In the name of God

Cancer in Children

Bibi shahin Shamsian. MD

Common Fears

- Fear of pain
- Fear of being alone
- Fear of disappointing parents
- Fear of the unknown
- ……..

Pediatric Oncology

- Hematologic Cancer:
  - Acute & Chronic leukemia
  - Lymphoma: Hodghkin & Non H-Lymphoma

- Solid tumors:
  - Brain tumors
  - Neuroblastoma
  - Wilm's tumor
  - Rhabdomyosarcoma
  - Retinoblastoma
  - Osteosarcoma
  - Ewing's sarcoma
  - Germ cell tumors .
  - ....

Leukemias

- 25–30% of all childhood cancers.
- USA /per year 2500–3,000 children
- ALL: 3–4 cases per 100,000 white children
- AMl 500 new cases in the United States per year
- Peak incidence between ALL ;2 - 5 years of age
- Acute leukemias represent a clonal expansion and arrest at a specific stage of normal myeloid or lymphoid hematopoiesis.
- They constitute 97% of all childhood leukemias

ü Acute lymphoblastic leukemia (ALL) – 75%
ü Acute myeloblastic leukemia (AML), also known as acute non lymphocytic leukemia (ANLL) – 20%
ü Acute undifferentiated leukemia (AUL)
ü Acute mixed-lineage leukemia (AMLL)

- Chronic myeloid leukemias constitute 3% of all childhood leukemias:
- Philadelphia chromosome positive (Ph positive) myeloid leukemia
- Juvenile myelomonocytic leukemia (JMML)

ETIOLOGY

- Unknown
- Ionizing radiation
- Chemicals (e.g., benzene in AML)
- Drugs (e.g., use of Akylating agents either alone or in combination with Radiation
- Therapy increases the risk of AML

- Genetic considerations:Identical twins
- If one twin develops leukemia during the first 5 years of life the, risk of the second twin developing leukemia is 20%.
- Incidence of leukemia in siblings of leukemia patient is 4 times greater

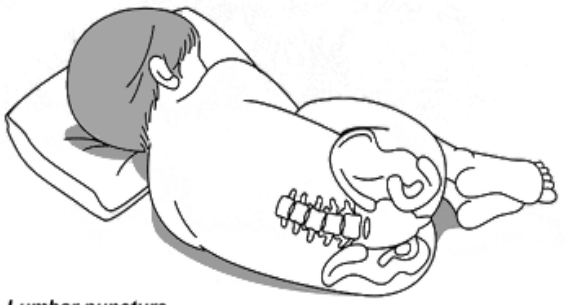
- Chromosomal abnormalities: Down syndrome , Fanconi Anemia , Kostmann disease, Ataxia telangiectasia

CLINICAL FEATURES OF ALL

- Fever (60%).
- Lassitude (50%).
- Pallor (40%)
- Anemia ,Neutropenia ,Thrombocytopenia , Pancytopenia,
- Lymphadenopathy
- Splenomegaly ,Hepatomegaly
- Central Nervous System (CNS) Involvement< less than 5% of children with ALL at initial diagnosis
- Testicular Involvement . painless enlargement of the in 10–20% of boys
- Bone and Joint Involvement (aArthragy , Arthritis)

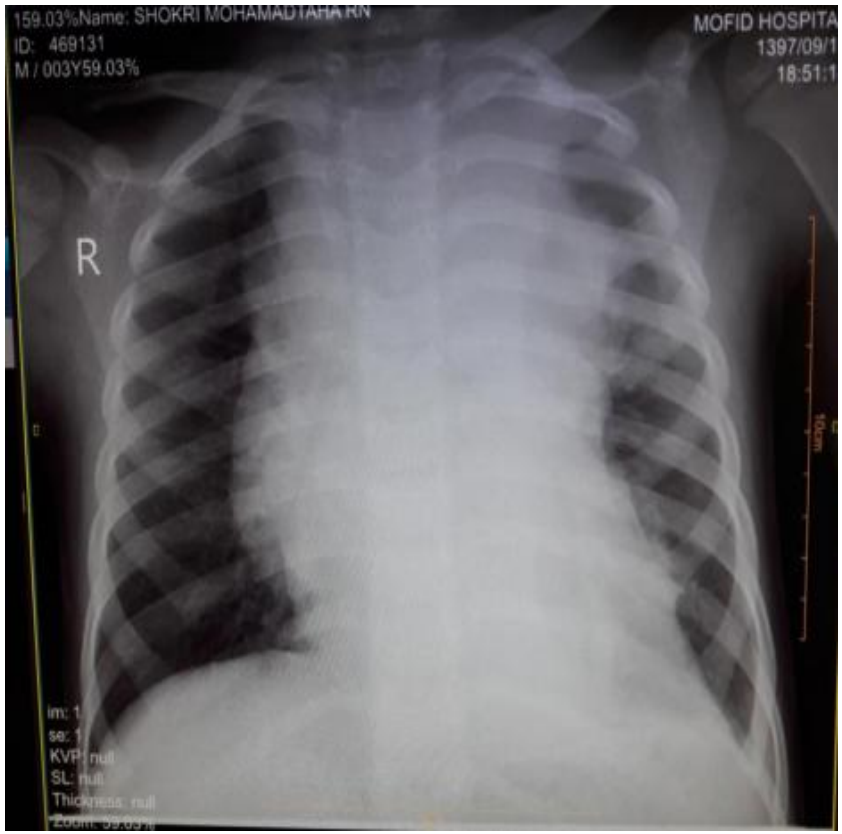
Diagnosis

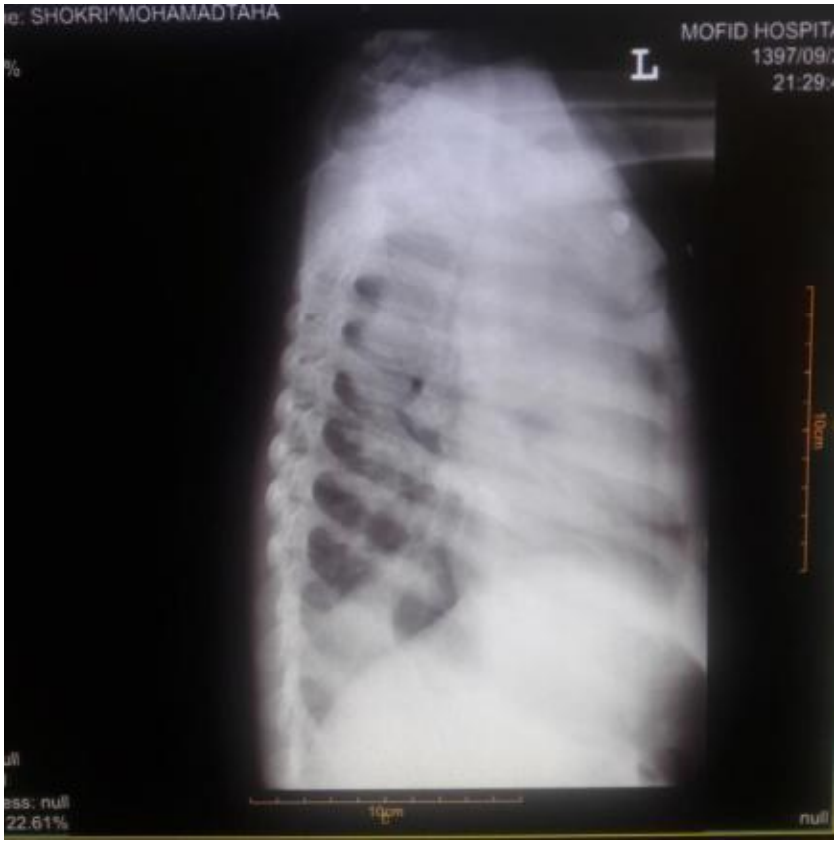
- CBC ,Blood chemistry; Electrolytes, blood urea, uric acid,LDH, liver function tests
- Immunoglobulin levels.
- Bone Marrow: , Morphology, Immunophenotyping, Cytogenetics
- CXR: Mediastinal mass in T-cell leukemia.
- Cerebrospinal fluid: Chemistry and cells
- Coagulation profile (AML M3,....)
- Cardiac function:Echo
- Infectious disease profile: Virology



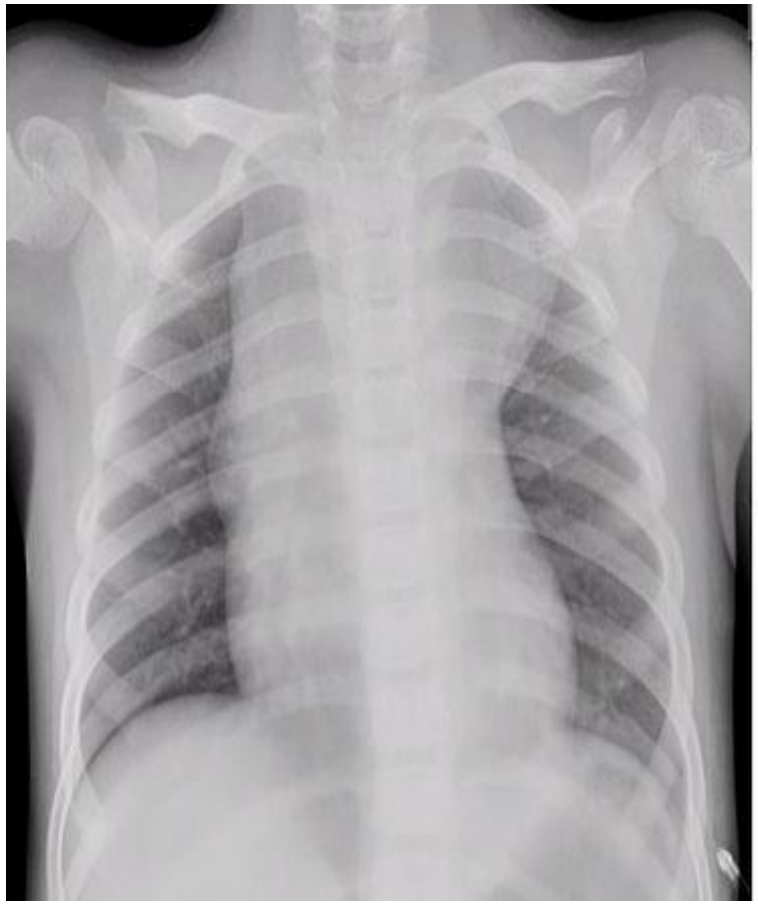
Lumbar puncture

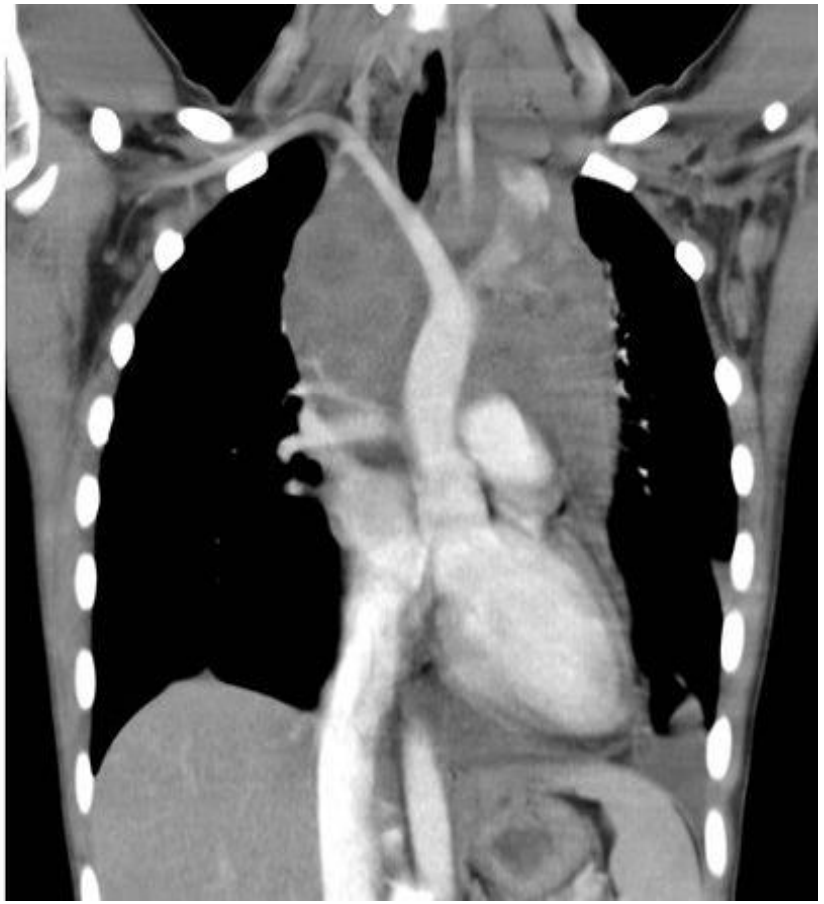
CXR PA& LAT(Ant Mediastinal Mass)



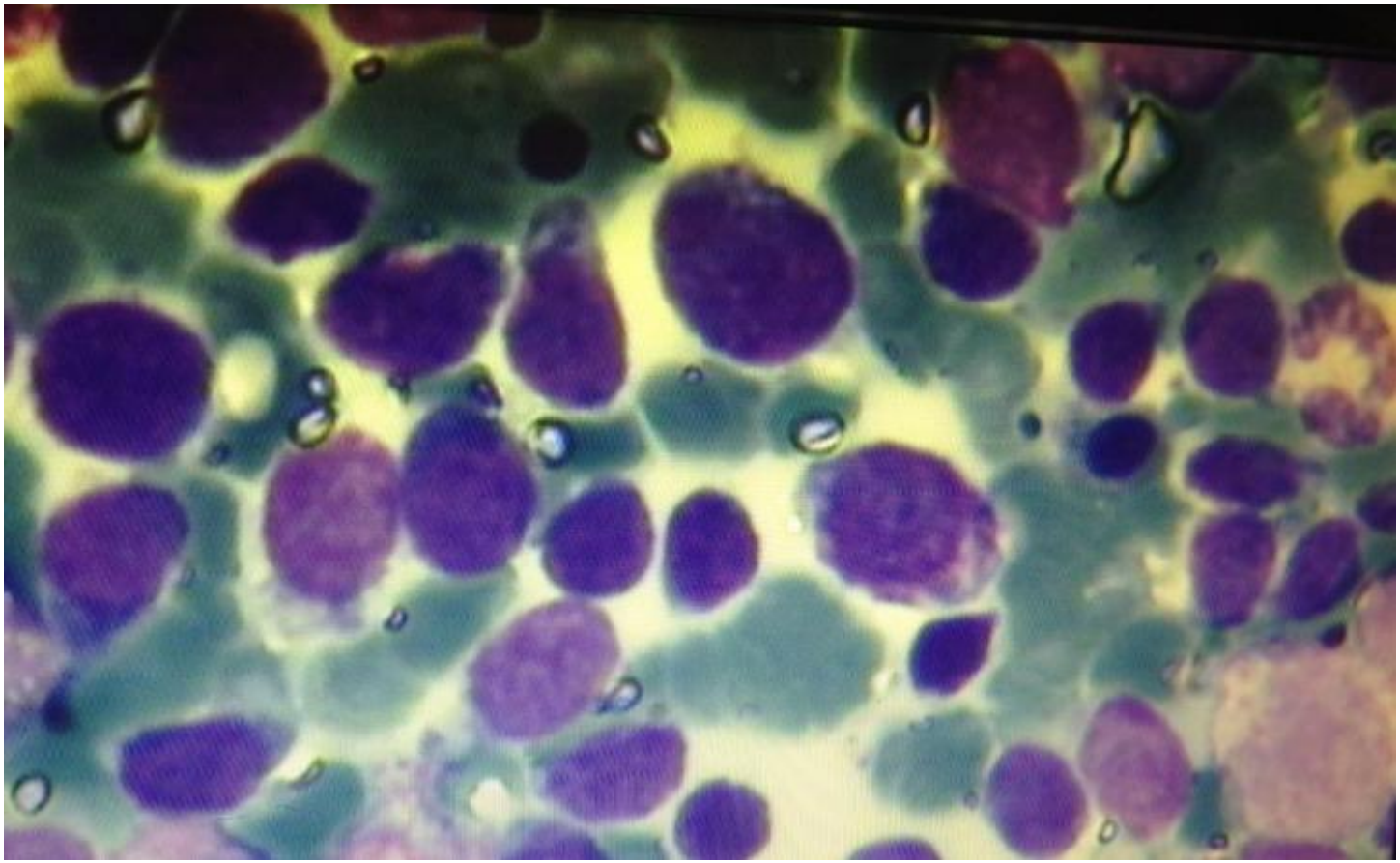


SVC &SMS / CXR & CT





BMA : Full Blast (Acute Lymphoblastic Leukemia)



Classification

- Lymphoblasts- ALL {French–American–British (FAB) Classification; L1, L2, L3
- Myeloblast in AML

ü Immunopheotyping : CD10, CD19 CD20, Cd22 for B lineage, CD7 for T lineage and CD13,CD33 for myeloid cells

- o Pre-B cell :80% of ALL,
- o 15-20% : T cell -Older age ;High initial WBC , extramedullary disease, Poor prognosis
- o B cell :1–2%

ü World Health Organization ;new classification of ALL (*cytogenetic and molecular characteristics) :*

World Health Organization Classification of ALL

B lymphoblastic leukemia/lymphoma

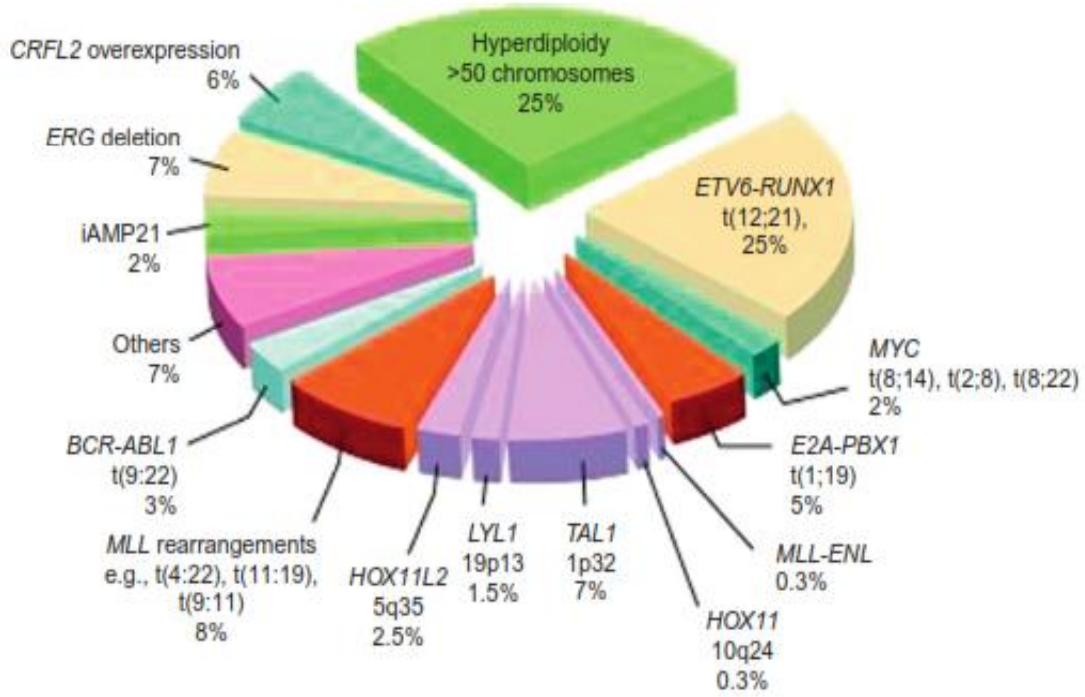
- B lymphoblastic leukemia/lymphoma, not otherwise specified (NOS)
- B lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
  - B lymphoblastic leukemia/lymphoma with t(9;22)(q34;q11.2);*BCR-ABL 1*
  - B lymphoblastic leukemia/lymphoma with t(v;11q23); *MLL* rearranged
  - B lymphoblastic leukemia/lymphoma with t(12;21)(p13;q22) *TEL-AML1 (ETV6-RUNX1)*
  - B lymphoblastic leukemia/lymphoma with hyperdiploidy
  - B lymphoblastic leukemia/lymphoma with hypodiploidy
  - B lymphoblastic leukemia/lymphoma with t(5;14)(q31;q32) *IL3-IGH*
  - B lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3);*TCF3-PBX1*

T lymphoblastic leukemia/lymphoma

Genotypes of ALL in childhood leukemias

Tel–AML1 fusion gene t(12;21) , Excellent prognosis

BCR–ABL fusion gene t(9;22); older age, higher WBC count ,CNS involvement at diagnosis



Treatment

- General Care
- Main treatment: Remission induction, Consolidation (intensification of remission),prevention of CNS leukemia , Maintenance therapy.

- Remission induction rates with three or four drugs (i.e., vincristine, prednisone, L-asparaginase,intrathecal Chemotherapy,produce a 95% remission induction rate.
- The aim of therapy in acute leukemia is to cure the patient and includes the following:

q induce a clinical and hematologic remission

q maintain remission by systemic chemotherapy and prophylactic CNS therapy

q Treat the complications of therapy and of the disease.

Prognostic Factors in Childhood Acute Lymphoblastic Leukemia

Factor	Favorable	Intermediate	Unfavorable
Age (years)	1–9	≥10[a]	<1 and *MLL*+
White blood cell count ($\times 10^9$/L)	<50	≥50[a]	
Immunophenotype	Precursor B cell	T cell[a]	
Genetics	Hyperdiploidy >50 chromosomes or DNA index >1.16 Trisomies 4,10 and 17 t(12;21)/*ETV6-CBFA2*	Diploid t(1;19)/*TCF3-PBX1*[a]	t(9;22)/*BCR-ABL1* t(4:11)/*MLL-AF4* Hypodiploid <44 chromosomes
CNS status	CNS1	CNS2[a] Traumatic spinal tap with blasts	CNS3
MRD (end of induction)	<0.01%	0.01% to 0.99%	≥1%

ACUTE MYELOID LEUKEMIA

- Abnormal proliferation and differentiation of myeloid precursors in the bone marrow
- AML ;20% of childhood leukemia.
- Incidence: 500 new cases of childhood AML in the United States per year.
- Age distribution: Peaks in neonatal period and during adolescence.
- Etiology;
- Twin concordance
- Genetic Syndromes;Down syndrome, Fanconi anemia
- Therapy-related - secondry:Vp16,Cyclophosphamide

AML Classifications

- AML ;20% blasts are required for the diagnosis of AML

q French–American–British (FAB) classification of AML. ;

q M0-undifferentiated leukemia

q .....

q M7- Acute Megakaryoblastic leukemia;

- Clonal cytogenetic abnormalities: t(8;21) ,inv(16) ,t(16:16) and (t(15;17)

- Receptor tyrosine kinase mutations (FLT 3 mutations): poor prognosis

Clinical Manifestations

- Fever, Weakness
- Anemia, Neutropenia
- Thrombocytopenia to life-threatening Coagulopathy
- Extramedullary disease (EMD) ;10-20% patients, It can occur as a myeloid sarcoma (MS) or chloroma
- Gingival hypertrophy
- Lymphadenopathy
- Leukemia cutis
- CNS , Orbit, periorbital areas, and paraspinal areas

DIAGNOSIS

- CBC & Biochemistry , LDH
- Leukocytosis, Auer rods, needle-shaped intracytoplasmic azurophilic inclusion bodies
- Anemia, Thrombocytopenia
- BMA ; Immunophenotype , Molecular Genetics
- Cerebrospinal fluid(CSF)
- Coagulation profile
- Cardiac function
- Infectious disease evaluation

TREATMENT

- General Care;

ü Management of Infectious

ü Transfusions

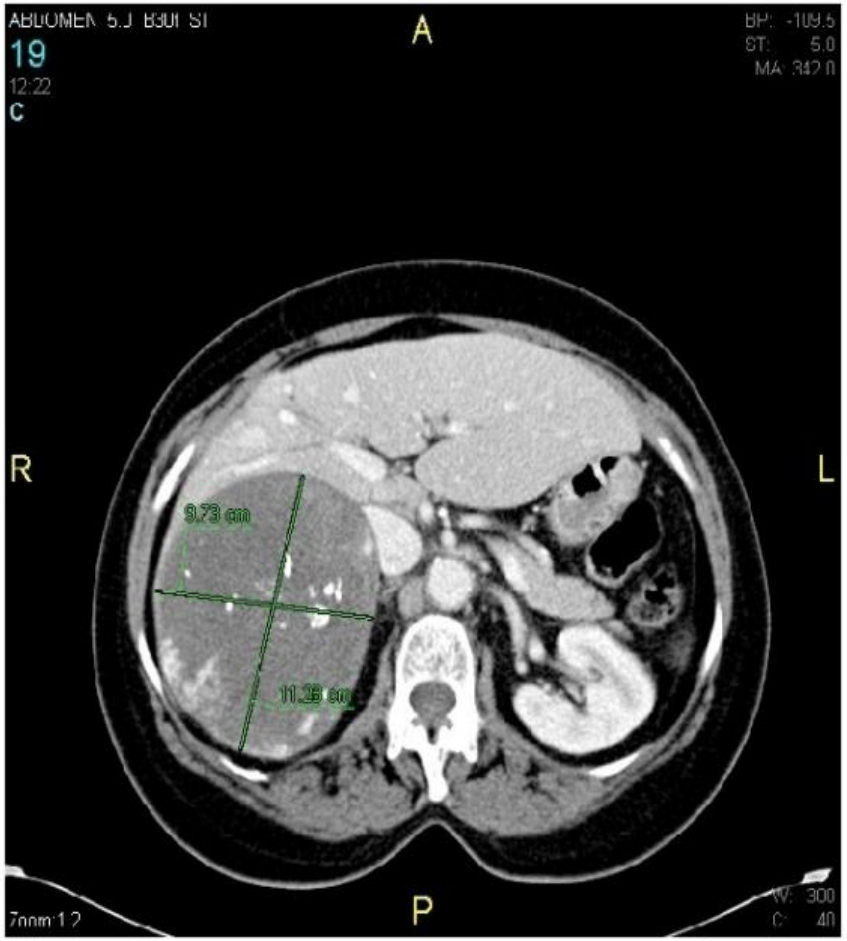
ü Tumor Lysis Syndrome

ü Hyperleukocytosis

- Chemotherapy
- Allogenic HSCT

Pedaitric Solid Tumors

CT scan showing 11.3 cm × 9.7 cm right adrenal mass with scattered calcifications



Solid Tumors

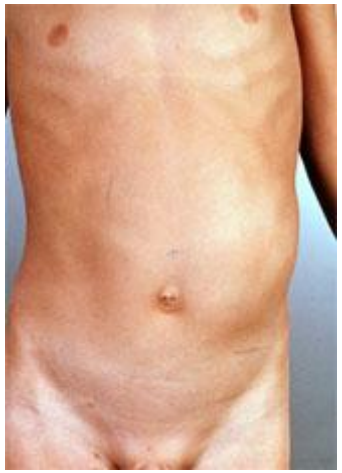
- Neuroblastoma is the most common extracranial solid tumor in children
- Renal tumors comprise approximately 6% of all childhood cancers
- Malignant bone tumors constitute ; 6% of all childhood malignancies. Osteosarcoma (56%), the Ewing sarcoma family of tumors (34%)

- Soft-tissue sarcomas (STS) derived from primitive mesenchymal cells
- Classification ;Rhabdomyosarcoma (RMS, Non rhabdomyosarcoma soft-tissue sarcomas (NRSTS). STS account for 7% of childhood malignancies. RMS accounts for 40% of STS and RMS is the most common pediatric STS

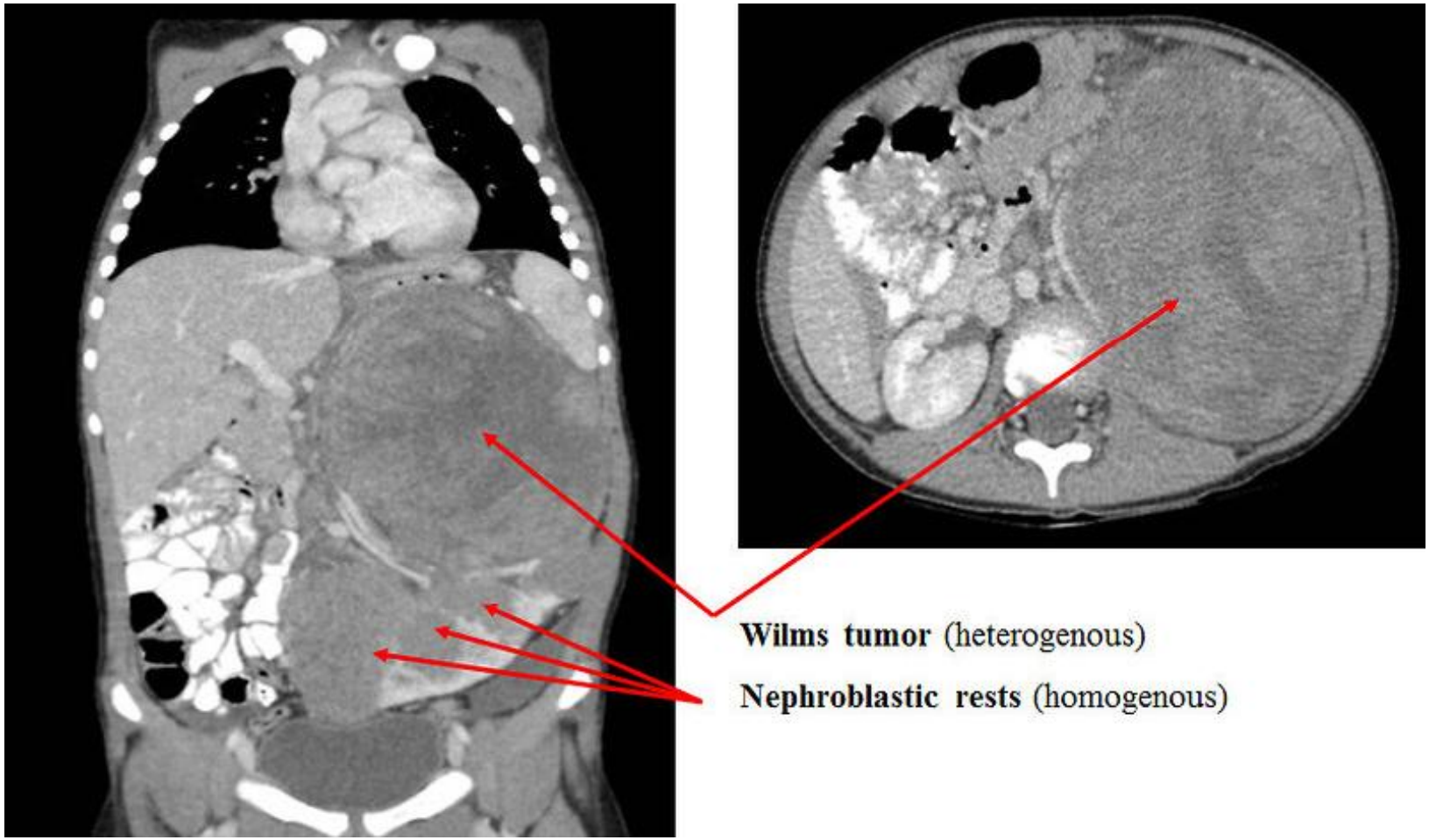
Ø Retinoblastoama
Ø Germ cell tumors
Ø Hepatobalstoma
Ø ....

Renal tumors/wilms

- Renal tumors comprise approximately 6% of all childhood cancers
- Nearly 10% of all malignancies among children aged 1 -4 years.
- Wilms' tumor (Nephroblastoma) ;most common primary renal tumor childhood
- Presentaion : Renal mass
- Metastasis: most Lung
- Treatment:
- Surgery , Chemo and Radiation



Wilms Tumor



Wilms tumor (heterogenous)

Nephroblastic rests (homogenous)

Neuroblastoma

- Neuroblastoma is the most common extracranial solid tumor in children
- Peak age of incidence is 2 year
- Small round blue cell tumors
- Histologically: Favorable or unfavorable
- 7% of all childhood malignancies
- 15% of childhood cancer mortality.
- Neuroblastoma :most common malignancy in infants
- At diagnosis;

ü 50% of patients < 2 years of age

ü 75% < age 4

ü 90% < age 10

CLINICAL FEATURES

- Non specefic-Lethargy, anorexia, pallor, weight loss, abdominal pain,weakness, and irritability.
- usually ;Adrenal mass
- Sweating, flushing, pallor, headaches, palpitations, hypertension
- Distant metastases detected at the time of diagnosis in 75% of cases.
- Paraneoplastic Syndromes;

Ø watery diarrhea ,FTT -abdominal distention a-hypokalemia

Ø Opsoclonus myoclonus ataxia syndrome (OMAS)

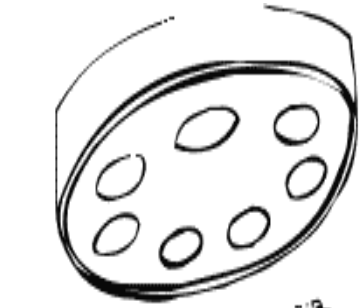
- Metastasis: Bone, BM, LN, Brain

DIAGNOSIS &STAGING

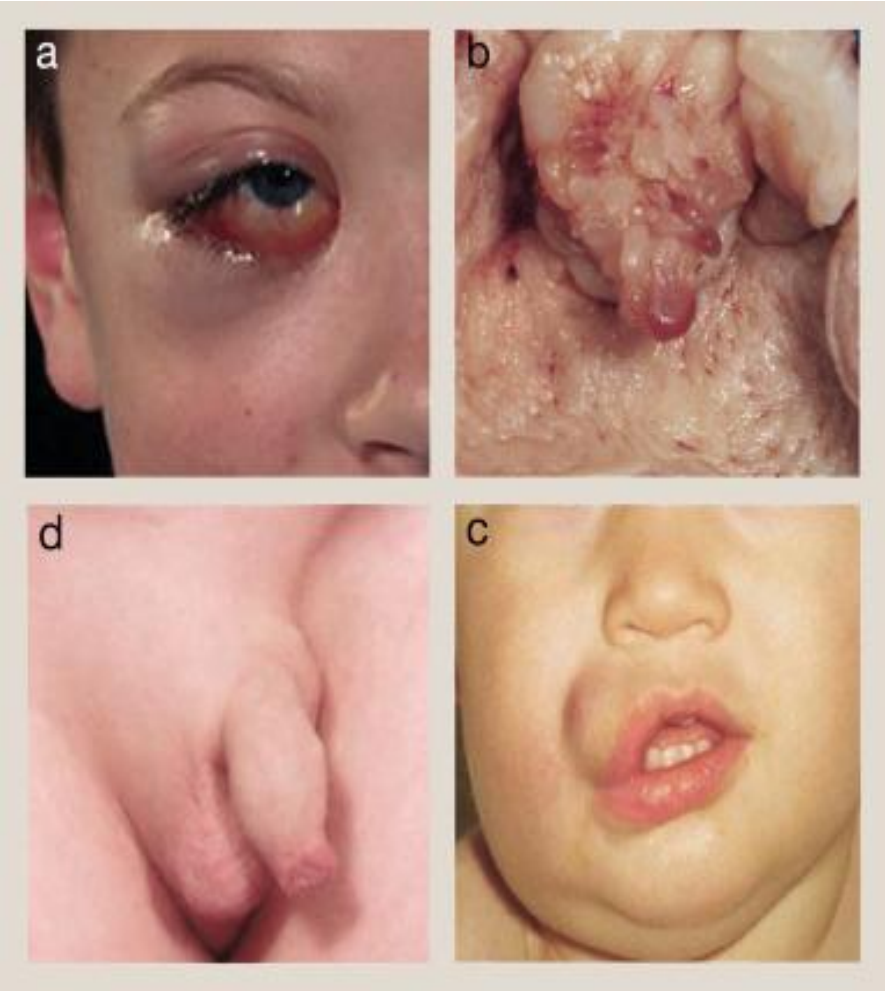
- CBC , BIO, LDH , Ferritin
- Urine 24hour HVA &VMA
- Imaging: Sono, Computed tomography (CT), MRI, (FDG-PET) ,123 & 131 I MIBG
- BMA+ BMB
- Bone survey , Bone scan
- NMYC (Ch2) amplification
- Open biopsies, Tissue diagnosis

TREATMENT/Neuroblastoma

- Surgery
- Chemotherapy
- Immunotherapy
- Radiotherapy X
- HR patients : HSCT: Auto HSCT



Soft Tissue sarcoma: Rhabdomyosarcoma



- Rhabdomyosarcoma
- (RMS) is the commonest soft tissue sarcoma (STS) in children

Rhabdomyosarcoma

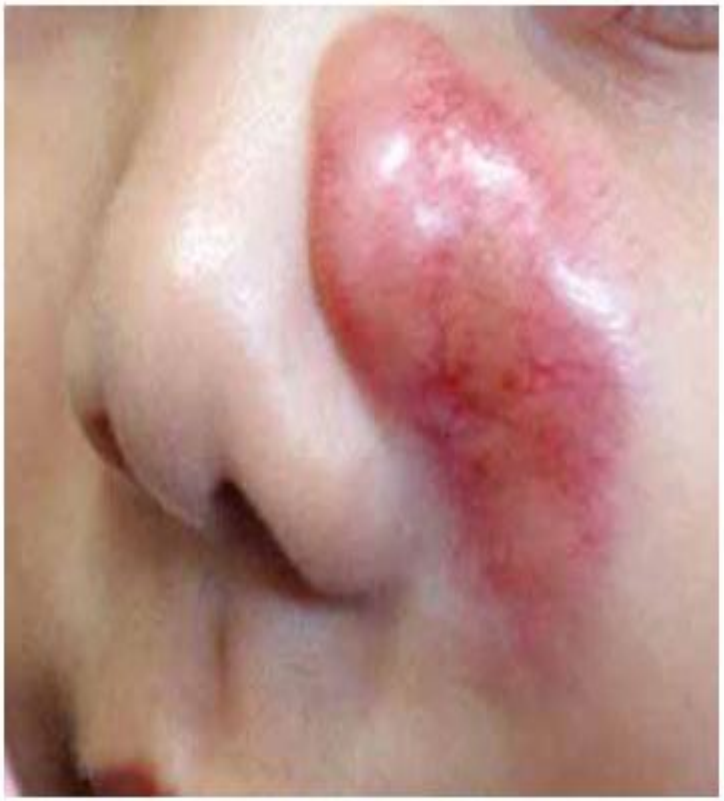
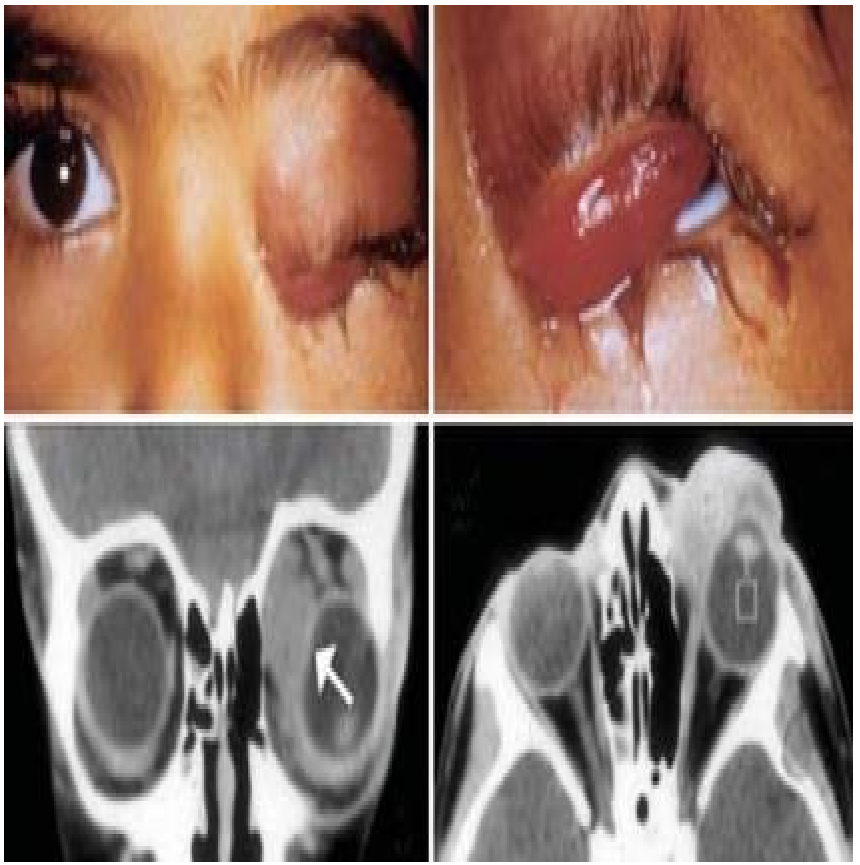
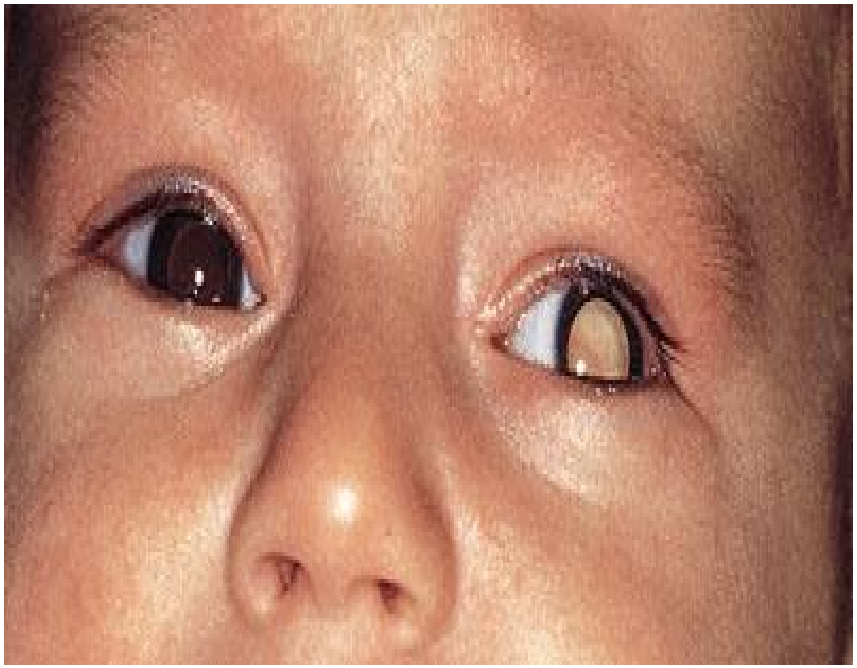


FIGURE 2: Erythematous, lobulated nodule with telangiectasias on its surface, measuring 3.2 x 2.4 cm, located on the left paranasal region



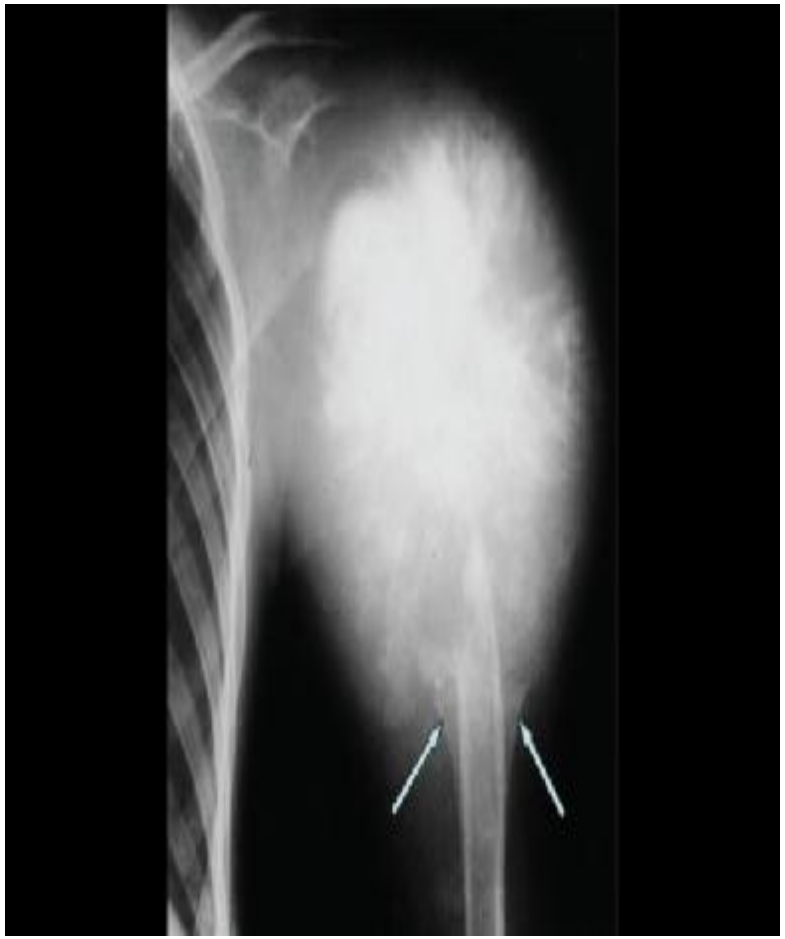
Retinoblastoma



- Retinoblastoma occurs in 1/15,000 to 1/30,000 live births
- about 3% of childhood cancers
- usually : in children < 2 yr; < 5% of cases are diagnosed in those > 5 yr.
- leukocoria (a white reflex in the pupil), strabismus, and, less often, inflammation and impaired vision.

- Diagnosis is based on ophthalmoscopic examination and ultrasonography, CT, or MRI.
- May be Hereditary

Bone tumors



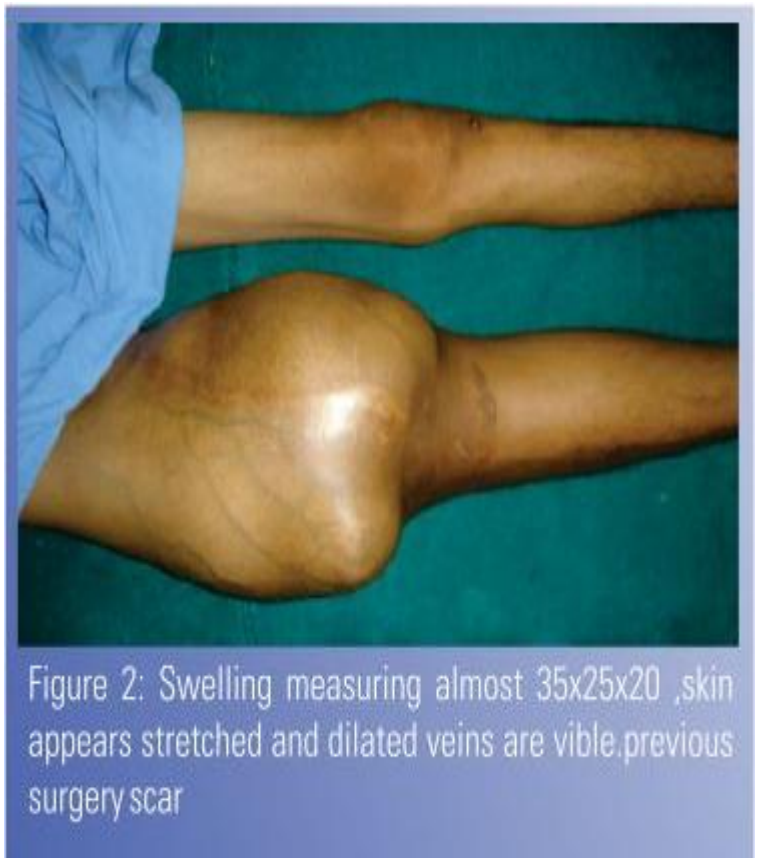
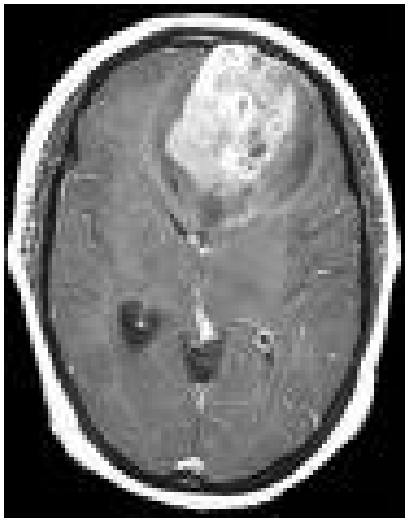
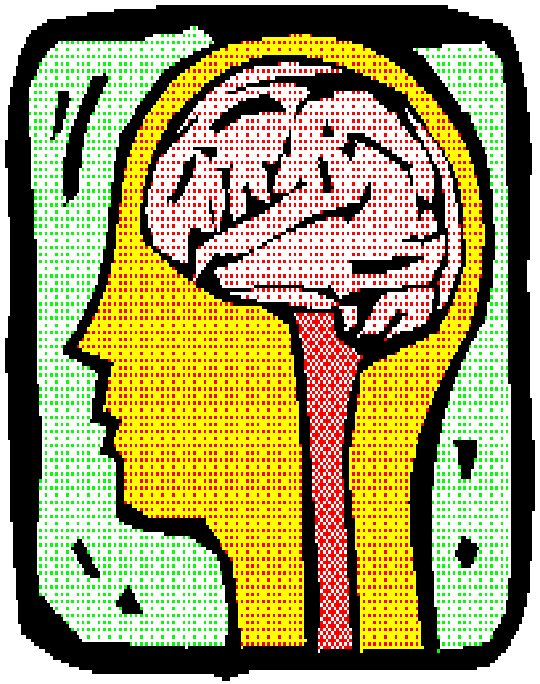


Figure 2: Swelling measuring almost 35x25x20 ,skin appears stretched and dilated veins are vible.previous surgery scar

Brain tumors umors of the central nervous system (CNS) are the second most common group of cancers in childhood, accounting for 20% of all childhood malignancies





Family support

Follow Up

Long-term Survival & Care

Cancer management needs :A large Team work