Pathologic Quiz Case

A Newborn With Seizures

Angela Spencer, MD, MS; Richard A. Prayson, MD

The patient was the product of a gestation complicated by first-trimester maternal bleeding and a cesarean section at 37 weeks, necessitated by fetal bradycardia. The birth weight was 7 lb 5 oz, with Apgar scores of 8 at 1 minute and 9 at 5 minutes. On the third day of life, the patient had a witnessed seizure that consisted of rapid eye blinking, right gaze preference, altered respiratory pattern, and right eyebrow twitching. These were followed by frequent similar episodes, occasional jackknife movements, and left-sided hypoactivity. Interictal left hemiparesis was apparent.

Magnetic resonance imaging showed right hemispheric megalencephaly with areas of hypointense signal on T1-weighted images and hyperintense signal on T2-weighted images; in addition, 2 small left frontal lobe heterotopias, a smaller-than-normal submental plate, and focal calcifications were observed. An electroencephalogram localized the seizures to the right occipital, parietal, temporal, and frontal lobes in a decreasing manner. The seizures were unresponsive to multiple drugs and continued at a frequency of 20 episodes per hour; on one occasion, the seizure lasted for 4 hours.

At the age of 4 months, the patient underwent a right hemispherectomy. An 18 × 13.5 × 3.5-cm segment of brain parenchyma (447 g) was excised. Grossly, pachygyria was observed in the occipital lobe region (Figure 1, arrow). On sectioning, there was focal thinning of the cortex with large areas in which there was obliteration of the gray-white interface (Figure 2). Microscopically, there was widespread cortical architectural disorganization, marked by a malpositioning of neurons in the cortex, abnormal cortical lamination, and abnormal orientation of cortical neurons (Figure 3). Focal extension of neuroglial tissue into the pia-arachnoid region was observed. Areas of prominent calcification (Figure 4) and reactive astrocytosis were noted in the disordered areas. Neuronal cytomegaly and mild neuronal dysmorphic features were observed. There was no evidence of balloon cells. There was no neoplasm recognized.

What is your diagnosis?

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From the Departments of Anatomic Pathology, Cleveland Clinic Florida, Weston, Fla (Dr Spencer), and Cleveland Clinic Foundation, Cleveland, Ohio (Dr Prayson).

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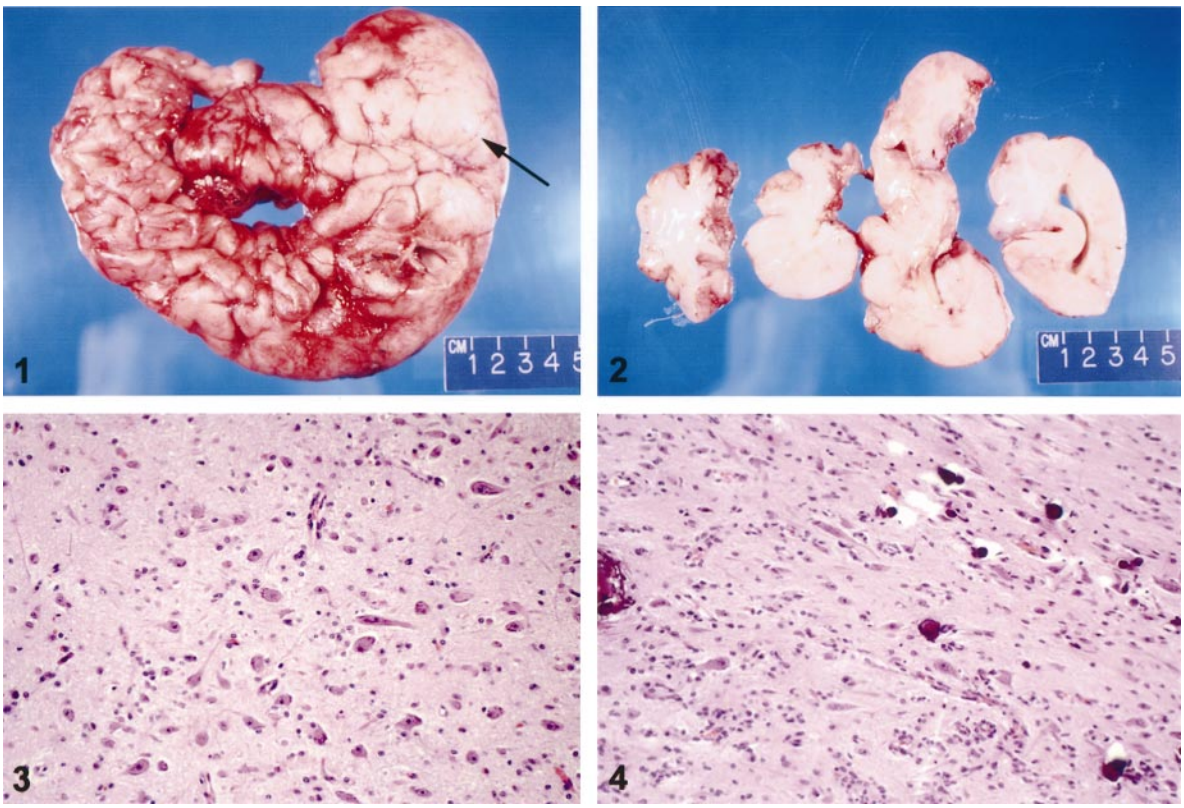
Corresponding author: Richard A. Prayson, MD, Department of Anatomic Pathology (L25), Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195 (e-mail: praysor@ccf.org).



Pathologic Diagnosis: Cortical Dysplasia (Malformation of Cortical Development)

A variety of gross patterns of cortical dysplasia is recognized, including polymicrogyria, hemimeganencephaly, and nodular heterotopias. Hemimeganencephaly is the result of a developmental abnormality, manifested by marked enlargement of one of the cerebral hemispheres.[1] The weight of the hemisphere is increased, often exceeding the customarily accepted total brain weight of an age- and sex-appropriate cohort. Other central nervous system structures usually retain their normal size and configuration. The phenomenon may be associated with ipsilateral craniofacial enlargement and/or dysmorphia, rarely with enlargement of the entire ipsilateral body, contralateral hemiparesis, and visual disturbance.[2] The most common early clinical presentation is epilepsy,[3,4] which is frequently intractable to pharmacologic agents and life threatening. Concomitant delayed achievement of developmental landmarks and mental retardation are frequently observed.

On gross inspection, the cortex may demonstrate visible abnormalities; failure of sulcation, pachygyria, and polymicrogyria have been reported.[5] In severely affected cases, broadened gyri may resemble a tuberous sclerosis tuber, firm and pale. These lesions may represent a forme fruste of tuberous sclerosis and are frequently associated with genetic defects.[3,4] On cross section, loss of demarcation between gray and white matter areas may be evident.[3,6]

Microscopically, the cortex may or may not be clearly discernible, as in this case, due to arrested layer formation secondary to severe neuronal migration defect. Abnormalities in the number of cortical layers present may exist. Focal dysgenesis may lead to linear or nodular gray matter heterotopias in the white matter region.[7] Abnormal orientation of neurons may be demonstrable (ie, dendritic processes are perpendicular with respect to the surface of the brain). Neurons may not be positioned in their proper location; large pyramidal neurons, normally present in cortical layers 3 and 5, can be found in cortical layers 1, 2, and 4. In addition, other observable findings include neuronal cytomegaly, dysmorphic neurons with cytologic alteration, and balloon cells characterized by abundant eosinophilic cytoplasm and eccentric nuclei. The pia-arachnoid region may contain glioneuronal tissue.

A number of syndromes with known chromosomal alterations have been associated with cortical dysplasia. The most common include tuberous sclerosis (*TSC1* gene, chromosome 9q34 and *TSC2* gene, chromosome 16p13.3), neurofibromatosis type 1 or von Recklinghausen disease (chromosome 17q11.2), and Miller-Dieker syndrome (*LIS1* gene, deletion on chromosome 17p13.3). Certain low-grade glial-neuronal neoplasms, including the dysembryoplastic neuroepithelial tumor and ganglioglioma, are often associated with cortical dysplasia.

Drug-resistant or life-threatening seizures necessitate surgical removal of the dysplastic foci.[8] At times, extensive resection, such as hemispherectomy, may be required. Younger patients generally have a better long-term outlook, secondary to functional compensation by the remaining brain. Battaglia et al[9] further attributed the overall improved quality of life to the additional increased social and parental involvement following the surgery.

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