Focal cortical dysplasia

Case report

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A histologically confirmed case of focal dysplasia of the cerebral cortex is presented. The computerized tomographic, electroencephalographic, pathological, and angiographic findings are discussed with respect to this rare developmental disorder. A review of the literature is presented with a possible etiology for this condition.

KEY WORDS • focal cortical dysplasia • heterotopia • epilepsy

The diagnosis of focal cortical dysplasia has been rare and elusive since this entity was originally described in 1971. With only a dozen clearly documented cases, most of them reported prior to computerized tomography (CT) scanning, its radiographic presentation has not been adequately described. Mental retardation and intractable seizures are early symptoms and are associated with abnormal electroencephalographic (EEG) findings and CT scan changes similar to those of neoplasia. Although gross pathological changes are occasionally seen, the diagnosis is ultimately based on the histopathology, which is characterized by a disorganization of the subcortical architecture and bizarre neuronal patterns.

Case Report

This 32-year-old woman was admitted to the Erie County Medical Center with recent exacerbation of seizures. She had long-standing mental retardation (intelligence quotient < 20) and had suffered from epilepsy since childhood. Her seizures were of the psychomotor type with staring episodes, and until 1 month prior to admission had been well controlled with carbamazepine (Tegretol, 300 mg four times daily) and phenobarbital (60 mg twice daily).

Examination. Neurological examination revealed hyperreflexia on the right, bilateral extensor plantar responses, and a mild spasticity of the right leg. The patient's gait showed right-leg circumduction and moderate ataxia. There were no frontal lobe release signs.

On CT scanning without contrast enhancement (Fig. 1 upper) and after intravenous injection of a 50-ml bolus of 60% contrast material (Fig. 1 lower), a slightly enhancing, deep-seated parenchymal abnormality with mixed density was seen in the left frontal lobe. The lesion appeared atrophic and caused no shift of the midline structures. On the basis of the CT scan, the differential diagnosis was an inflammatory lesion versus a possible infiltrating tumor. A four-vessel angiogram was normal. The EEG tracings showed mild to moderate diffuse cerebral dysfunction, maximal in the left frontotemporal area. The background rhythm was slightly reduced. Rare discharges in both frontal areas suggested the presence of epileptiform foci in these regions.

Operation. A left frontal craniotomy revealed an abnormal-looking brain that appeared avascular and was rubbery to the touch. The gyri and sulci were of normal size. Multiple frozen sections revealed gliosis. A partial frontal lobectomy was performed. The patient's postoperative course was uncomplicated and her seizures were well controlled with anticonvulsant therapy.

Pathological Findings. The specimens consisted of three irregular fragments of brain tissue, the largest measuring 3 cm in greatest dimension. Microscopic
FIG. 1. Computerized tomography scans without (upper) and with (lower) contrast enhancement. These 10-mm thick sections which were obtained at the base of the brain (left) and at the low ventricular level (right) show a slightly enhancing lesion of mixed density in the left frontal lobe.

sections were stained with hematoxylin and eosin (H & E), Nissl, Luxol fast blue, and Bodian’s method for axons; staining for neuron-specific enolase and glial fibrillary acidic protein (GFAP) was performed using immunoperoxidase techniques.

Microscopic examination revealed a lesion infiltrating the cerebral cortex and subcortical white matter. The corticomedullary junction was sharply demarcated. The involved gyri appeared abnormally narrow. The normal laminar arrangement of the cortical neurons was disturbed such that foci of the cortex were replaced by somewhat hypercellular sheets of neurons arranged in a haphazard manner, but sparing the first cortical layer (Fig. 2 upper left). Numerous large neurons were seen in both the deep and superficial layers of the cerebral cortex, but not in the molecular layer. Some of these had large, rounded, vesicular nuclei with prominent nucleoli. Others had irregularly shaped or lobular single nuclei, while occasional binucleated or multinucleated neurons were encountered (Fig. 2 upper right). A number of enlarged neurons displayed central chromatolysis or vacuolation of the cytoplasm which was strongly positive for neuron-specific enolase (Fig. 2 lower right). Occasional neurons contained neurofibrillary tangles which were demonstrated on H & E and Bodian stains (Fig. 2 lower right). Many smaller neurons containing abundant neuron-specific enolase were found in the disordered portions of the cortex which failed to exhibit the usual laminar architecture. The white matter beneath the dysplastic cortex was pale and poorly stained in the Luxol fast blue preparations and combined reduced numbers of axons with Bodian staining. Occasional large neurons were identified within the white matter. These contained neuron-specific enolase within the cytoplasm. The nuclei of some cells were large, rounded, and vesicular with prominent nucleoli. Increased numbers of astrocytes were identified within these areas of the white matter as well as within the abnormal zones of the cerebral cortex. The cytoplasm of the astrocytes was often intensely stained using the immunoperoxidase method for GFAP. The molecular layer was free of gliosis and no “wheat sheaf” formations of glial fibrils were detected in the subpial regions of the cortex. No areas of calcification were associated with the dysplastic lesions.

Discussion

Focal cortical dysplasia is a rare developmental formation involving subcortical architecture. Intractable seizures, abnormal EEG findings, and mental retardation are the hallmarks of its clinical presentation. In the small number of reported cases, the interval between onset of symptoms and treatment has varied from 2 to 35 years. Before the availability of CT scanning, the diagnosis depended solely on the pathological findings. Indeed, all recent cases have been described as a result of surgical lobectomy for intractable seizures.

With the advent of high-resolution CT, discrete atypical lesions may be recognized preoperatively. On CT scans, the lesion is poorly defined and of mixed density, containing a stellate low-density center and a higher-density periphery. The lesion involves white as well as gray matter and is without mass effect. In fact, the midline structures are shifted slightly toward the lesion and the gyri appear slightly atrophic. With contrast enhancement, the CT scans show a slight but definite increase in density of the peripheral portion of the lesion while the central portion remains of low density. The first diagnostic consideration would be that of an infiltrating low-grade glioma, the atrophic feature apparently representing changes secondary to central infarction. The characteristics of the contrast enhancement suggest the same diagnosis. Consistent with these findings, a chronic brain abscess could also be considered in the differential diagnosis.

These lesions were first described histopathologically in 1971 by Taylor, et al. These authors reported 10 cases among a series of 300 lobectomies. The distinguishing features were solely histological. Bizarre subcortical neurons with obvious disruption of the normal cerebral architecture was characteristic of these lesions. These aberrant neurons could be found in all but the first molecular layer. They typically occurred around a gyrus in patches no larger than 2 cm. Malformed cells with scant cytoplasm and large or multiple nuclei were also noted in a majority of the specimens. Calcifications and cysts were conspicuously absent. Various authors have described similar cytoarchitectural abnormalities.

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Fig. 2. Photomicrographs of the excised specimens. Upper Left: Low-power view of the dysplastic cortex in which the laminar arrangement of neurons is replaced by randomly distributed neurons of varying size. H & E, x 37. Upper Right: An abnormal binucleate neuron is seen within the dysplastic cortex. H & E, x 238. Lower Left: View of a dysplastic neuron with a large nucleus and cytoplasm exhibiting central chromatolysis. H & E, x 238. Lower Right: The neuron at the center contains conspicuous neurofibrillary tangles within the cytoplasm. H & E, x 238.

in the cerebellum along with diffuse cerebral involvement. Sections from these areas exhibited significant gross pathological changes, including lissencephaly, microgyria, pachygyria, or macrocephaly. The etiology of focal cortical dysplasia is unknown; however, similarities with tuberous sclerosis and various heterotopias have been noted. It has also been linked with congenital muscular dystrophy (Fukuyama type). Although similar to these disorders in clinical presentation, focal cortical dysplasia may be distinguished by its roentgenographic and histological appearance.

It should be emphasized that, despite the similarities between cortical dysplasia and the cortical tuber found in tuberous sclerosis, many distinguishing features exist between these two conditions, both clinically and pathologically, as described in detail by Taylor, et al. With respect to our patient, none of the clinical stigmata associated with tuberous sclerosis were present. There was no family history of neurocutaneous disease, nor was there evidence of adenoma sebaceum, subungual fibromas, retinal phakomata, or intraventricular candle-guttering. From a pathological standpoint, in contrast to Bourneville's disease, the external surface of the cortical lesion was visually unremarkable and it lacked the firm consistency of a tuber. Microscopically, the subpial region was spared and did not exhibit the striking fibrillary gliosis resembling sheaves of wheat that is so typical of tuberous sclerosis. Unlike a tuber, the dysplastic cortex was cellular rather than pale in its staining properties and was not abnormally widened.

In 1978, Mikhael and Mattar described four cases of heterotopia, one of which presented as focal cortical dysplasia. They proposed a developmental malformation in cortical organization as the etiology; this proposal was supported by noting the heterotopic giant neurons in the white matter with obvious disruption of lamination. These combined with the defects in gyrination certainly pointed toward developmental disorders originating in utero. Takada, et al., and McBride and Kemper supported this notion, emphasizing that subcortical ectopic neurons indicate a destructive process before 18 weeks of gestation (that is, before neuronal migration is completed). Changes in the gyri occur in the 6th intrauterine month, well after this neuronal migration. Thus, developmentally, the gross and histopathological changes are isolated events although often
linked clinically. Other theories include that of Manz, et al., who concluded that biochemical defects in the control of metabolism accounted for this dysplasia. They offered evidence of heteroploidy with enhanced DNA (deoxyribonucleic acid) transcription and translation. Current basic science research further supports this view. Cerebral cell migration takes place at 10 to 17 weeks' gestation. It involves active movements of gliophilic and neurophilic structures and follows selective pathways. It is restricted and dependent to both place and time. Each cortical layer divides at specific times, and migration only occurs after the last cell division.

Our case illustrates for the first time this rare dysplastic lesion on high-resolution CT scanning. Of note is its location, mixed CT density, lack of calcification, and enhancement with contrast material. These features can help to distinguish it from other lesions with similar clinical presentation. At this time no definitive conclusions about focal cortical dysplasia and its presentation can be drawn. However, certain characteristics of a distinct entity seem to be surfacing. Foremost is its histopathological presentation. The CT findings may be of increased benefit as more of these lesions are discovered. There is certainly great potential for magnetic resonance imaging in analysis of these lesions. Surgery may be indicated for diagnosis, potential treatment, or possible seizure palliation. Clearly, there is a full spectrum of clinical and research indications and applications for treatment of this type of lesion.

References

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