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BRAIN NEOPLASMS

OUTCOME OF INFANTS WITH INTRACRANIAL TUMORS

Investigators at British Columbia Children's Hospital, Vancouver, Canada evaluated by retrospective chart review the long-term outcome and its predictors in all infants with a primary intracranial tumor seen at BCCH in the 23-year period, 1982-2005. Of 35 infants (18 [51.4%] male) diagnosed with tumors, 30 underwent surgical resection, 14 received adjuvant chemotherapy, 5 had delayed radiotherapy; 20 (57%) survived, 12 (34%) had a good outcome and 23 (66%), a poor outcome. Of those with poor outcome, 15 (43%) died before age 5 years, 6 (23%) were alive with partial or severe disability, and 2 died at ages 5.5 and 7 years.

Intracranial pressure was raised at presentation in 21 (60%) patients, with increasing head size in 20 (57%), and vomiting in 16 (45.7%). Seizures occurred in 5 (14.3%), limb weakness in 4 (11.4%), and poor feeding in 4 (11.4%). Less frequent presenting features included nystagmus in 3 (8.6%), torticollis in 2 (5.7%), and apnea in 2 (5.7%). Among survivors, 14 of 20 (70%) had neurologic deficits; these included seizures in 8 (40%), speech difficulties 8 (40%), limb weakness 6 (30%), ataxia 3 (15%), and cranial nerve deficits in 2 (10%). Other complications included endocrine dysfunction in 5 (25%), visual deficits in 9 (45%) and auditory deficits in 3 (15%) children. Other late, treatment related, problems in 10 (50%) patients included alopecia, VP shunt, and 2nd malignancies. Ten of 20 survivors were attending regular school or had a skilled job.

Location of tumor was supratentorial in 25 (71%) (32% astrocytoma) and infratentorial in 10 (29%) (50% atypical teratoid rhabdoid tumor). Older age and an infratentorial tumor location are predictors of a poor outcome. The histological grade of tumor (I-IV) is the only independent predictor of survival ($p=0.002$) and functional outcome ($p<0.001$). (Pillai S, Metrie M, Dunham C, Sargent M, Hukin J, Steinbok P. Intracranial tumors in infants: long-term functional outcome, survival, and its predictors. *Childs Nerv Syst* 2012 April;28(5):547-555). (Respond: Dr Steinbok. E-mail: psteinbok@cw.bc.ca).

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COMMENT. More than half of infants with brain tumors survive more than 5 years after diagnosis, and a third have a good functional outcome. Older infants and those with infratentorial tumors have a poor prognosis. The histological grade of tumor is the most reliable predictor of 5-year survival and functional outcome. For an infant with an infratentorial or high-grade III or IV tumor the chances of survival are small. Extent of resection and adjuvant chemotherapy are not reliable prognostic indicators.

Compared to brain neoplasms in childhood, those originating in infants are more likely to be supratentorial, more aggressive, and patients who survive have a high incidence of neurological, endocrine, and developmental complications. Because of frequency of adverse effects, post-surgery radiation therapy is delayed, and chemotherapy is preferred.

Seizures and Brain Tumors. Symptoms of raised intracranial pressure, with bulging fontanelle and vomiting, are most frequent presenting manifestations of infants with intracranial tumors, but seizures may also occur early, especially with supratentorial tumors. Seizures associated with infratentorial tumor are typically manifested by opisthotonus and respiratory irregularities, including vertigo in older patients. Penfield W and Jasper HH (*Epilepsy and the Functional Anatomy of the Human Brain*. Boston: Little, Brown, 1954;p284) coined the term *ictus infratentorialis* for seizures thought to originate in the brainstem; they found no clinical evidence of seizures due to involvement of the cerebellum itself.

In the British Columbia study, seizure was an early symptom of infantile intracranial tumor in 14% of the cohort. In a total of 291 children with intracranial tumors treated at the Mayo Clinic, 1950-1960, seizures occurred in 50 (17%). The seizure-associated tumor was supratentorial in 62% and infratentorial in 38%. The EEG was abnormal in 96% of patients with supratentorial tumor and of localizing value in 88% of tumors that involved the cerebral cortex. (Millichap JG et al. *Neurology* 1962;12:329-336).

BIOLOGICALLY TARGETED THERAPY OF PEDIATRIC BRAIN TUMORS

Investigators at the Mayo Clinic, Rochester, MN; George Washington University, and Children's National Brain Tumor Institute, Washington, DC review the molecular pathways implicated in pediatric brain tumors, biologic agents that target these pathways, and current clinical trials of these novel therapies. Two major classes of newer biological agents include monoclonal antibodies against growth factor ligands or ligand-binding sites and the small molecule inhibitors that target the intracellular tyrosine kinase domains. The overexpression of the epidermal growth factor receptors found in brainstem gliomas, ependymomas, and medulloblastomas make these receptors a rational therapeutic target. Other targets for biological therapy include the platelet-derived growth factor receptor, angiogenesis inhibitors, and the Sonic Hedgehog pathway that plays a role in embryogenesis and is implicated in the pathogenesis of medulloblastoma. Tumors exhibit immune tolerance, and the induction of immunological responses to tumors using tumor vaccines offers a further promising approach to treatment. (Nageswara Rao AA, Scafidi J, Wells EM, Packer RJ. *Pediatr Neurol* 2012 Apr;46(4):203-211).(Respond: Dr