

PEDIATRIC NEUROLOGY BRIEFS

A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

Vol. 21, No. 12

December 2007

BRAIN TUMORS

MOLECULAR BIOLOGY OF MEDULLOBLASTOMA

Current methods of diagnosis and treatment of medulloblastoma, and the influence of new biological advances in the development of more effective and less toxic therapies are reviewed by researchers at Children's National Medical Center, The George Washington University, Washington, DC. Medulloblastoma accounts for 16% of all pediatric brain tumors, and 40% of cerebellar tumors. The incidence peaks bimodally at 3 to 4 and 8 to 9 years of age. Associated disorders in 1-2% of patients include a nevoid basal carcinoma (Gorlin's syndrome), and familial adenomatous polyposis (Turcot's syndrome). CNS dissemination in 11-43% of patients, especially infants, is a predictor of poor outcome. Diagnosis is made on clinical presentation (vomiting 67%, headache 60%, ataxia 40%), CT findings of midline, homogeneous, contrast-enhancing cerebellar vermian mass in 30-55% patients, and MRI showing a heterogeneous hypointense mass on T1-weighted imaging. T2-weighted sequences are intermediate between grey and white matter. Drop metastases having a "zuckerguss" (icing sugar) appearance occur in up to 40% patients, in spinal MRIs. Magnetic resonance spectroscopy (MRS) determines the biochemical composition of the tumor (increase in choline and decreased N-acetyl aspartate and taurine). SPECT helps differentiate postradiation changes and tumor recurrence. Changes in diffusion tensor imaging after treatment are associated with poor intellectual outcome. Variants of medulloblastoma (classic, desmoplastic, anaplastic large cell, and nodular) are distinguished only by histological examination. Staging (M0-M4) and risk stratification are crucial in management, and are determined by lumbar CSF analysis and MRI. Risk is based on age, extent of disease, and dissemination.

Advances in molecular biology show that medulloblastoma arises from two germinoma zones of the cerebellum, the ventricular zone for midline tumors, and the

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2007 covers selected articles from the world literature and is published monthly. Send subscription requests (\$68 US; \$72 Canada; \$75 airmail outside N America) to **Pediatric Neurology Briefs - J. Gordon Millichap, M.D., F.R.C.P.-Editor**, P.O. Box 11391, Chicago, Illinois, 60611, USA. The editor is Pediatric Neurologist at Children's Memorial Hospital and Professor Emeritus, Northwestern University Medical School, Chicago, Illinois.

PNB is a continuing education service designed to expedite and facilitate review of current scientific information for physicians and other health professionals. Fax: 312-943-0123.

external granular layer for lateral desmoplastic tumors. Research involving the signal transduction mechanisms that promote oncogenesis includes sonic hedgehog (Shh), wingless (Wnt) growth factor receptors, receptor tyrosine kinases, retinoids that induce apoptosis, and notch and CXCR4 signalling ligands and inhibitors of apoptosis proteins that are associated with a poor prognosis. Determining the mechanisms of signal transduction in neuro-oncogenesis and the genetics of medulloblastoma will aid the development of more specifically targeted therapies. (Crawford JR, MacDonald TJ, Packer RJ. Medulloblastoma in childhood: new biological advances. **Lancet Neurol** December 2007;6:1073-1085). (Respond: John R Crawford MD, Children's National Medical Center, The George Washington University, 111 Michigan Ave NW, Washington DC 20010).

COMMENT. The addition of chemotherapy in the past 2-3 decades has increased the survival rate compared to surgical resection and radiotherapy alone. Controversial methods of management include total tumor resection that might account for the increased incidence of posterior fossa mutism; whole body radiation that causes long-term intellectual deterioration; and the incorporation of biological therapeutics in combination with radiation or chemotherapy. Altered classification of tumors based on more advanced neuroimaging may explain an apparent improvement in survival rates in response to new treatments.

OUTCOME OF INFANT EXTRACEREBRAL FLUID COLLECTIONS

Cases of benign infantile extracerebral fluid collections and nontraumatic chronic subdural hygroma or hematoma were reviewed retrospectively at Nebraska Medical Center, Omaha. Thirty-nine patients with benign extracerebral fluid collections presented at 3-12 months of age with macrocephaly. The birth was premature in 15 cases. Head size was normal at birth, 3 required shunt placement, but in most the accelerated head growth leveled off, approaching the 98th percentile after 24 months of age. Long-term developmental outcome was normal in 30 and mildly delayed in 3.

Of 9 patients with subdural hygroma, 3 presented with a large head and 3 with seizures. Birth was premature in 4. Five required subdural punctures and/or subduroperitoneal shunt placement. All developed normally. (Hellbusch LC. Benign extracerebral fluid collections in infancy: clinical presentation and long-term follow-up. **Jrnl Neurosurgery: Pediatrics** 2007;107(2):119-125). (Respond: Dr Leslie C Hellbusch, Department of Surgery (Neurosurgery), Nebraska Medical Center, Omaha, Nebraska).

COMMENT. In this patient series, infants with benign extracerebral fluid collections had a favorable long-term outcome, and 44% of patients with nontraumatic subdural hygroma resolved without surgical intervention. Previous follow-up studies of infants with idiopathic macrocephaly and orbito-frontal extradural fluid collections have shown variable results regarding neurological, radiological, and neuropsychological outcome. Some showed normalization of head circumference by 18-24 months, and others had persistent radiological changes. A study of 41 infants with idiopathic macrocephaly and extradural fluid collections followed to young adulthood showed resolution of the fluid collection but neuropsychological impairments in visuomotor skills and attention. (Muenchberger H et al. **Child's Nerv Syst** 2006;22(10):1242-1248; **Ped Neur Briefs** Nov 2006;20:81-82).