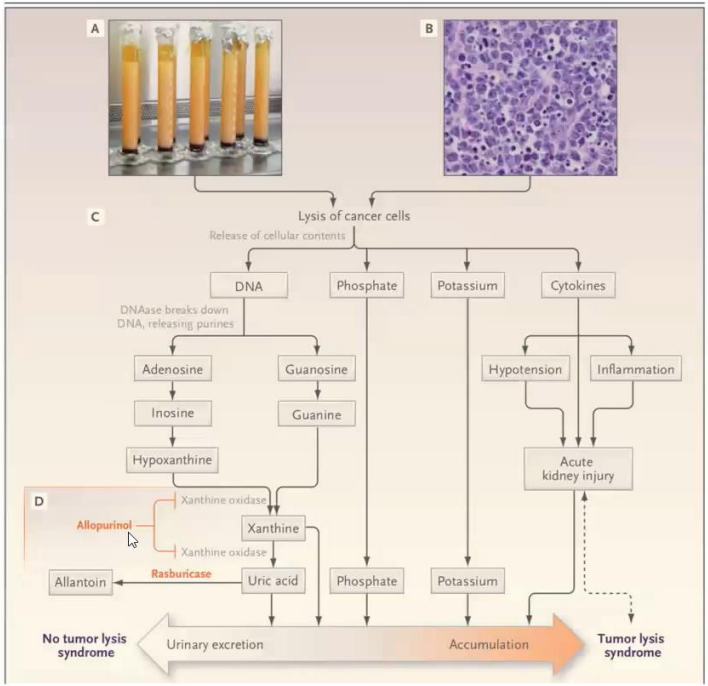
- Tumors: T-ALL, NHL, thymoma, teratoma
- Others: TB, thrombosis

It can happen with B-ALL but it more with T cell.

NHL>HL.

In adults thymoma and teratoma can all cause superior vena cava syndrome.

- When you have lysis of the cancer cells because they are multiplying quickly or because of the effect of the initial therapy it release DNA, phosphate, potassium and cytokines.
- DNA will eventually be converted to uric acid and phosphate and potassium will accumulate, so when we do tumor lysis lab we check for all of these.
- For the uric acid we give allopurinol (oxidase inhibitor that decreases formation of uric acid), if the volume leukemia or lymphoma cells is huge then allopurinol alone might not be enough so we give rasburicase (rasburicase clear the uric acid it's not an enzyme inhibitor so it will give quick drop in uric acid, the disadvantage of it is if the patient G6PD we can can't give it).
- If we don't treat the uric acid it will precipitate in the kidney and cause renal failure.
- Potassium can cause life threatening hyperkalemia, so we give kayexalator and limit the potassium and phosphate intake .
- For phosphate we give phosphate binder.
- And the first few week we check tumor lysis lab more frequently



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?

- Basically this child is coming with febrile neutropenia.
- Give broad spectrum Abx to cover pseudomonas and gram -ve, if there is cellulitis or evidence of line infection we also cover gram +ve and consider giving them vancomycin.
- Febrile thrombocytopenia is another oncological emergency and we always ask the ER to administer antibiotics within 15 to 20 minutes from showing to ER, because we can loose the patient if they are not given stat, so always the first dose has to be given right away

This historical now a days any one who comes with fever we start therapy right away we don't wait for culture

Febrile neutropenia:

- High mortality when antibiotics started after blood cultures became positive.

We use broad spectrum because:

- 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

And hypotensive we have to give both gram -ve and +ve coverage.

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]	25	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	52
Pseudomonas aeruginosa	530	R	R	R	75	76	62	77	82	---	94	85	R	R
Salmonella spp.	36	67	---	---	100	100	100	88	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

- Here an e.g from 2019 if you see the pseudomonas : Piperacillin-Tazobactam (TZP) (77%) alone is not enough we will miss 23% of pseudomonas cases, as for Amikacin it has (94%) sensitivity which is very good, so in general we combine them now.
- We use 2 Abx TZP and Amikacin, but this is after discussing with ID and with microbiology lab.
- if you see in the past we used to give gentamicin instead of amikacin but now with resistance evolving you can see gentamicin is not as good as Amikacin. In general for gram negative Amikacin is better

J Clin Oncol 35:2082-2094

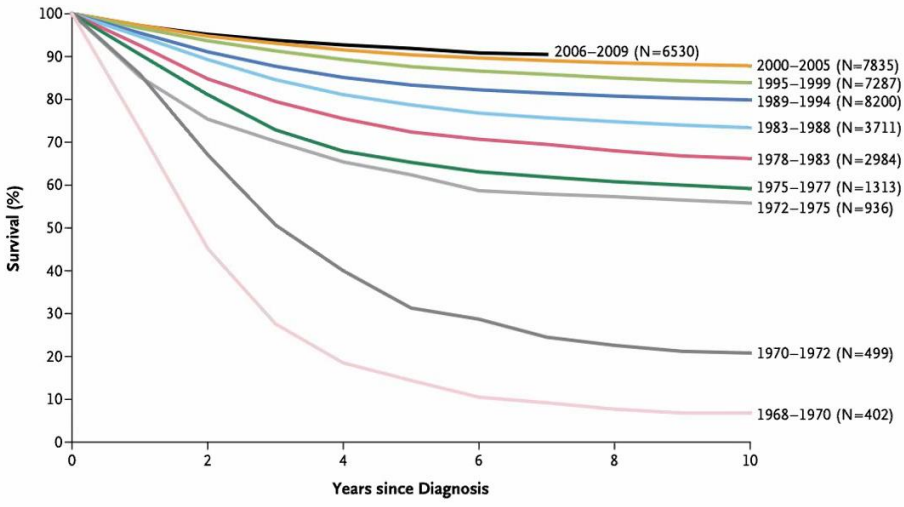


Figure 1. Overall Survival among Children with Acute Lymphoblastic Leukemia (ALL) Who Were Enrolled in Children's Cancer Group and Children's Oncology Group Clinical Trials, 1968–2009.

- The good part is that survival in ALL which is the most common here is excellent. It's a curable disease and most pt. do very well.
- AML is not common in children and the outcome is still about 50-60%.

Brain tumors

Brain tumors in children:

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

Brain tumors

- Clinical presentation: It depends on where is the tumor and wither it's causing pressure effect and increase in ICP or not.
  - General and non-localizing symptoms

    (e.g. headache, vomiting, behavioral changes, learning problems, weight loss/gain) Weight gain depending on the hypothalamus or not
  - Increased intracranial pressure

    (e.g. irritability, vomiting, bulging fontanelle, papilledema, parinaud syndrome) look at the upper gaze, it doesn't follow normally
  - Localizing signs Especially in the cerebellum like mudlloblastoma (ataxia -> medulloblastoma)

    (depend on tumor location e.g. ataxia)

Brain tumors

- Workup:
  - Brain MRI/Spine Because spine can be involved
  - CSF cytopathology If not contraindicated
  - Surgical biopsy or resection is the only way to confirm the diagnosis
  - CSF tumor markers (B-HCG/AFP) if germ cell tumor is suspected

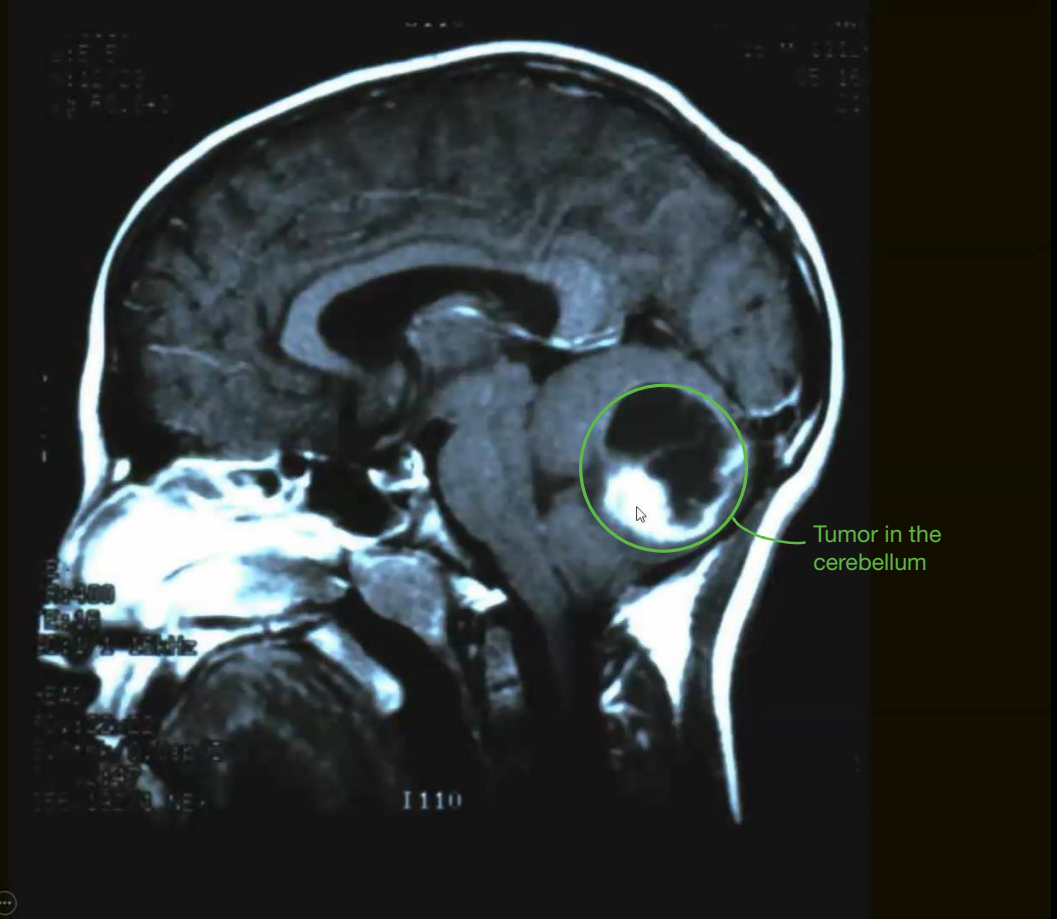
Brain tumors

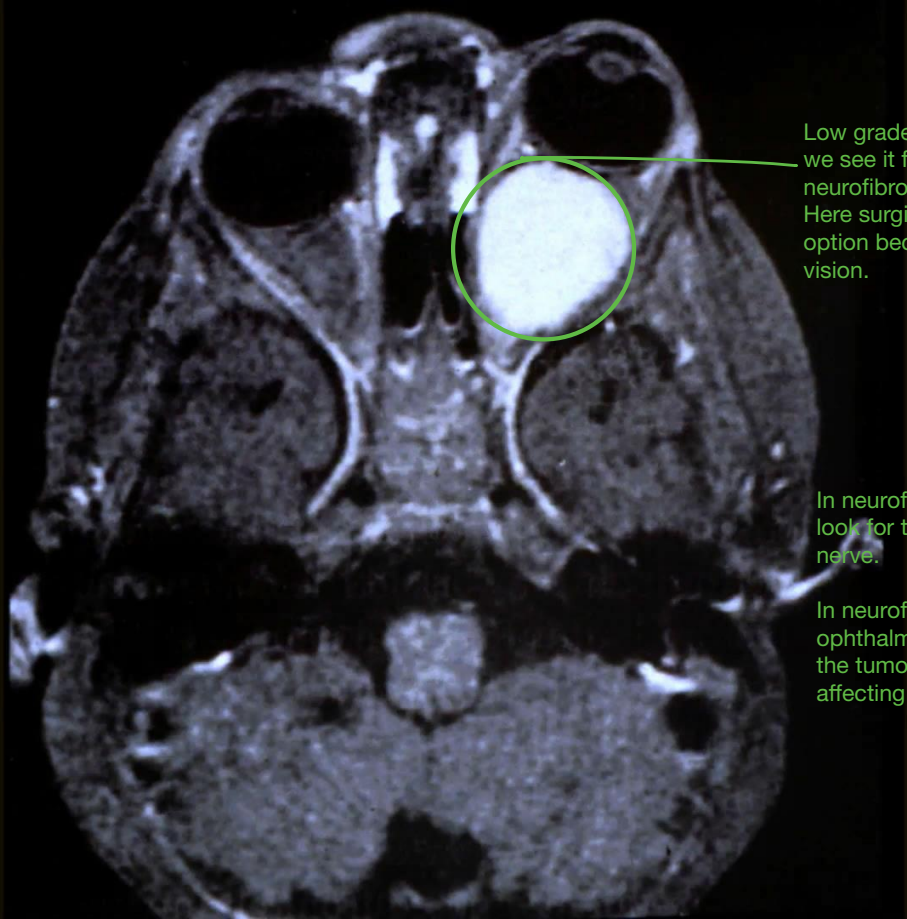
- Treatment: Depends on the type of the tumor
  - Surgery The better the the resection the better the outcome.
    - Gross total resection if feasible
  - Radiotherapy
  - Chemotherapy

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)


Tumor in the
cerebellum
I110

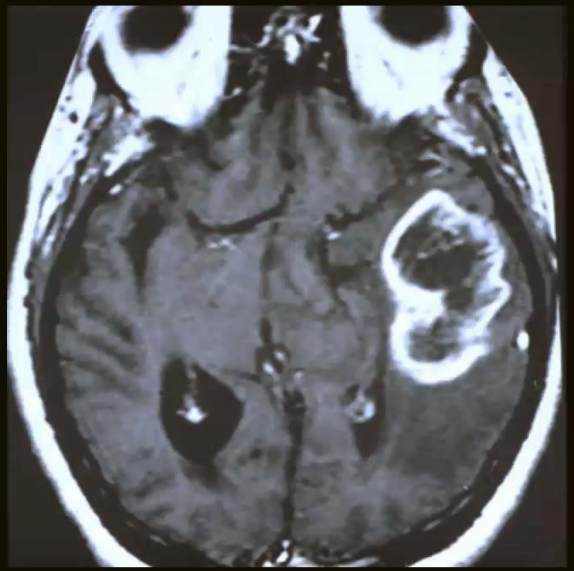


Low grade glioma in the optic nerve, we see it frequently in neurofibromatosis patients.
Here surgical management is not an option because patient may loose his vision.

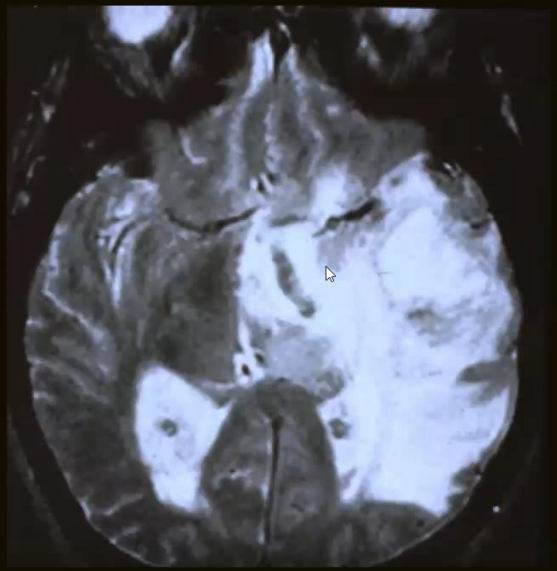
In neurofibroma we do annual MRI to look for tumors especially in the optic nerve.

In neurofibromatosis we do annual ophthalmological examination even if the tumor is small to see if it's affecting the visual field or not.

Here you can see the difference between the previous one (the previous slide) which was well demarcated and looks relatively benign compared to this one



This is the GBM which is grade 4, very infiltrative and impossible to have full resection most of the time.

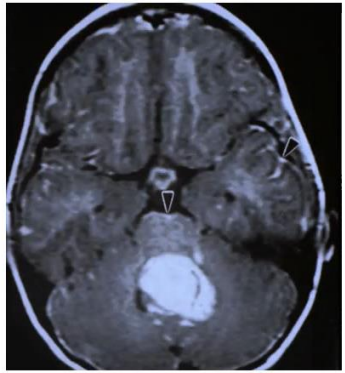


Medulloblastoma

Common malignant tumor in children

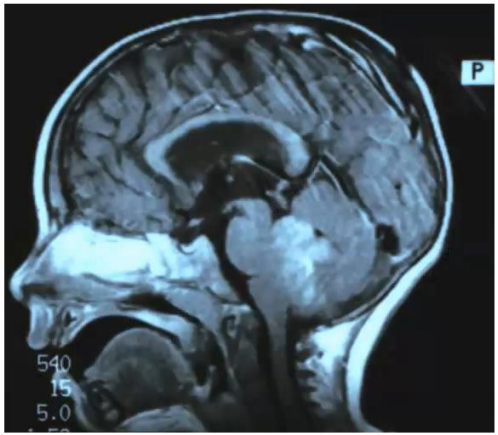
- Location: posterior fossa (PNET) Can spread to the spine
- Small blue round cell tumor
- Treatment: surgery/radiation/chemotherapy
- Prognosis: 85% survival (non metastatic)
  50% survival (metastatic)

The issue is if they receive radiation at a younger age they usually have behavioral and learning prombles later in life.



Ependymoma

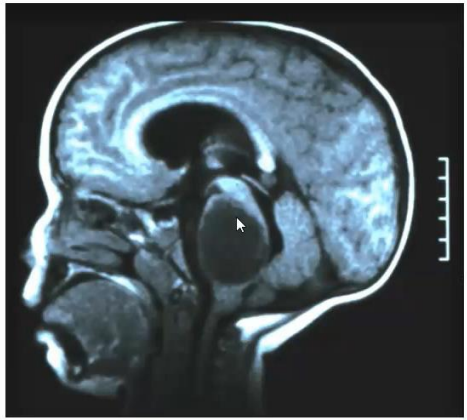
- Site: ventricular lining
- Treatment: surgery and radiation
- Prognosis: 50-60% if fully resected



Brain stem glioma

- Highly aggressive tumor And it forms in the pons
- Treatment: radiation
- Progress in about 12 months

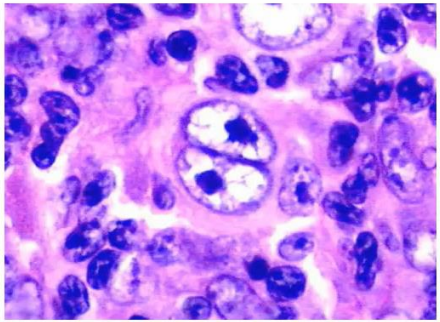
You cannot resect, chemo doesn't benefit and they usually progress very quickly after stopping the radiation.



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.

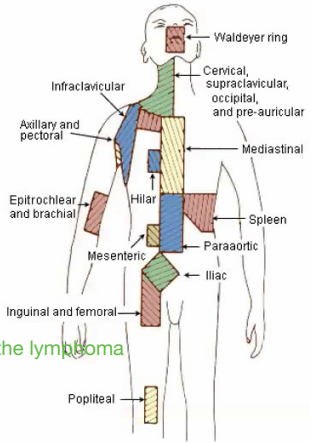
Reed sternberg cell in hodgkin lymphoma



Hodgkin Lymphoma

If we see lymphoma in children younger then 5 years we always question if the child has immunodeficiency, because some immunodeficiency can cause immune disregulation and increase the risk of lymphoma especially if triggered by EBV infection

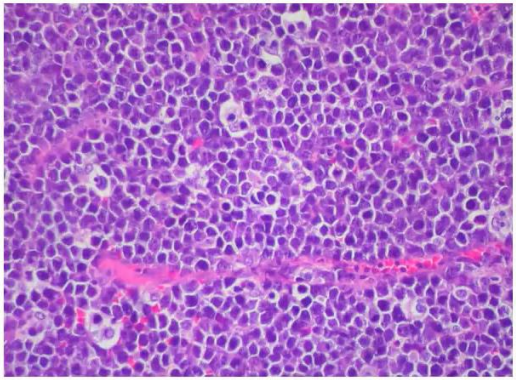
- Bimodal: 15-34 years and after 50 yr.
  - Rare under the age of 5 years
- Ann Arbor staging
- B symptoms:
  - Fever (>38 C) usually > 3 consecutive days
  - Unexplained weight loss of 10% - preceding 6 months
  - "Drenching" night sweats
- Workup:
  - Labs: CBC, ESR, LDH, uric acid, LFT, Renal
  - Biopsy of the lymph node
  - Bone marrow biopsy (bilateral) To make sure it's not involved by the lymphoma
  - CT scan/PET scan Gold standard
- Treatment:
  - 90-95% of all children can be cured Rarely relapse and even if they relapse we do salvage therapy.
  - Chemotherapy +/- radiotherapy Surgery has no role in this type of tumor
  - Aim is to minimize late effects



Because of the excellent outcome new protocols are trying to minimize long term side effects of any intervention that we do.

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.



starry sky presentation in Burkett lymphoma

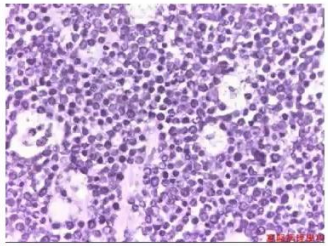
Burkitt Lymphoma

Under the group of non-Hodgkin lymphoma and Burkett in children is a common one

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

In contrast to Hodgkins which doesn't usually involve extra nodal disease



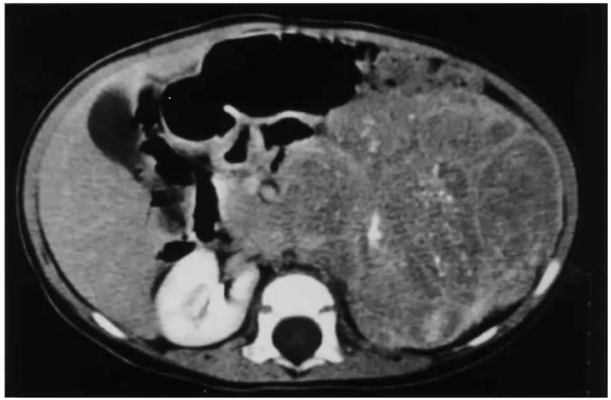
The difference between Hodgkin and non-Hodgkin:

- In **Hodgkin**: the family tells you that their child had lymph nodes increasing slowly for the last 3-6 months and they thought it's nothing (slowly increasing in size).
- In **Burkett** we approach it as an emergency because it can increase in size very quickly, especially if it's in the mediastinal area it can cause significant compression on their airway and can be life threatening, we try our best to do quick diagnosis so we can start therapy.
- Because it's rapidly growing the risk of tumor lysis syndrome is even higher than in leukemia and this is why it's almost routine to give rasburicase not only allopurinol because we can't control the hyperuricemia
- Superior vena cava syndrome is also frequent because of the of the reasons I mentioned above.

Case

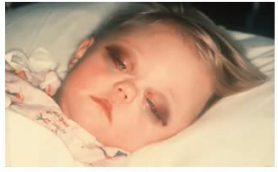
A one year old male infant was discovered by his mother to have abdominal mass. On your assessment, there is abdominal mass that crosses the midline. CT scan showed large calcified mass as shown in the figure. Urine VMA and HVA are high.

Dx: neuroblastoma



Neuroblastoma

- Second most common solid neoplasm in childhood
- Originates from neural crest tissue (sympathetic nerve pathway) Mostly in the adrenals
- Median age of diagnosis is 22 months
- Clinical Presentation:
  - Asymptomatic mass (e.g. abdomen or chest) Most common
  - Horner's Syndrome
  - Spinal Cord Compression (medical emergency) Comes in the para-spinal area and cause compression
  - "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) CT scan of the head, neck and chest. MIBG because the nuclear materials will be up-taken by the neuroblastoma tissue so it's a very useful way to assess the staging of neuroblastoma
  - Biopsy: MYCN
- Treatment:
  - Low risk: Surgery +/- chemotherapy Low risk and intermediate do very well
  - Intermediate risk: surgery + chemotherapy
  - High risk: High dose chemo/ autologous stem cell transplant + surgery + radiation+ immunotherapy and the outcome is still around 50% , don't do very well.

Wilms tumor

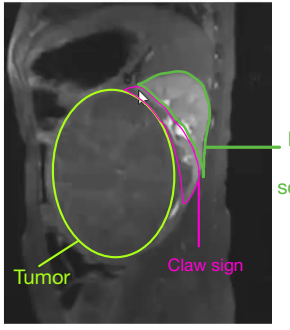
- Most common primary malignant renal tumor of childhood
- 5-10% of patients have bilateral tumors
- Median age at presentation: Unilateral 44 months Bilateral 31 months

  Less then 5 years
- Clinical features: asymptomatic abdominal mass/hypertension/hematuria/pain

  Detected by the mother during diaper change.

  Because of compressions on the blood vessels.
- Associated anomalies:
  - WAGR syndrome (wilms tumor, aniridia, genitourinary malformation, mental retardation)
  - Hemihypertrophy and Beckwith-Wiedemann syndrome

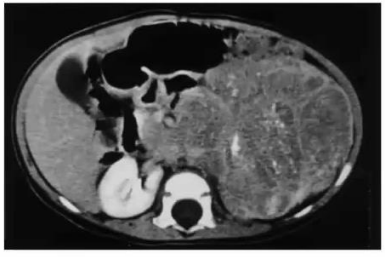
  In ophthalmology when they see a child with aniridia they do abdominal US every 3 months to screen for wilms tumor. In general the risk decreases after 5 years so most screening should be done in the first 5 years.
- Workup:
  - CBC, renal and liver function tests
  - CT abdomen and chest We do CT chest because wilms usually metastasize to the lungs and less likely to other organs.
- Treatment:
  - Surgery + chemotherapy +/- radiation



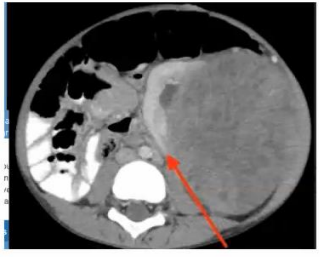
Usually there is no calcification

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



Cross the midline



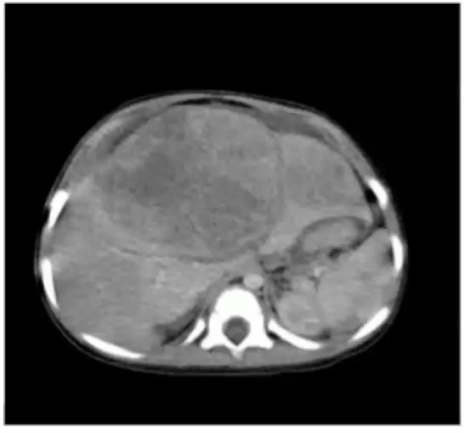
Doesn't cross the midline

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.

Dx: hepatoblastoma

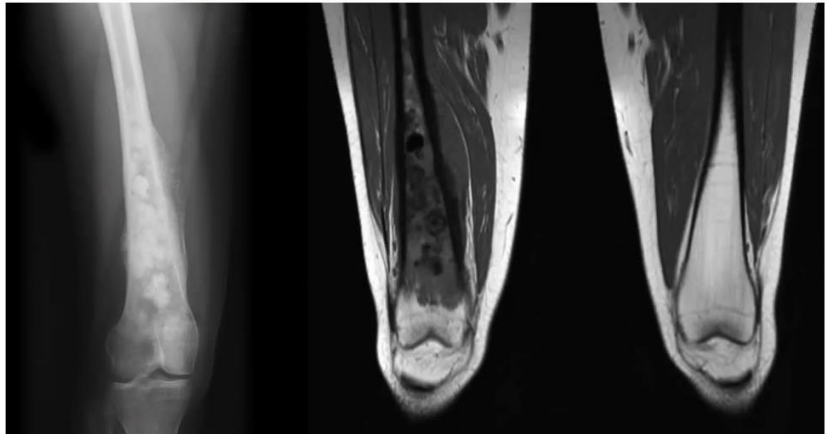


- Hepatoblastoma is the most common type of hepatic cancer in children.
- A rare pediatric tumor
- Age: usually < 3 years

We have to take care if we see thrombocytosis in children, always do Us abdomen because it could be a sign of tumor (and it's this probably because they secrete thrombopoietin)

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.



What makes you worry is that it's a sever thigh pain after minimal trauma and this is frequent when the patient comes with bone tumor. The degree of trauma doesn't explain the severity of the symptoms, and they don't usually respond to over the counter pain medications.
So this is a red flag when you assess a child who has sever bone pain.

Bone tumor can also present without trauma, they will have bone pain.

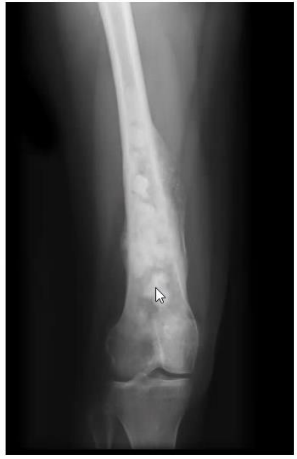


TABLE 1

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.

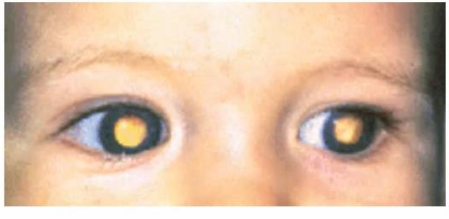
Codman triangle: triangular area of new subperiosteal bone that is created when the tumor raises the periosteum away from the bone. Seen in primary bone tumors.

periosteal Reaction

Case

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

Retinoblastoma



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

This why it's very important to do red reflexes as part of your routine in baby clinic assessment.

To make sure there is no spread beyond the orbit

Enucleation is done if other measures failed because the priority is to save the child no only the eye.