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CNS MALFORMATIONS

GENETIC BASIS FOR CLASSIFICATION OF CNS MALFORMATIONS

A new classification of malformations of the nervous system based on patterns of genetic expression integrated with descriptive morphogenesis is proposed by specialists in pediatric neurology, neuropathology and embryology at the University of Washington School of Medicine, Seattle, WA, now at Cedars-Sinai Medical Center, Los Angeles, CA. The authors point out the problems with classifications based exclusively on either descriptive morphogenesis or on genetics. Their new genetic based etiological classification lists 7 main categories, each with subtypes: I, II and III, involving upregulation or downregulation of organizer genes, or over- or under-expression of ventralizing or dorsalizing genes (eg duplication or agenesis of the neural tube and spinal cord); IV, disorders of rostrocaudal gradient and/or segmentation (including Chiari II malformation, and agenesis of corpus callosum); V, aberrations in cell lineages by mutation (including hemimegalencephaly, tuberous sclerosis, and gangliogliomas); VI, involving genes that mediate migrations; VII, involving genes that attract or repel axonal growth cones; and VIII, disorders of symmetry, including hemimegalencephaly and hemihyperplasia of the cerebellum. For some malformations, as in hemimegalencephaly, the malformation is listed under two categories, V and VII, recognizing there are sometimes multiple mechanisms, involving different genes and different patterns of genetic expression. Furthermore, lesions such as infarcts acquired in fetal life may disrupt radial glial fibers and result in heterotopia from disruption of nerve cell transport and incomplete migration (included in category VI). The authors appeal for semantic precision in describing developmental disorders of the nervous system. (Sarnat HB, Flores-Sarnat L. A new classification of malformations of the nervous system: an integration of morphological and molecular genetic criteria as patterns of genetic expression. Eur J Paediatr Neurol 2001;5:57-64). (Respond: Dr Harvey B Sarnat, UCLA School of Medicine, Cedars-Sinai Medical Center, 1165 West Tower, 87800 Beverly Blvd, Los Angeles, CA 90048).

COMMENT. The authors have written extensively on this subject, and their new etiological classification of malformations of the nervous system based on

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genetic expression permits inclusion of recent advances in molecular genetics integrated with morphological data. In the following article involving hemispherectomy for cortical malformations and epilepsy, the outcome was correlated with the MRI findings and cerebral morphology. Future research may facilitate correlations with genetic data based on the Sarnats' classification.

SEIZURE DISORDERS

SEIZURE OUTCOME AFTER HEMISPHERECTOMY

MRI features of hemispheric malformations of cortical development (MCD) were correlated with post-hemispherectomy seizure outcome in 13 children treated at The Cleveland Clinic Foundation, OH. At surgery, 11 patients were between 4 months and 2 years of age, and two were aged 8 and 12 years. MRIs were classified in 3 groups: 1) hemimegalencephaly (6 patients); 2) hemispheric MCD with partial cortical sparing (4 patients); 3) hemispheric MCD with atrophy (3 patients). All patients had hemiparesis and developmental delay, and 6 of 7 tested had homonymous hemianopia. Three had epidermal nevus syndrome. Seizures (infantile spasms and focal motor) began in the neonate in 11, and at 6 months and 4 years in the remainder; they recurred daily in the majority. Three had hypsarrhythmia or hemihypsarrhythmia; focal EEG seizures arose from the affected hemisphere in all patients. At functional hemispherectomy (FH), all patients had pathological confirmation of cortical dysplasia. Ventriculoperitoneal shunt for post-surgery obstructive hydrocephalus was required in 3 patients. There was no mortality.

At follow-up (mean 19 months, range 12-48 months), five of 6 patients (83%) in MRI group 1 (with hemimegalencephaly) had persistent although improved seizures after FH, whereas 5 of 6 patients (83%) in MRI groups 2 and 3 (with partial cortical sparing or atrophy) were seizure free. Outcome was not correlated with EEG findings; seizure control was similar among patients with or without bilateral interictal epileptiform discharges, infantile spasms, hypsarrhythmia, or hemihypsarrhythmia. Postoperative video-EEG monitoring in 5 hemimegalencephaly (MRI group 1) patients with persistent seizures showed a seizure focus in the operated hemisphere in 3 and the contralateral hemisphere in 2 patients. (Carreno M, Wyllie E, Bingaman W et al. Seizure outcome after functional hemispherectomy for malformations of cortical development. Neurology July (2 of 2) 2001;57:331-333). (Reprints: Dr Elaine Wyllie, Head, Section of Pediatric Epilepsy, The Cleveland Clinic Foundation, S-51, 9500 Euclid Ave, Cleveland, OH 44195).

COMMENT. Patients with hemimegalencephaly and other types of hemispheric malformations of cortical development, as distinguished by MRI, have varying seizure outcomes after surgical functional hemispherectomy. Patients with partial preservation of cortical architecture in one lobe or with atrophy have a better prognosis than those with hemimegalencephaly. Despite the relatively poor seizure outcome in this series, the authors advocate surgery because of an expected improvement in alertness and social interaction and lessened seizure severity. The distinction of various forms of cortical maldevelopment by MRI and molecular genetics before surgery should permit a better prediction of prognosis.