Tumors of the childhood

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Children tumors

Tumor - incorrect, palpable or visible structure

The tumor's etiology

- congenital
- inflammatory
- cancerous

To differentiate

- interview
- physical examination
- knowledge of the tendency to localize tumors in a particular location at a specific population (age, gender, etc)
- additional tests: imaging, histopathological, immunochemical, etc

Examination

Interview

- How long it last
- Alergies, diet, skin changes
- Drugs, vaccinations
- Contact with animals
- Weight loss
- Changes in child character

Physical examination- the tumor and its:

- localization (local / generalized, symmetrical / asymmetrical)
- size and shape
- consistency, splashing
- soreness, swelling, appearance of the skin
- nodes - single / packages

Tumors

BENIGN

- Lipoma
- Fibroma
- Hemangioma
- Nerve tissue tumors (neurofibromas, schwannoma)
- Teratoma

MALIGNANT

- Leukemia
- Lymphomas
- CNS tumors
- Sarcomas
- Neuroblastoma
- Retinoblastoma

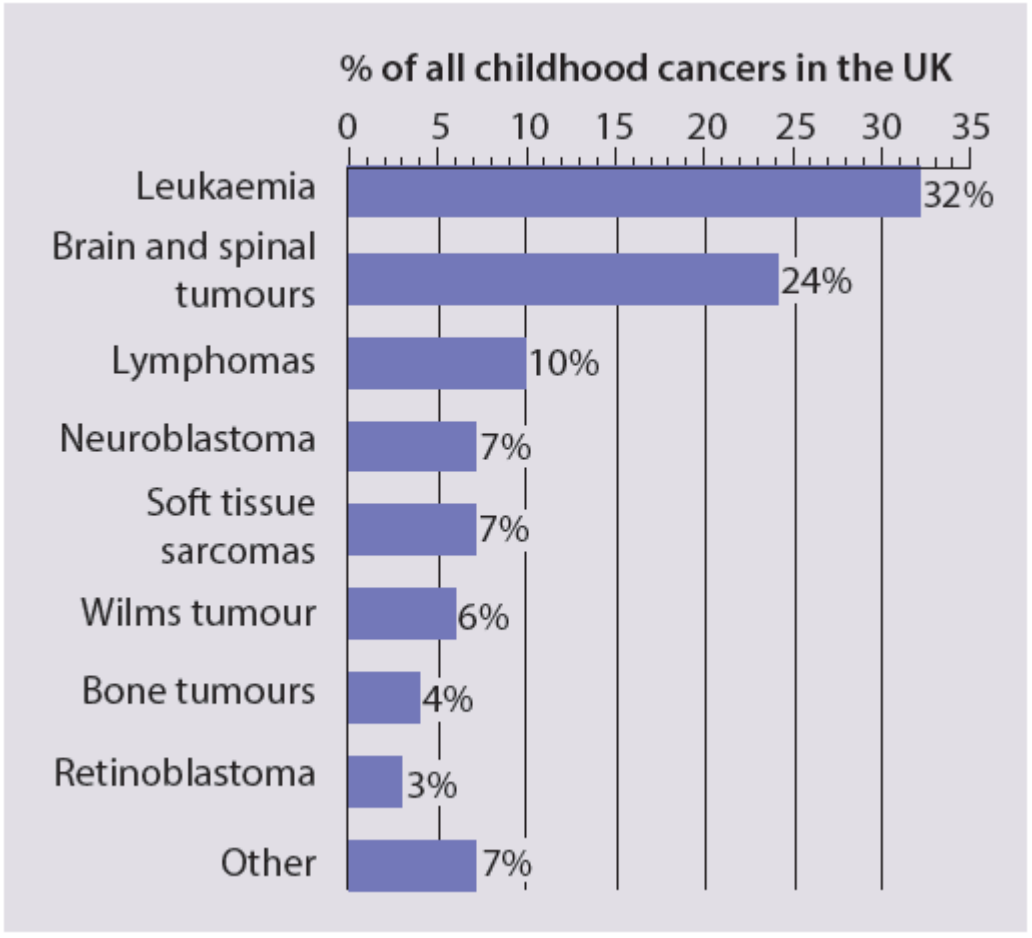
Children's oncology

1. Around 1 child in 500 develops cancer by 15 years of age.
2. Childhood cancer comprise 2% of all malignant tumours but they are the leading cause of death in this age group
3. Both benign and malignant tumors occur in childhood.
4. Benign tumors are more common than malignant tumors but they are generally of little immediate consequence
5. Most malignant tumors in children arise from hematopoietic, nervous and soft tissues.
6. The 5-year survival of children with all forms of cancer is about 75%, most of whom can be considered cured, although cure rates vary considerably for different diagnoses.

Differences between pediatric and adults cancers

	Pediatric cancers	Adult cancers
Incidence	• Rare • Depends on age	• Relatively common • Increased incidence with increasing age
Localization	• Hematopoietic system • Neural tissue • Soft tissue	• Epithelial orgin - carcinomas (lung cancer, colon cancer, skin cancer)
Regression	• Tendency to regress spontaneously/ mature	
Histology	• Primitive / embryonal appearance	• Pleomorphic- anaplastic appearence
Genetics	• Simple karyotype	• Complex karyotypes
Management	• Curable - chemotherapy/ radiotherapy • Even resectable may need chemo • May develop second malignancy	• Often chemo-insensitive • Low stage - surgically curable

Frequency of different kind of cancer



Predsposing factors

- Genetic- mutations, neurocutaneous disorders, chromosomal abnormalities
- Immunodeficiencies
- Infections – EBV, HIV
- Environmental
- Chemotherapy
- Ionising radiation
- Electromagnetic radiation

Leukemia

ACUTE (95%)

ALL – acute lymphocytic/ lymphoblastic leukemia

- 80-85% all childish leukemia
- The peak incidence at 3-6 years of age, mostly boys
- Short duration of the disease- 2-6 weeks

ANLL – acute nonlymphocytic leukemia (acute myeloid anemia, AML)

- The same incidence in both sexes
- 8 types with different clinical course and response for treatment (M0- M7)

CHRONIC (5%)

CML – chronic myeloid leukemia

- Rare incidence in children population
- Possibility to transform to ALL after 3-5 years
- Classify to myelodysplastic disorders

ALL

ALL- symptoms

- Initially nonspecific - anorexia, irritability, lethargy, loss of apetite, loss of weight
- Pallor
- Bleeding
- Petechiae
- Fever
- Lymphadenopathy, splenomegaly, hepatomegaly
- Bone pain and arthralgia
- Rarely headache and vomiting

Lab test

- Anemia, thrombocytopenia, increases erythrocyte sedimentation rate
- WBC ↓ N ↑
- Presence of blast cells on peripheral smear
- Bone marrow – leukemic lymphoblasts

Differential diagnosis

- Aplastic anemia
- Myelofibrosis
- Infections mononucleosis

Treatment ALL

The aim is to induce a lasting remission, defined as the absence of detectable cancer cells in the body.

- Chemotherapy
- Steroids
- Radiation therapy
- Bone marrow or stem cell transplants

Prognosis overall cure rate 80% . It is assumed that the 5-year disease-free survival (counted from the end of therapy) is synonymous with cure the child. After this period of ALL relapse are already very rare.

ALL- prognosis

Worse prognosis

1. Age child below 12 months
2. WBC count less then 50 000/ul
3. Chromosomal transactions t(22:9), t (4:10), Down syndrome
4. Gender- male
5. Cancer spread into the Central nervous system (brain or spinal cord)
6. Morphological, immunological, and genetic subtypes
7. Patient's no response to initial treatment

Acute myeloid leukemia

Symptoms:

- Pallor, fatigue, petichae,
- Enlarged nodes and hepatosplenomegaly
- Gingival hyperplasia in AML M4 i M5

Investigation:

Anemia, trombotythopenia, neutropenia

WBC count in most cases enlarged

Presence of blast cells on peripheral smear

Diagnosis: 25% myeloblasts in bone marrow

Treatment

Chemotherapy

Radiotherapy

Bone marrow transplantation

Worse outcomes: no responce after induction therapy

M5 type

Non Hodgkin lymphoma

- Abdominal form (B) and mediastinal form (T)
- asymmetrical enlargement of lymph nodes, mainly supraclavicular (figure mediastinal), sometimes extranodal site
- rare in infants, increasing incidence after 3 years
- Burkitt's lymphoma virus (EBV)
- a huge rate of change (days!) and large malice (CNS and bone marrow)

DIAGNOSIS

uric acid levels

LDH activity reflects the size of the tumor

Treatment: mainly chemotherapy (few indications for radiotherapy)

Hodgkin lymphoma- Hodgkin disease

- Sign - painless, firm, cervical or supraclavicular adenopathy
- Rarely hepatosplenomegaly
- Less common: Pruritus, lethargy and anorexia
- Additional tests: mild anemia, reduced number of eosinophilic cells, elevated ESR
- Hispatologically: Reed-Sternberg cells
- Treatment: The association of chemotherapy and radiotherapy

Oral lesions in the hematopoietic and lymphatic diseases

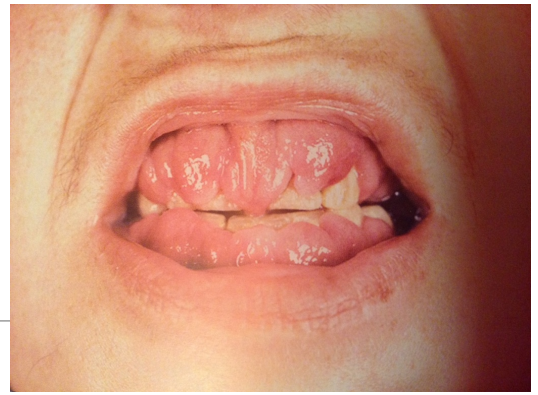
Cause of the occurence the changes in the oral cavity:

- the presence of neoplastic lesions
- peripheral blood cytopenia
- immune deficiency

The changes in the oral cavity:

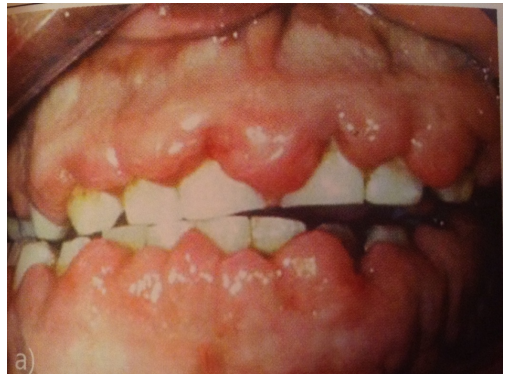
- gingivitis
- periodontitis
- bleeding
- gingival hyperplasia
- petechiae
- erosions
- ulcers of the mucous membranes

Changes in oral cavity

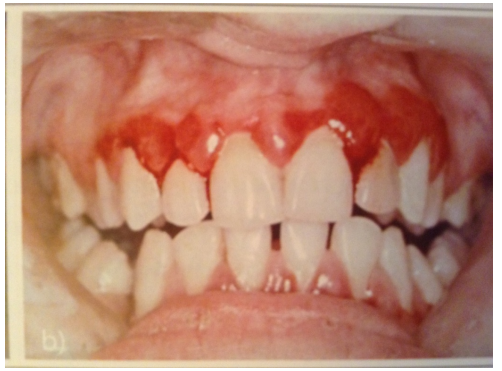


Gingivial hyperplasia- cause:

- leukemic infiltrates (patients with chronic myelomonocytic leukemia (CML) or acute leukemia nonlymphocytic (ANLL - M4 and M5))
- primary neoplastic proliferation originating from the lymphatic system (rare)
- drug-induced gingival hyperplasia (phenytoin , cyclosporin A, calcium channel blockers)



- agranulocytosis can cause inflammatory changes and / or fungal infections of tonsils and oral mucosa
- thrombocytopenia -> development of thrombocytopenic bleedings with symptoms of bleeding gums and petechiae of the oral mucosa
- anemia ->pale mucous membranes



Changes in oral cavity

Patients with NHL (usually from mature B cells)-> increase bacterial and fungal infections in the oral cavity, dry mucous membranes, decreased saliva secretion, viral vesicular lesions on the mucous membranes of the mouth, on the hard palate, soft posterior wall of the pharynx.

EBV - development of post-transplant lymphoproliferative syndrome (PTLD) - local or generalized in patient with immune deficiency

- varying degrees of severity (from reactive hyperplasia, to the development of lymphoma); the cause of hairy leukoplakia, erosions, ulcers

HPV – oncogenic virus

- clinical picture may be asymptomatic, or may be the cause of change of squamous papilloma (7-8% of tumors in children)

Neuroblastoma

Second most common solid tumor of infants (up to 2 years)

metastasis to bone marrow

2/3 of the cases, the diagnosis of <5 years of age (mean age of onset 2.5 years)

the most common malignant tumor in neonatal age (34-54 %)

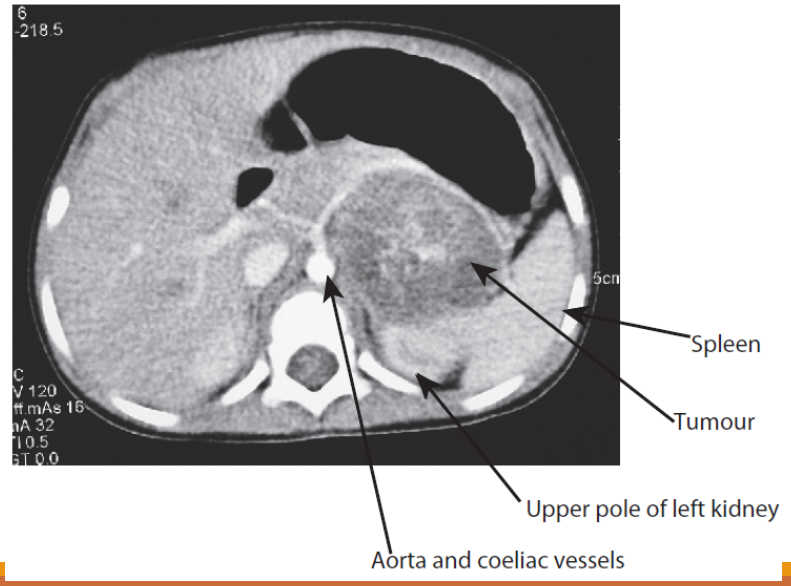
Location:

- retroperitoneal space (70-75 %)
- Rear mediastinum (20%)
- neck (5%)

metastatic form of the disease in 70 % of the time of diagnosis

Diagnosis- CT, MRI → tumor mass, Tumor markers → HVA, VMA, Biopsy

Treatment: surgical chemotherapy and radiotherapy



NBL symtoms

abdominal mass

loss of appetite, weight loss

fever

abdominal pain, bone pain

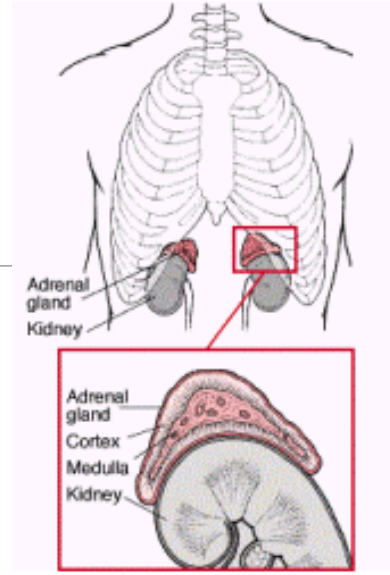
multiple subcutaneous nodules

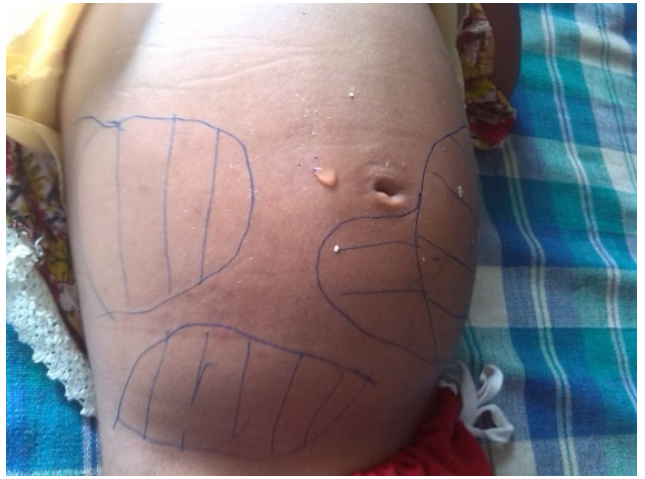
exophthalmos

Horner's syndrome (not characteristic)

overproduction of catecholamines:

- Diarrhea (escape potassium overproduction VIP)
- Episodes of sweating
- skin redness
- Hypertension





Wilms tumor- nephroblastoma

derived from renal tissue with low differntiation

the peak incidence of 3-4 years of age

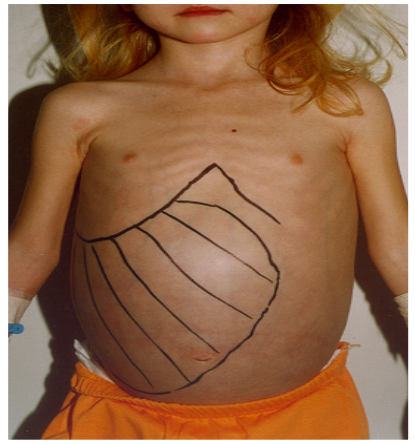
7-10% of childhood cancers

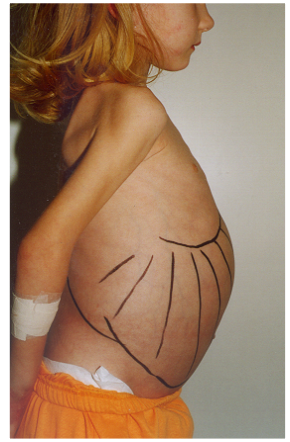
can coexist with other congenital defects

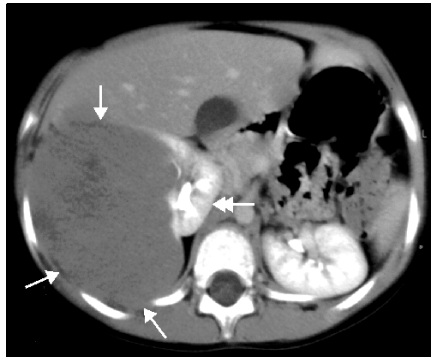
bilateral Wilms tumor

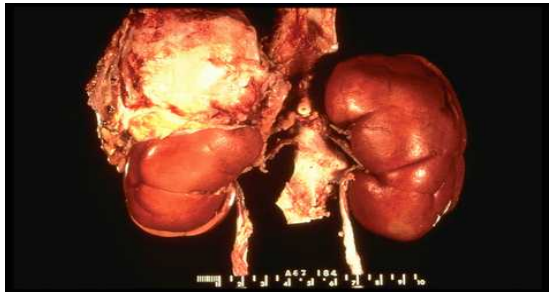
Genetic predisposition:

- WAGR syndrome - Wilms , aniridia , genito - urinary malformations , mental retardation , del 11p13
- Beckwith - Wiedemann syndrome - omphalocoele , macroglossia , gigantism , hepatoblastoma , nephroblastoma, gonadoblastoma , del 11p15
- Denys - Drash syndrome - nephropatia , nephroblastoma, pseudohermaphroditism , point mutations in the WT1 gene









Wilms tumor- symptoms

- recurrent symptoms of urinary tract infection
- hematuria
- hypertension (renin secretion)

Symptoms of a tumor in the abdomen:

- Abdominal distension
- abdominal pain, nausea , vomiting, abnormal intestinal transit
- bulge of abdominal wall

Diagnosis- USG, CT, Chest X-ray, CT

Treatment- surgical removal, chemotherapy: Vincristine, actinomycin & doxorubicin, Radiotherapy

Retinoblasoma

Symptoms: leukocoria, strabismus, orbital infalmation, pain

- Monocular form, unifocal occurs sporadically , diagnosed between 3-4 years of age, 60% of all cases
- Multifocal form, predominantly in the form of a binocular hereditary recognized in most cases in 1 yr of life, 25% of all cases

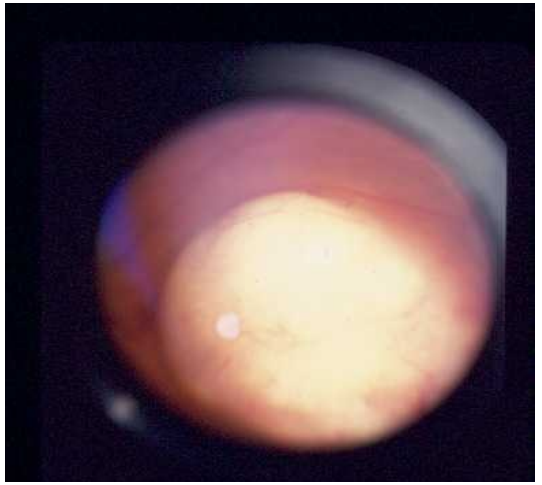
develops intraocularly , then invades the structure of periocular and penetrates into the cranial cavity

It can give distant metastases.

Diagnosis → Opthalmology – orbital USG and CT

Treatment – u/l enucleaton

Laser photocoagulation, cryotherapy, radiotherapy



B/l → enucleation of the more several effected eye.

There is a significant risk of second malignancy (especially sarcoma) among survivo hereditary retinoblastoma.

Brain tumors

The most common solid tumors (20-25 % of all cancers)

The average age of 7 years 10 months .

Etiology:

- Hereditary : neurofibromatosis type I and II , tuberous sclerosis , Li - Fraumeni syndrome , Gardener , Turcot , von Hippel -Lindau
- Environmental factors : pesticides , nitrosamines , exposure to ionizing radiation , electromagnetic
- Primary and secondary immune deficiencies

Diagnosis:

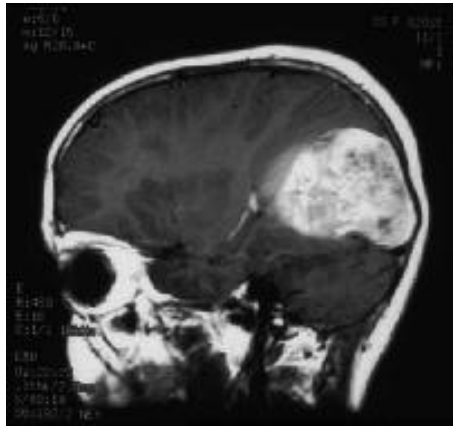
- neuroimaging – MRI
- Cerebrospinal fluid
- Biochemical tests (AFP , hCG)

Treatment- surgery, radio and chemiotherapy

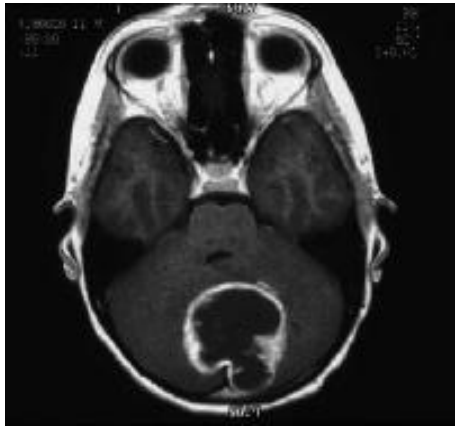
Brain tumors classification

Localisation

- Supratentorial (gliomas, ependymomas , PNET tumors, midline - germ cell tumors , pineal tumors)
- Infratentorial-> the cerebellum (medulloblastoma), Brainstem (gliomas)



The supratentorial glioblastoma multiforme



The juvenile pilocytic astrocytoma of the cerebellum

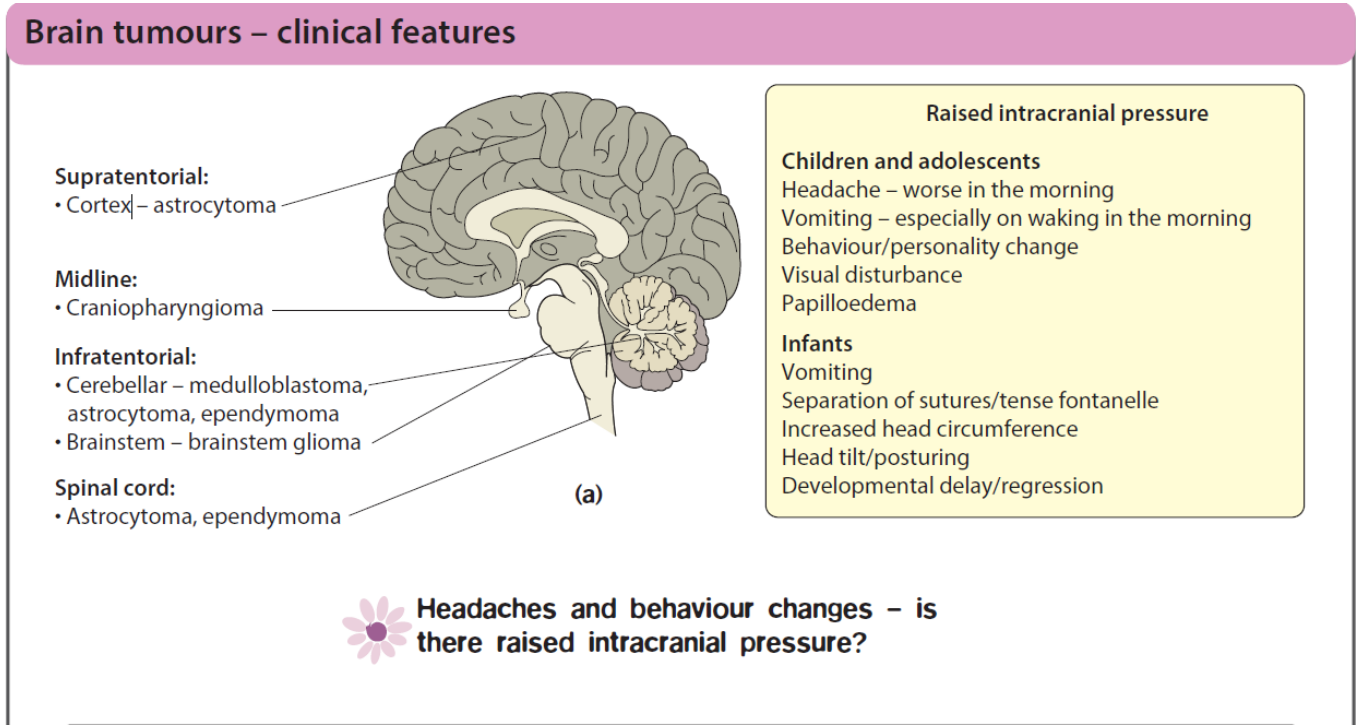
- Astrocytoma (~40%) – varies from benign to highly malignant (*glioblastoma multiforme*)
- Medulloblastoma (~20%) – arises in the midline of the posterior fossa. May seed through the CNS via the CSF and up to 20% have spinal metastases at diagnosis
- Ependymoma (~8%) – mostly in posterior fossa where it behaves like medulloblastoma
- Brainstem glioma (6%)
- Craniopharyngioma (4%) – a developmental tumour arising from the squamous remnant of Rathke pouch. It is not truly malignant but is locally invasive and grows slowly in the suprasellarregion.

Brain tumors- symtoms

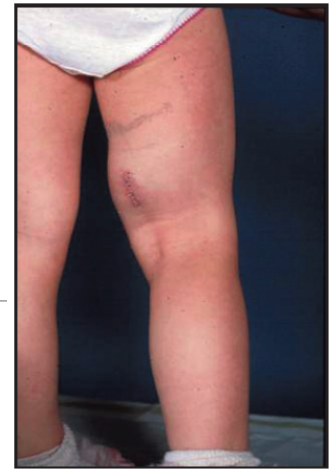
Posterior fossa tumors
- the increase in intracranial pressure
- ataxia
- headache
- nausea
- vomiting

Supratentorial tumors
- Seizures
- hemiparesis
- focal symptoms

Tumors midline
- Visual field defect
- visual acuity,
- diabetes insipidus
- growth disorders



Rhabdomyosarcoma

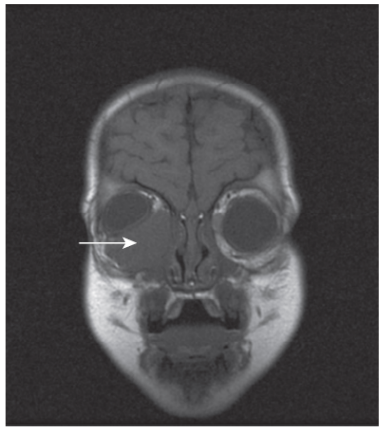


The most common form of soft tissue sarcoma in childhood- 2-6 years of age, more boys

Head and neck are the most common sites of disease (40%),

Clinical symptoms :

- exophthalmos , squint , narrowing of the eyelid
- nasal speech, difficulty swallowing
- occupation of the middle ear with the leak and polyps in the external auditory canal
- intracranial pressure , cranial nerve palsies



Genitourinary tumours may involve the bladder, paratesticular structures or the female genitourinary tract.

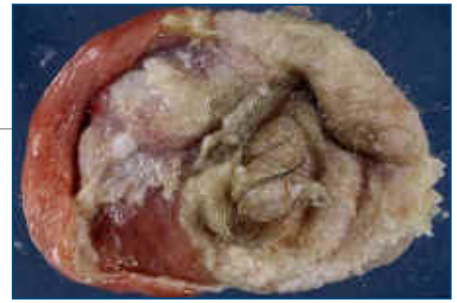
Symptoms include

- dysuria and urinary obstruction,
- scrotal mass
- bloodstained vaginal discharge.

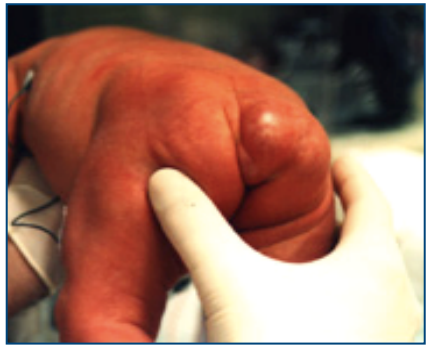
Metastatic disease (lung, liver, bone or bone marrow) is present in approximately 15% of patients at diagnosis and is associated with a particularly poor prognosis.

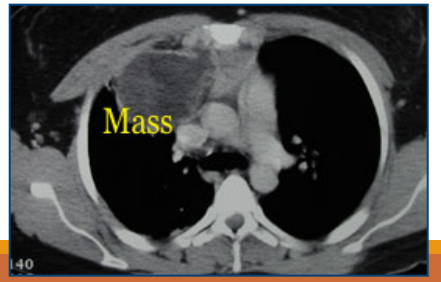
Multimodality treatment (chemotherapy, surgery and radiotherapy)

Germ cell tumours



- 3-3.7 % of all malignancies in children
- benign or malignant
- M : F - 1 : 2-4
- They arise from the primitive germ cells which migrate from yolk sac endoderm to form gonads in the embryo.
- Benign tumours are most common in the sacrococcygeal region, and most malignant germ cell tumours are found in the gonads.
- Serum markers (αFP and β-HCG) are invaluable in confirming the diagnosis and in monitoring response to treatment.
- Two incidence peaks:
  1. 0-3 yr (mainly tumors of sacrococcygeal region, testinal tumors)
  2. > 12 years of age (mainly ovary tumors)
- Good response to chemotherapy





Liver tumors

0.5-2 % of cancers developmental age

Primary malignant liver tumours are:

1. hepatoblastoma (65%), the peak incidence 1 yrs, genetic factors- Beckwith- Wiedeman sydrome, WAGR, neurofibromatosis
2. hepatocellular carcinoma (25%), the peak incidence 12 years of age, HBV infection, tyrosinemia, billary atresia

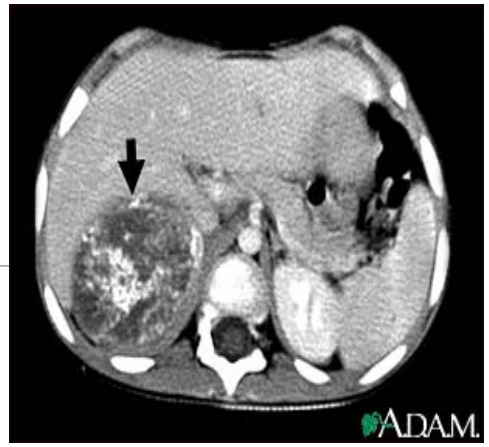
Symtoms: loss of appetite,weight loss, vomiting, abdominal tumor, hepatomegaly

Elevated serum α-fetoprotein (αFP) is detected in nearly all cases of hepatoblastoma and in some cases of hepatocellular carcinoma.

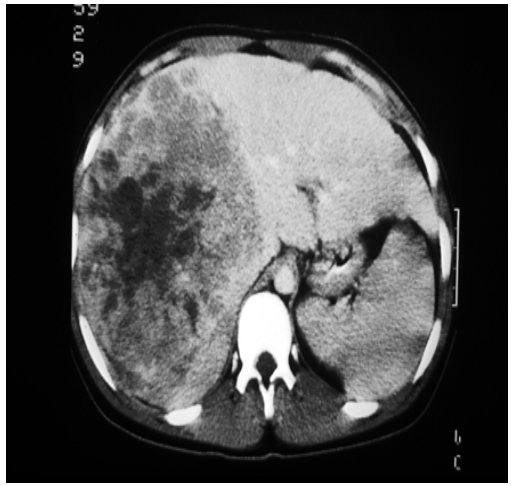
Diagnosis- USG, CT, MRI, biopsy

Management includes chemotherapy, surgery and, in inoperable cases, liver transplantation.

The majority of children with hepatoblastoma can now be cured, but the prognosis for children with hepatocellular carcinoma is worst.



Computed tomogram of hepatoblastoma



Computed tomogram of hepatocarcinoma

Bone tumors

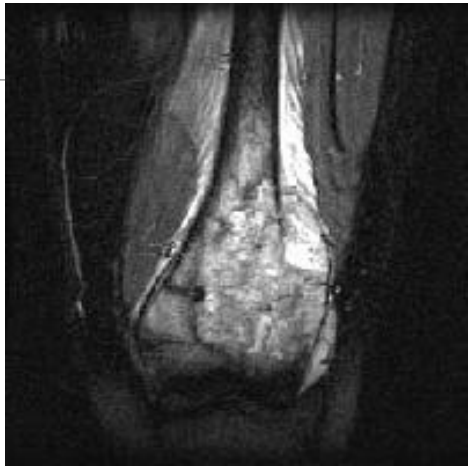
Malignant bone tumours are uncommon before puberty.

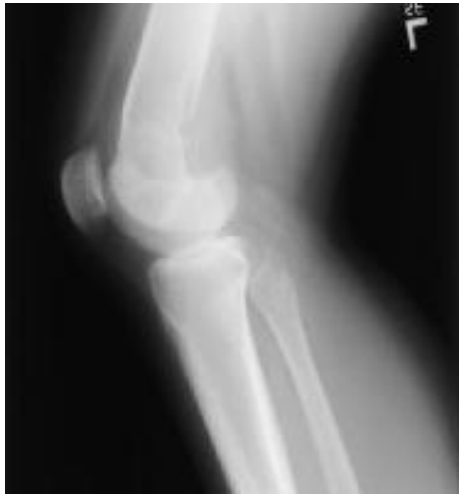
Osteogenic sarcoma is more common than Ewing sarcoma, but Ewing sarcoma is seen more often in younger children.

Both have a male predominance

Osteosarcoma:

- The most common malignant bone tumor in children
- The peak incidence 15-19 years of age
- The most common location - metaphyseal distal femur and proximal tibia metaphyseal

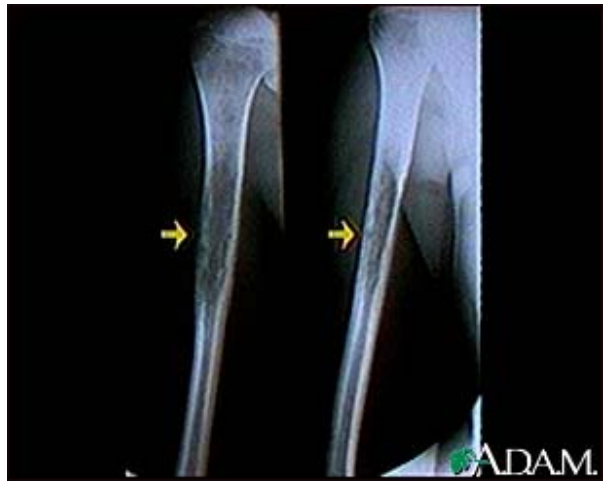




Bone tumors

Ewing sarcoma

- It can occur at a younger age
- The most common location - flat bone of the pelvis, shoulder, ribs, long bones- femur, tibia, arrow
- there is often a substantial soft tissue mass
- 1/3 patients at diagnosis is metastatic to the lung, bone

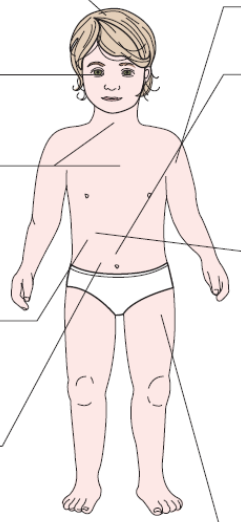


Treatment- combination chemotherapy given before surgery. Whenever possible, amputation is avoided by using *en bloc* resection of tumours with endoprosthetic resection.

In Ewing sarcoma, radiotherapy is also used in the management of local disease, especially when surgical resection is impossible or incomplete, e.g. in the pelvis or axial skeleton.

Summary

Presentation of malignant disease in children



Brain tumours:
- Raised intracranial pressure
- Neurological signs – depends on anatomical position

Retinoblastoma:
- Screening if positive family history
- White pupillary reflex or squint

Lymphomas:
- Enlarged lymph nodes in the head and neck or abdomen
- Mediastinal mass – may cause superior vena caval obstruction.

Wilms tumour:
- Large abdominal mass in a well child
- Occasionally anorexia, abdominal pain, haematuria

Langerhans cell histiocytosis:
- Seborrhoeic rash
- Widespread soft tissue infiltration
- Bone pain, swelling or fracture
- Diabetes insipidus

Soft tissue sarcomas:
- Mass any site

Neuroblastoma:
- Abdominal mass, crosses the midline
- Spinal cord compression
- Weight loss and malaise
- Pallor, bruising
- Bone pain

Acute lymphoblastic leukaemia (ALL):
- Malaise, anorexia
- Pallor, lethargy
- Infections
- Bruising, petichiae, nose bleeds
- Lymphadenopathy
- Hepatosplenomegaly
- Bone pain

Malignant bone tumours:
- Localised bone pain

Pre-school (<5 years old)	School-aged	Adolescence
Acute lymphoblastic leukaemia (ALL) – peak incidence Non-Hodgkin lymphoma	Acute lymphoblastic leukaemia (ALL)	Acute lymphoblastic leukaemia (ALL) Hodgkin lymphoma
Neuroblastoma	Brain tumours	Malignant bone tumours
Wilm tumour		Soft tissue sarcomas
Retinoblastoma		

Dental care on the oncological patients

As quick as possible!

Chemotherapy : miniumum one week earlier

Radiotherapy : a min 2 weeks earlier

Oral hygiene : use a soft toothbrush- toothpaste for children

Liquid to mouth: saline, baking soda, infusions of chamomile ,

Removal of braces

Restrictive diet

Complications of chemotherapy and radiotherapy

A generalized inflammation of the oral mucosa (mouthwashes with pain killers, antifungal, steroids)

reduced saliva secretion (pilocarpine , Vit. A)

opportunistic infections (Fluconazole prophylactically)

tooth caries, necrotic bone inflammation because of radiation

periodontitis

Trismus

dysgeusia, dysphagia

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