CNS malignancies in childhood

Epidemiology :Pediatric Brain tumors – Epidemiology ~2200 primary brain tumors , 1994 – 3.45 per 100,000. Primary Brain tumors are the most common malignancy of children (now overtaken non-solid tumors). Most common cause of cancer-related deaths in children. Mortality 45% Highest morbidity of all childhood malignancies (d/t Dz and Tx) Generally multimodal Tx has improved over yrs d/t advancements in NeuroSx, Radiation, ChemoRx

Etiology : Not well defined Familial/hereditary syndromes in 5% Exposure to ionizing radiation Familial w/o heritable syndrome in sporadic cases Molecular events not well understood. Multiple genetic markers involved in some

Familial/Hereditary Syndromes (all autosomal dominant) : Neurofibromatosis 1 (NF1) Neurofibromatosis 2 (NF2) Tuberous Sclerosis Li Fraumeni Syndrome Von Hippel Lindau Cowden Turcot Nevoid Basal Cell

Childhood Brain Tumor Consortium (location of tumors) : Infratentorial tumors (43.2%) Supratentorial Tumors (40.9%) Spinal Cord (4.9%) Multiple Sites (11%)

Age-related differences :Age-related differences <12mo: most are supratentorial (mostly Choroid Plexus, Complex Tumors and Teratomas 1-10yr: most are infratentorial (juvenile pilocytic astrocytoma and medulloblastomas) >10yr: Most supratentorial (diffuse astrocytomas) Children/adolescents have more tumors of optic pathway, hypothalamus, brainstem, pineal-mid-brain than adults

Clinical Manifestations –Depends on tumor site and type and age of child Intermittent early a.m. HA, nausea (months) then more frequent and more intense Sx d/t ? ICP (irritability, personality ?, HA, vomiting [esp early am], diplopia) Signs – ? head circ., papilledema, head tilt [herniation or CN IV palsy], CN VI paresis. In very young ?ICP – vomiting, irritability, lethargy and later macrocephaly In very young Sx may be similar to other common illnesses Seizures, tremors, sleepiness

Clinical Manifestations – Location : Infratentorial Tumors: equilibrium, gait, coordination problems. Blurred vision, diplopia, nystagmus Brainstem region: gaze palsy, cranial nerve palsies, UMN deficits (clonus, hyperreflexia, hemiparesis) Supratentorial tumors: can be focal w/ motor weaknesses, sensory loss/?, speech, mentation ? and personality deficits, seizures. Infants may present w/ hand preference. Mid-line or Infratentorial Tumors: Classic triad of HA, N/V, Papilledema

Optic Pathway Tumors: ? visual acuity, Marcus Gunn pupils, visual field defects, nystagmus Suprasellar Tumors and 3rd Ventricle tumors: neuroendocrine defects (DI, galactorrhea, hypothyroid, precocious (or delayed) puberty. Diancephalon Syndrome: FTT, ? appetite, emaciation, euphoria (infants/young children) Pineal Region tumors: Parinaud syndrome – upward gaze paresis, pupils accommodate but don't react, nystagmus, eyelid retraction

Diagnosis : H+P plus ophthalmic exam MRI and MRA (tumor vascularity) If midline or Pituitary/optic chiasm/ suprasellar regions, eval for neuroendocrine dysfxn Serum and CSF ß-HCG, a-FP for germ cell tumors LP: medulloblastoma/PNET, ependymoma, germ cell tumors that spread to the leptomeninges LP contraindicated if newly dx'd hydrocephalus d/t CSF outflow obstruction or infratentorial tumors. Delay if newly dx'd intracranial tumors and Sx of ICP Bx

Treatment – Multimodal : Dexamethasone – ? cerebral edema around tumor (but temporary and side effects) Surgery – for histology, debulking, resecting, re-establishing CSF flow VP shunt – for CSF but malfxns and infxns Radiation – Typically 5d/wk for 5-6wk. Depends on age (try to defer in infancy d/t ? intellectual fxn), and SE's (HA, ?appetite, risk of stroke years later, short stature, scoliosis..) Chemotherapy – usually = 1 drug better

World Health Organization – Classification : Based on morphology, cytogenetics, molecular genetics, immunologic markers TNM based classification not used Tumor size not as important as histology No Lymphatics in CNS, Mets not common d/t ? mortality before mets can develop. M0 no spread, M1 into CSF..)

WHO Grading : WHO grade I – low proliferative potential. Possible cure with surgery alone WHO grade II – infiltrating, but low in mitotic activity. Can recur and progress to other grades WHO grade III – Histologic evidence of malignancy (mitotic activity), infiltrative, anaplastic WHO grade IV – mitotically active, necrosis,

rapid pre and post-surgical progression

World Health Organization : WHO classification >100 histologic categories and sub-types 5 types account for 80% 1. Juvenile Pilocytic Astrocytoma 2. Medulloblastoma/Primitive Neuroectodermal Tumor (PNET) 3. Diffuse Astrocytomas 4. Ependymoma 5. Craniopharyngioma

Tumor types : Astrocytomas Oilgodendrogliomas Mixed gliomas Ependymal tumors Choroid plexus tumors Embryonal tumors Pineal Parenchymal tumors Neuronal/mixed neuronal glial tumors Craniopharyngioma Meningeal tumors Germ cell tumors Brainstem tumors Metastatic tumors