

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

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COMMENT. With a clearer understanding of tumorigenesis, molecular growth pathways, and immune mechanisms in pathogenesis of brain tumors, clinical trials of novel biologic agents are showing better CNS penetration and lower toxicity profiles compared with conventional chemotherapy. The effects of newer targeted agents on the developing nervous system must be further investigated since the pediatric brain may be more vulnerable to toxicity. (Wells EM et al. *Pediatr Neurol* 2012 Apr;46(4):212-221).

PATHOPHYSIOLOGY OF IDIOPATHIC INTRACRANIAL HYPERTENSION

Investigators at Emory University, Atlanta, GA review the epidemiology, pathophysiology and management of idiopathic intracranial hypertension (IIH), sometimes called pseudotumor cerebri or benign intracranial hypertension, terms now considered inappropriate. Theories regarding the pathophysiology of IIH involve obesity in young women and adipose tissue as an actively secreting endocrine tissue, vitamin A metabolism, and cerebral venous abnormalities, but the definitive etiology is unknown. No evidence based consensus or formal guideline is developed regarding management. Diagnostic lumbar puncture (CSF opening pressure >25 cm water) is a valuable intervention in treatment, and dietary modification to correct obesity is essential. The efficacy of acetazolamide, CSF shunting and cerebral transverse venous sinus stenting remains to be established.

Male patients are affected less frequently than female but their visual prognosis is worse. Various medications may cause or precipitate IIH, including tetracycline, cyclosporine, lithium, oral contraceptives, and tamoxifen. Obstructive sleep apnea is an obesity and IIH-associated factor. Proposed mechanisms for IIH include increased brain water content, excess CSF production, reduced CSF absorption, and increased cerebral venous pressure. Stenosis (not thrombosis) of a dominant transverse sinus (TSS) is a frequent finding and can impair venous drainage; correction of TSS following lumbar puncture or CSF shunt may be associated with relief of IIH and headache. Venous sinus stenosis leads to venous hypertension, decreased CSF absorption, increased ICP, and venous sinus compression. MRI findings in IIH include TSS, flattening of the posterior pole of eyes, dilation and tortuosity of optic nerve sheaths, and empty sella.

Therapy involves lumbar puncture, weight reduction, and carbonic anhydrase inhibitors, acetazolamide and the weak inhibitor, topiramate. Surgery and optic nerve sheath fenestration or LP or VP shunt is performed in patients with visual loss and papilledema. (Biousse V, Bruce BB, Newman NJ. Update on the pathophysiology and management of idiopathic intracranial hypertension. *J Neurol Neurosurg Psychiatry* 2012 May;83:488-494). (Respond: Dr V Biousse, Neuro-Ophthalmology Unit, Emory Eye Center, 1365-B Clifton Rd NE, Atlanta, GA 30322. E-mail: vbiousse@emory.edu).

COMMENT. Factors independently cited by the authors as predictive of a worse prognosis in IIH include male gender, African American race, obesity, anemia, obstructive sleep apnea, and fulminant onset of IIH.