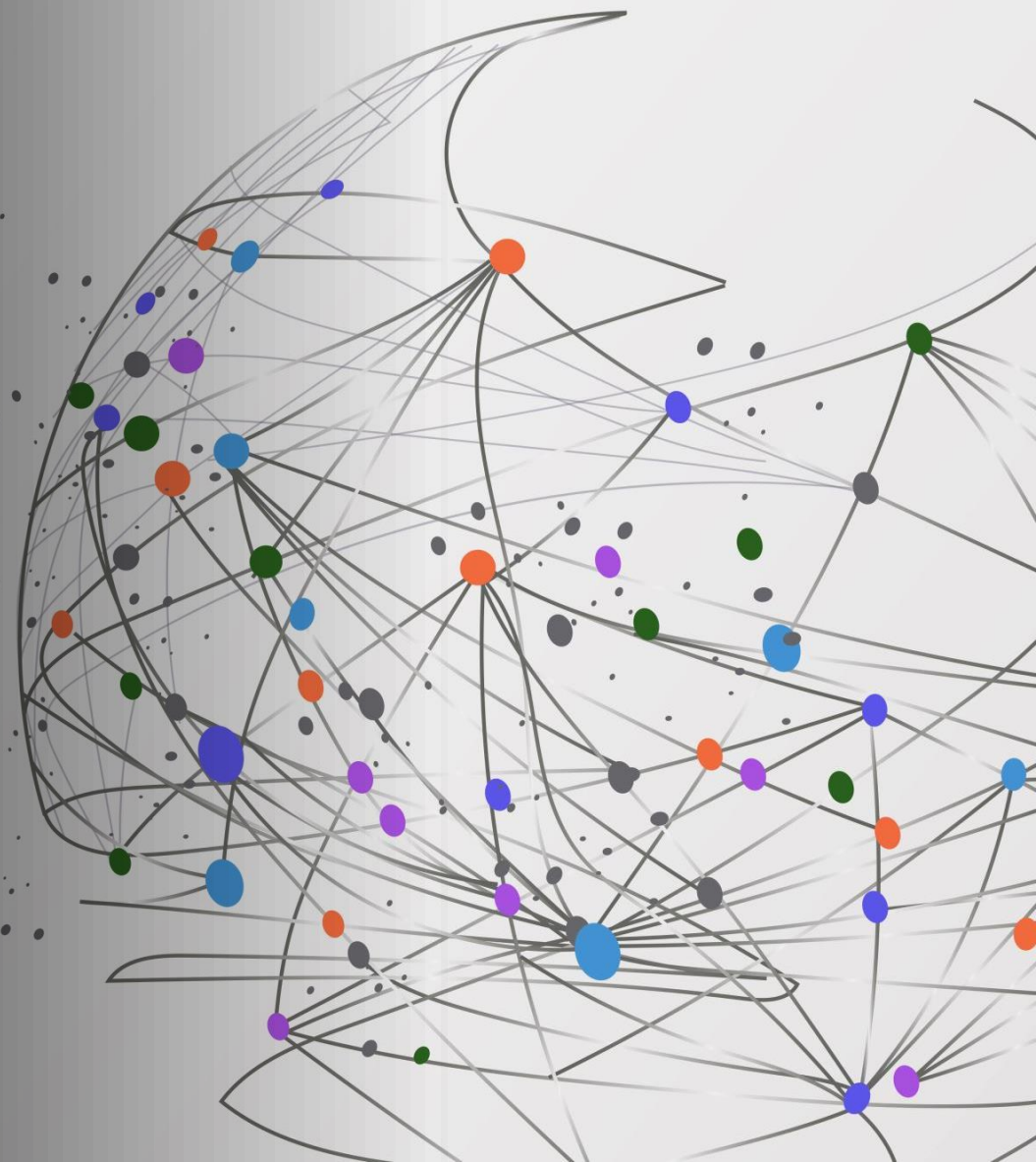




Pediatric Hematology- Oncology Series





Solid tumors

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April 2024

How does a Solid tumor present?

Latency in presentation.

Asymptomatic/ incidental finding.

Mechanical effect (depends on both mass size and location): pain, bowel obstruction, distention, headache with increased ICP.

Effect of mediators produced by the mass (as in VIP secreting tumors and pheochromocytoma)

Loss of function (Hypoglycemia in liver tumors. Paralysis in spine tumors).

How to work up a solid tumor?



H&P: family history.



Baseline labs.



Genetic evaluation.



Imaging studies: X ray, US, CT scan, MRI, PET, MIBG.

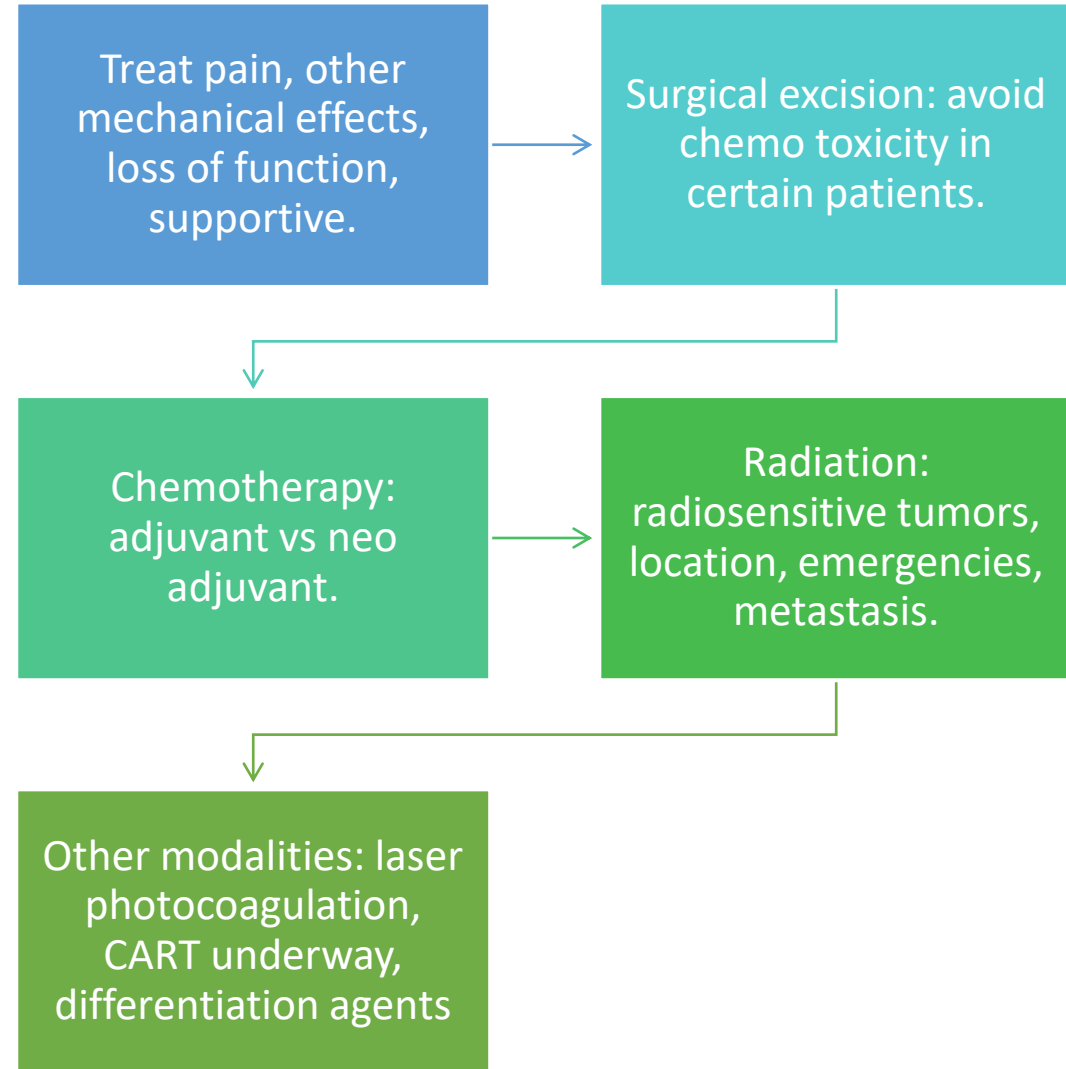


Look for mets: chest CT, BMX etc.



Look for mediators/ hormones etc secreted by tumors.

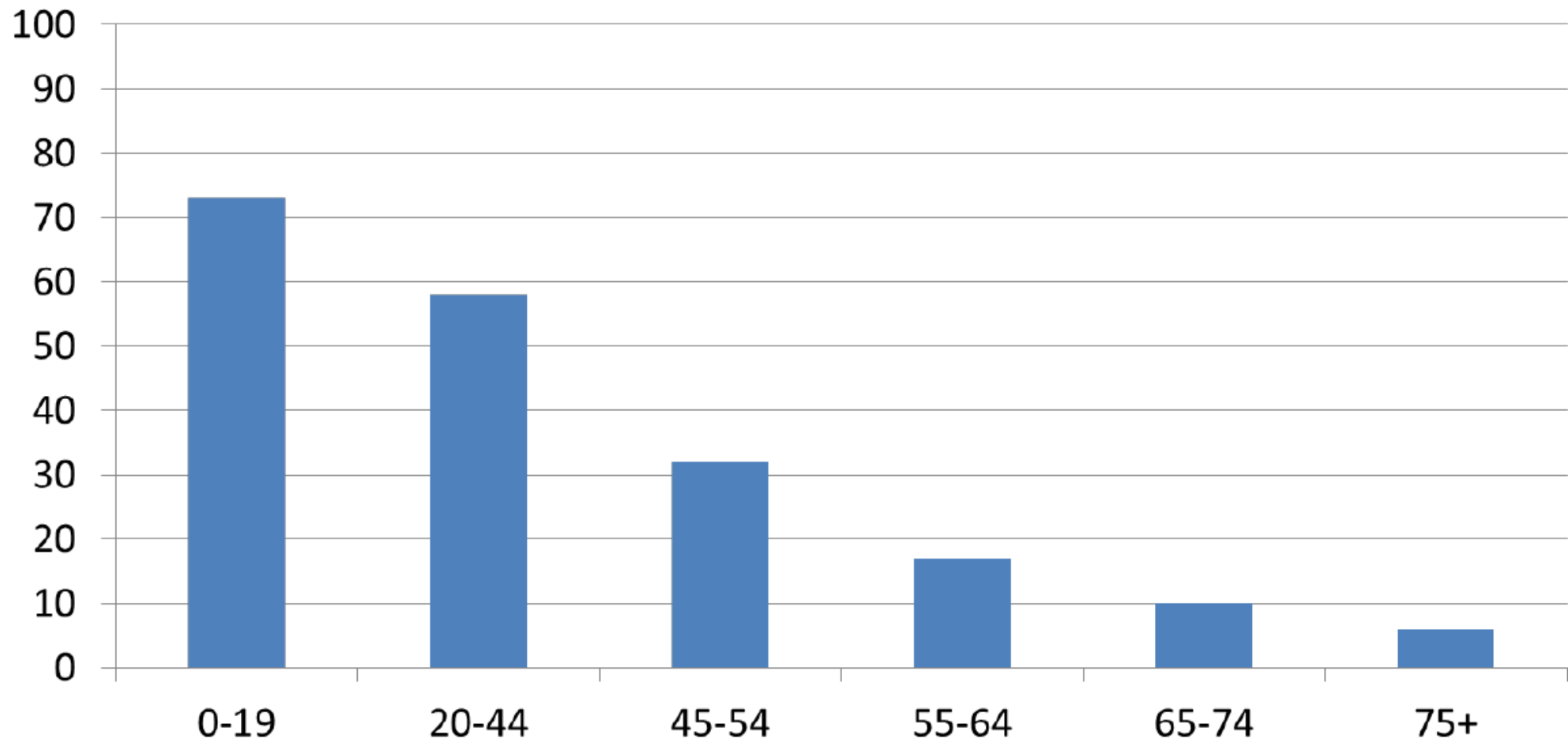
General solid tumor management



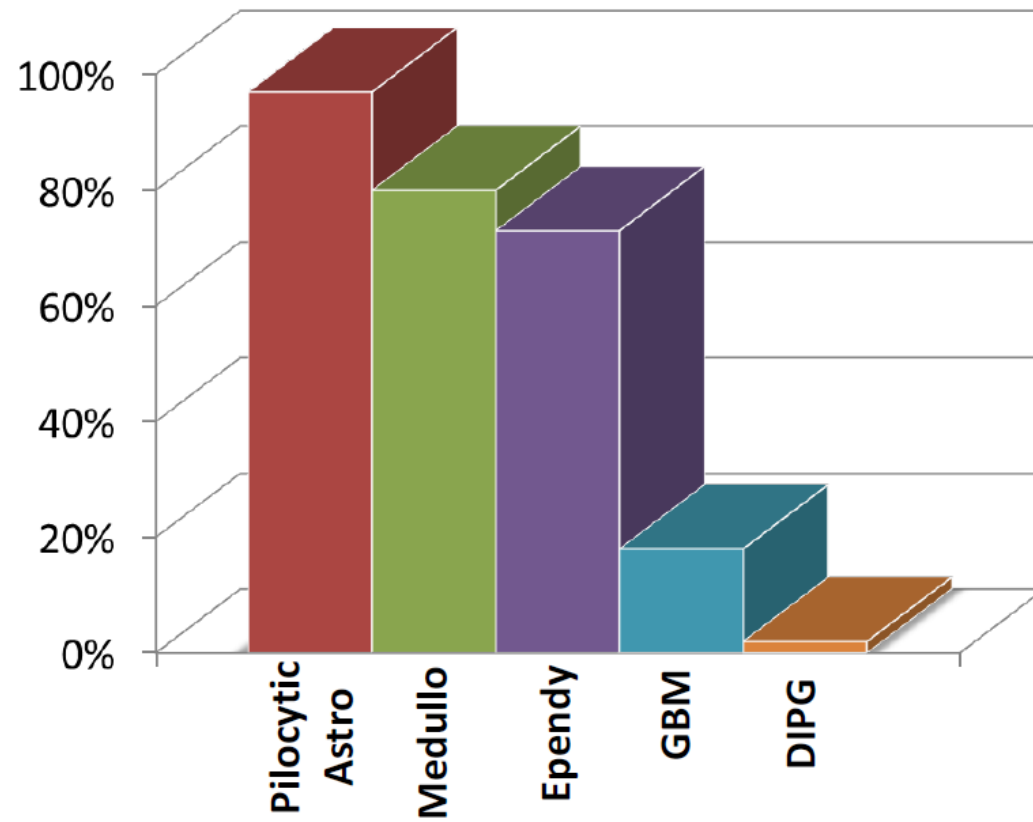
A dark, textured, organic shape resembling a brain tumor is positioned on the left side of the image. The shape is irregular and has a rough, porous appearance, with some lighter areas suggesting internal structure or shading. It is set against a light, speckled background that transitions into a solid light blue on the right side of the image. The overall composition is minimalist and focuses on the form of the tumor.

Brain tumors

5-year survival 1995-2009 (SEER data)



5-yr Survival Rates



Common presenting symptoms and signs



Nausea, vomiting, headache.



Behavioral and sleep cycle changes.



Weight changes, developmental delay.



Papilledema, bulging fontanel, cranial neuropathies, seizures, imbalance and loss of coordination/ ataxia.



Early preference of one hand before the age of 2 years or change of handedness.



Detailed history and
physical exam are
very important!

Medulloblastoma

Most brain tumors of childhood are infratentorial

The most common malignant pediatric BT is medulloblastoma

Embryonal origin.

Most are diagnosed under the age of 10 years.

Ataxia, signs of increased intracranial pressure.

Treatment: surgical excision; more complete the excision the better the outcome is, radiation and chemotherapy.

Overall cure rates are very good but long-term growth and neurodevelopmental delays in addition to endocrinopathies are common complications of radiation therapy.





Diffuse intrinsic
pontine glioma

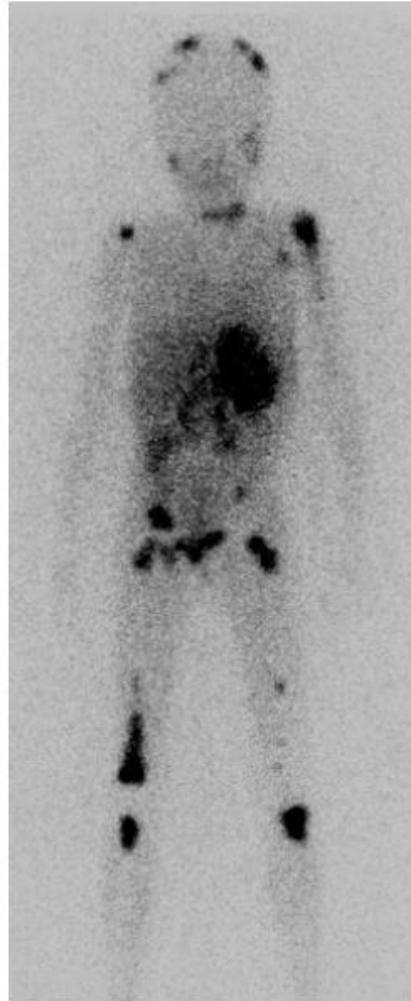
Neuroblastoma

- Third most common childhood malignancy.
- Its an embryonal malignancy, neural crest tissue of the sympathetic nervous system.
- The tumor can arise anywhere along the sympathetic chain, but the classical presentation is an abdominal suprarenal mass.
- Presentation depends on the location of the tumor (neck mass, intrathoracic mass or abdominal mass) and metastasis (skin lesions, anemia due to bone marrow replacement, bony masses and bone pain, proptosis and raccoon eyes).
- It may present with Horner's syndrome if the stellate ganglion is involved.
- Paraneoplastic effects: VIP secreting tumors and opsoclonus myoclonus syndrome were patients present with random eye movements, myoclonus and ataxia (good prognosis but long term neuro complications).

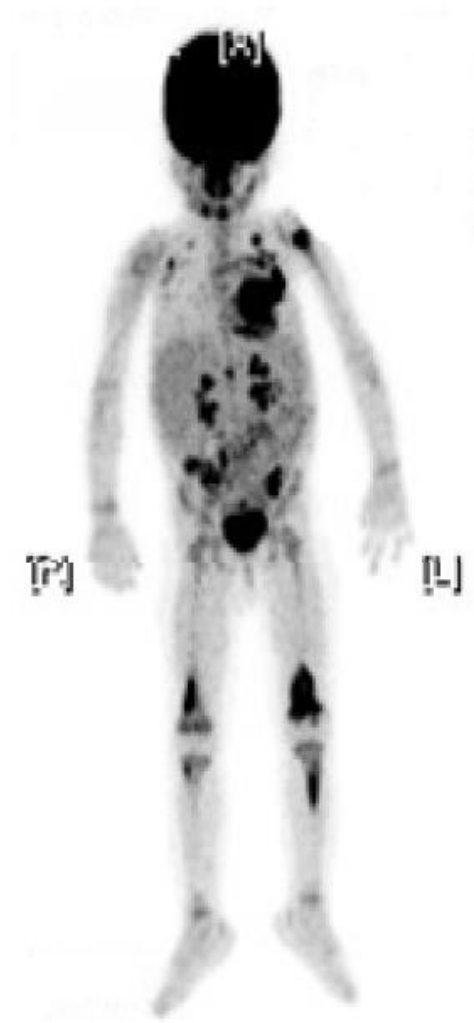
Neuroblastoma

- Poor prognostic features: normal diploid DNA content in tumor cells, advanced stage disease, age above 18 months at presentation, higher risk histologic features (poorly differentiated tumors) , and MYCN oncogene amplification.
- Exception stage 4S in infants (S for skin metastasis) prognosis is excellent.
- Evaluation includes: a chest/ abdomen/ pelvis CT scan, MIBG scan, bone marrow biopsy, spine MRI if involvement of the spine is suspected, urine/ serum testing for catecholamine metabolites (HVA and VMA), counts and chemistries.
- Prognosis was very poor with surgery, chemotherapy and radiation (for select cases). Significant improvement in outcome with addition of autologous stem cell transplant and antibody therapy.





I123-MIBG



FDG-PET

Wilms tumor

- Most common pediatric renal malignancy.
- Most are unilateral, up to 10% can be bilateral.
- It can be associated with some malformations in up to 10% of the cases.
- Aniridia, hemi-hypertrophy, Genito-urinary malformations and others.
- Malformations = earlier diagnosis.
- Patients with over growth syndromes including up to 10% of children with Beckwith- Wiedemann syndrome and some children with Perlman syndrome develop Wilms tumor.
- About 5% of patients with isolated hemi-hypertrophy also develop Wilms tumor.

Wilms tumor

- 2% of all Wilms tumor cases can be familial.
- Genes: WT1(Wilms tumor 1) WT2 and WTX genes.
- Most Wilms have favorable histology with excellent prognosis.
- About 8% have anaplastic histology.
- Presentation: asymptomatic abdominal mass. Occasionally, abdominal pain, hypertension, anemia and hematuria may be present.
- Evaluation: document blood pressure, check for congenital anomalies, evaluation by a geneticist, blood counts, UA, blood electrolytes, liver function testing and chest/ abdominal/ pelvic CT scan or MRI.
- While lower stage disease may be managed with surgical excision alone, higher stage disease require chemotherapy the possibility of radiation for situations like lung metastasis

Osteosarcoma

- Can occur de novo or as a long-term side effect to radiation therapy.
- Patients with hereditary retinoblastoma at high risk for developing osteosarcoma.
- It can be part of Li-Fraumeni syndrome (Tp53 mutation).
- Classical clinical presentation: pain and a mass at the site of the primary tumor.
- Typically involves the metaphysis of long bones.
- Most common sites are the distal femur followed by the proximal tibia followed by proximal humerus.

Osteosarcoma

- Can spread in skip lesions pattern or through hematogenous spread to the lung and other bone locations.
- Diagnostic work up: plain X ray (osteoblastic , osteolytic or a mixture)
Classical X ray findings include a Codman triangle caused by elevation of the periosteum and a sunburst pattern due to extension of the tumor through the periosteum. Chest CT scan is done to rule out pulmonary metastasis in addition to a biopsy.
- Treatment relies on surgery and chemotherapy administration.
Radiation is not part of treating osteosarcoma.

Ewing sarcoma

- Primitive neuroectodermal tumor.
- Tends to affect the axial skeleton more often than OS.
- Most common location: pelvis. Other locations: femur and ribs.
- Can present with systemic symptoms as fever and weight loss.
- Metastasis can affect the lungs, bone and bone marrow.
- Work up includes bilateral bone marrow biopsies (marrow mets).
- Plain X ray finding described is the onion skin appearance, but Codman triangles and sunburst patterns can be seen too.
- Treatment: surgery, chemotherapy and radiation.

Retinoblastoma

- Rare childhood tumor affecting the retina.
- Most present by the age of 5 years.
- 2 major forms: hereditary, 25% of patients, usually bilateral and multifocal and is due to germline mutations in the RB1. Median age of presentation is around 15 months.
- Non-hereditary form: majority of cases, unilateral or unifocal and is due to mutations in RB1 gene in somatic cells. Median age of presentation is about 30 months.

Retinoblastoma



Most common presenting feature is leukocoria, but strabismus, nystagmus, glaucoma, periorbital cellulitis, proptosis and buphthalmos, can be other features.



Diagnosis: examination under anesthesia of the retina for direct visualization of the tumors and evaluation of intraocular pressure in addition to ocular ultrasound, orbit and brain MRI, bone scan and bone marrow studies (evaluate for metastasis).



Most common metastatic sites: bone, bone marrow, liver and CNS.



Genetic counseling.



Treatment: multidisciplinary care aspects, depends on laterality and potential vision outcome / eye salvage chances.



Retinoblastoma

Surgical excision, chemotherapy , radiation and laser photocoagulation are all used modalities for this type of tumor.

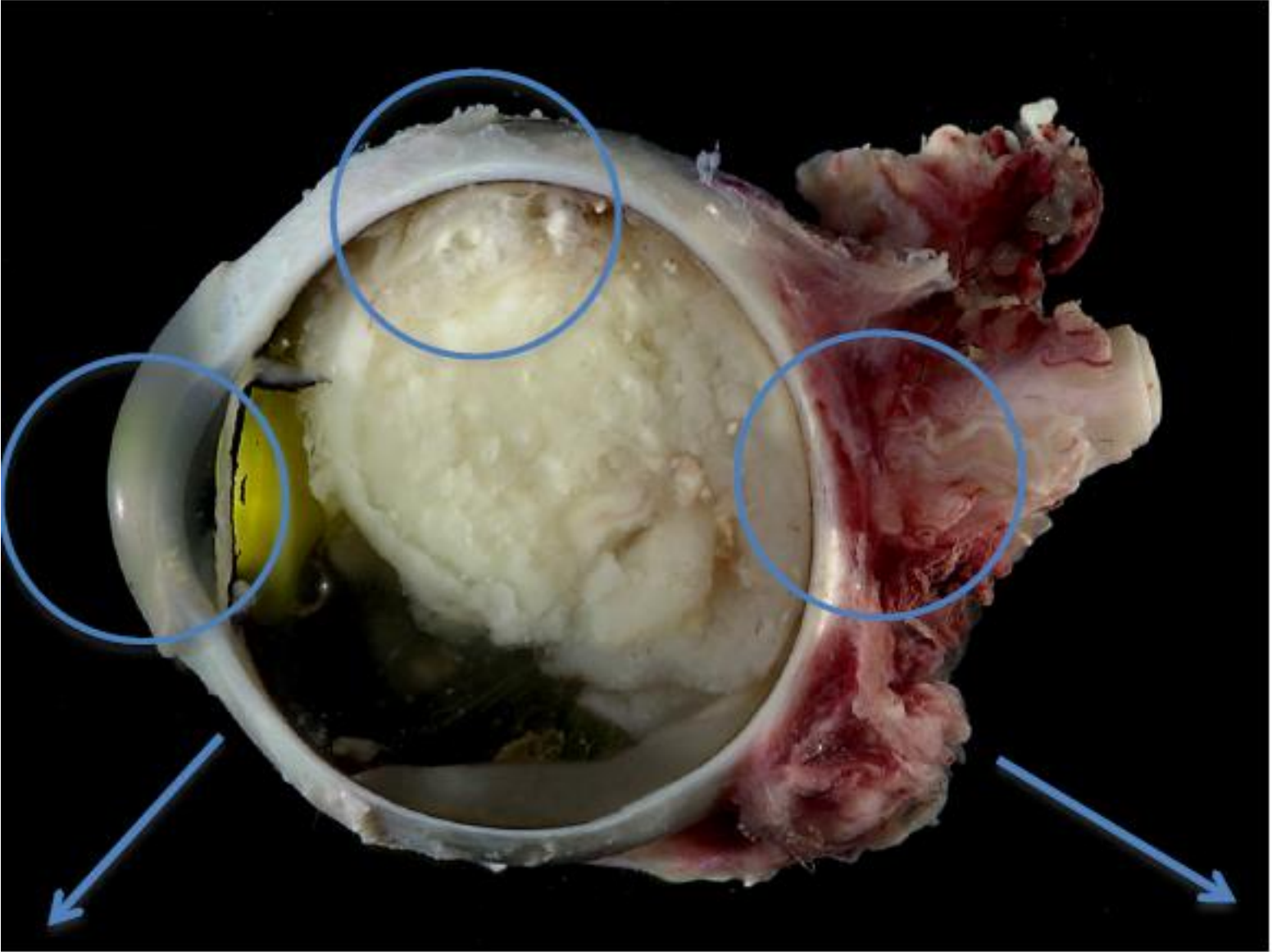
Survivors at high risk for second cancers post therapy.

Most of these second cancers, but not all of them are radiation induced.

The most common second cancer in these patients is osteosarcoma followed by soft tissue sarcomas, melanoma/ other skin cancers, lung cancer and others.

Trilateral retinoblastoma: presence of a midline pineoblastoma in a patient with bilateral retinoblastoma. very poor outcome.







Hepatoblastoma

Most common liver malignancy in children

Typically affects infants and young children with a median age at diagnosis of 19 months

Vast majority of patients less 15 years.

Prematurity and low birth weight are risk factors.

About 5% of hepatoblastoma patients also have familial adenomatous polyposis syndrome showing the importance of obtaining and accurate and complete family history.

Painless abdominal mass (pain present in advanced disease), weight loss, loss of appetite and most cases have elevated alpha feto protein level. If metastasis occurs, its usually to the lungs but other locations are also possible as the brain and peritoneum.

Hepatoblastoma

Workup: biopsy, CT scan imaging (or MRI), abdominal ultrasound and AFP levels.

Normal AFP levels can't rule out hepatoblastoma but are associated with a poorer prognosis and elevated levels can be followed to assess response to treatment.

Treatment is based on a combination of surgical resection and chemotherapy.

Those with unresectable tumors may need a liver transplant to achieve cure.

Practice Questions

- The parents of a 4-year-old boy bring him to the urgent care clinic because he has been increasingly fussy over the past few weeks and as of this morning stopped walking. All you notice on exam are purple to blue bruises under his eyes. You order multiple lab tests and his prothrombin and partial thromboplastin times are within normal range, but you note a slightly decreased platelet count at 100,000 cells/mm³ and a mild normochromic anemia with hemoglobin at 10.1 gm/dl. The rest of the CBC and electrolytes are normal.

- Which of the following is the most appropriate next step managing this child?

- A) Abdominal computed tomography.
- B) Brain computed tomography.
- C) Call the authorities to report potential child abuse.
- D) Platelet function studies.
- E) Administration of activated coagulation factor VII.

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Due to the finding of aniridia and hemihypertrophy in a 3-year-old child, he was worked up for the possibility of having Beckwith- Wiedemann syndrome and the suspicion is now confirmed. You counsel parents that the child's risk of developing certain tumors is significantly higher than the general population.

Which of the following tumors these patients are at the highest risk for?

- A) Osteosarcoma.
- B) Diffuse large B cell lymphoma.
- C) Wilms tumor.
- D) Acute lymphoblastic leukemia.
- E) Acute myelogenous leukemia.

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You evaluated a 2-year-old boy in your clinic who was born at 29 weeks of gestation due to worsening painless abdominal distention over the past month. You could appreciate a large abdominal mass on palpitation and lab work up is significant for a highly elevated alpha feto protein. On further questioning, the parents indicate a significant family history for familial adenomatous polyposis.

Which of the following conditions do you suspect based on this clinical picture?

- A) Neuroblastoma.
- B) Wilms tumor.
- C) Hepatocellular carcinoma.
- D) A liver hemangioma.
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The father of a 3-month-old male patient brings him to clinic today for evaluation of abnormal eye movements. On exam, you notice random, rapid bilateral eye movements in all directions. Neurological exam was significant for myoclonus in both lower limbs. You order an abdominal ultrasound that shows an upper right sided abdominal mass for which you schedule an abdominal computed tomography for follow up.

Which of the following is consistent with these clinical findings?

- A) Elevated alpha feto protein blood levels.
- B) Elevated carcinoembryonic antigen blood levels.
- C) Elevated urinary homovanillic acid levels.
- D) Leukemia cells on Cerebrospinal fluid exam
- E) Family history of short stature.

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You evaluate a 2-year-old male patient in your clinic. His mother brings him due to a worsening strabismus in his left eye. You note leukocoria on your exam on that eye and advise the mom that you are worried about a malignant condition that will need further evaluation by oncology, ophthalmology and genetics.

Which of the following is a valid statement about the suspected condition?

- A) This condition is most likely hereditary.
- B) The other eye is at very high risk for developing the same condition in the near to intermediate future.
- C) The child is at a high risk for developing osteosarcoma in the future.
- D) This tumor almost never metastasizes.
- E) This is a rare presentation as this tumor usually presents in patients older than 12 years old.

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A 15-year-old male presents with progressive pain above the left knee for the past 2 months. A plain x ray shows a sunburst appearance of the distal femur. You suspect this could be osteosarcoma.

Which of the following is not part of working up and managing osteosarcoma?

- A) A chest CT scan.
- B) Radiation therapy.
- C) Chemotherapy.
- D) Surgical excision.
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A 5-year-old boy presents to the emergency room with a 3-day history of worsening ataxia. His mother mentions that he was doing well until about 10 days ago when he started vomiting mostly in early mornings. Vomiting episodes have been increasing in frequency since then and did not seem to be preceded by nausea. A wide based gait was noted on physical exam.

Which of the following is most likely to be helpful in establishing the likely diagnosis?

- A) Brain magnetic resonance imaging.
- B) Brain magnetic resonance angiography.
- C) Spinal magnetic resonance imaging.
- D) Blood alcohol level.
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What is the most likely explanation for this child's hemoglobin value?

- A) Iron deficiency.
- B) Occult gastrointestinal bleeding.
- C) Metastasis of neuroblastoma to the bone marrow.
- D) Low erythropoietin levels due to neuroblastoma metastasis to the kidneys.
- E) Paraneoplastic effects of neuroblastoma.

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Which of the following is the most likely cause of this boy's pain?

- A) Osgood-Schlatter Disease.
- B) Cellulitis.
- C) Ewing sarcoma of distal femur.
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You meet the parents of a 12-month-old girl in your clinic for counseling 1 day after she was diagnosed with retinoblastoma of the right eye. As you review her chart, you notice that the presenting complaint was leukocoria noticed at home a few days ago. The child was born at term and has a significant family history of retinoblastoma in multiple relatives.

Which of the following statements regarding this child's condition is accurate?

- A) This condition is not curable.
- B) This condition is usually hereditary.
- C) Most familial retinoblastomas are bilateral.
- D) The best treatment for this child is observation.
- E) Most children affected by retinoblastoma are over 10 years of age.

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As part of workup for hematuria, an 11-year-old girl gets an abdominal CT scan that shows a renal mass suspicious for Wilms tumor which is confirmed by histopathology later.

What is the most common presentation for this disorder?

- A) Incidental finding of an otherwise asymptomatic abdominal mass.
- B) Hematuria.
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Which of the following tumors is most likely to be diagnosed on biopsy?

- A) Atypical rhabdoid teratoid tumor.
- B) Germ cell tumor.
- C) Diffuse intrinsic pontine glioma.
- D) Glioblastoma multiforme.
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Which of the following studies will be most helpful in this scenario?

- A) A chest CT scan.
- B) Serum alpha feto protein.
- C) Urine for homovanillic acid.
- D) Lumbar puncture with cytology looking for malignant cells.
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