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NEURORADIOLOGY
CASE REPORT

MR tractography of schizencephaly

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ABSTRACT
This report attempts to document the potential of magnetic resonance (MR) tractography in providing detailed information on white matter tract anomalies in schizencephaly. Diffusion tensor imaging with tractography was performed in four patients referred for neuroimaging. On conventional MR imaging, two of the patients had temporal lobe involvement and the other two had frontal lobe involvement. Tractography was successful in showing major tract abnormalities in two patients and subcortical involvement in three. Tractography was negative in one patient. MR tractography is a promising imaging method in developmental anomalies, beneficial for both clinical management and understanding the nature of the pathology.

Key words: • *malformations of cortical development* • *schizencephaly* • *magnetic resonance imaging*

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Diffusion tensor imaging (DTI) with tractography is a recently introduced imaging technique that is unique in providing detailed imaging of white matter tracts and connectivity between different regions of the brain not easily appreciated with other imaging methods. It has a growing list of various clinical applications, with developmental anomalies at the top (1). The purpose of this report is to emphasize the potential role of DTI and tractography in providing insights into the evaluation of white matter tracts in patients with schizencephaly.

Case reports

All patients underwent magnetic resonance imaging (MRI) on a 1.5 T system (GE Signa Excite HD, GE Medical Systems, Milwaukee, Wisconsin, USA) utilizing an 8-channel neurovascular coil. MRI sequences were obtained in accordance with the epilepsy protocol of my institution including sagittal SE T1-weighted (W), transverse propeller T2W, transverse propeller T2W FLAIR, coronal FSE T2W, and coronal 3D SPGR IR for the three patients referred for epilepsy. In addition, 3D SGPR IR sequence was added for the patient presenting solely with cognitive impairment upon noticing the schizencephalic cleft. Informed consent was obtained from the next of kin for each patient. DTI sequences were obtained in the axial plane in all patients and in the sagittal plane in two patients using a single-shot spin echo-planar imaging sequence with a FOV, 27 cm; slice thickness/gap, 5/0 cm; TR/TE, 7000/88 ms; NEX, 2; and matrix, 128 × 128. The diffusion sensitizing gradients were applied at a b value of 1000 s/mm^2/axis with 33 non-collinear directions and 3 b=0 images. Images were reviewed at the console using the commercially available Functool software with Fibertrak option (GE Medical Systems, Milwaukee, Wisconsin, USA). Whole brain tractography has been performed in all patients. After marking the schizencephalic clefts, tracts within the vicinity of clefts were specifically identified by selecting the seed ROI and target ROI, and since all the patients had unilateral involvement, tracts on the affected side were compared with those on the normal side.

Case 1

An 8-year-old girl presented with epilepsy since early childhood and was on antiepileptic treatment. She had a horizontal schizencephaly cleft involving the inferomedial right frontal lobe with a dilated subarachnoid space communicating with the frontal horn of the right ventricle. Although not wide, it was considered open-lip, since the lips were not fused. She had dilatation of the right lateral ventricle, particularly prominent at the occipital and temporal horns. Her left hemisphere was normal except for periventricular band heterotopia located posteriorly (Fig. 1). Whole brain tractography showed asymmetry of the tracts be-

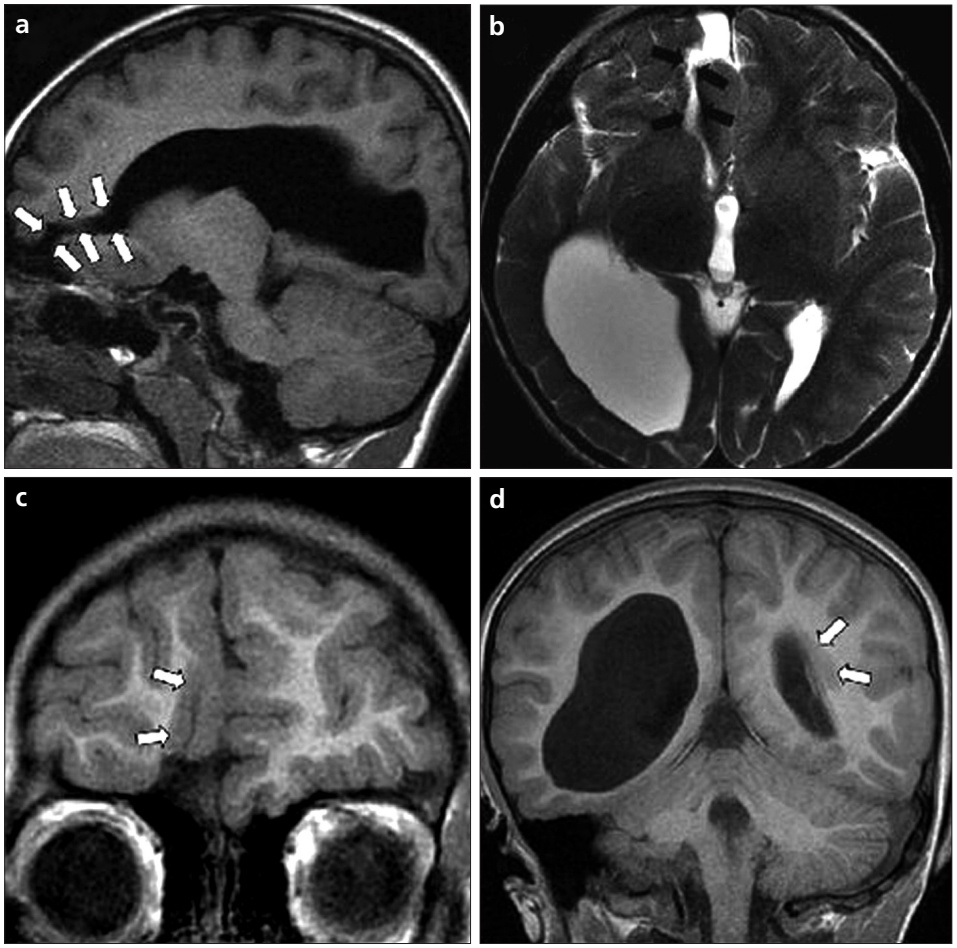

Figure 1. a–d. Conventional MRI of Case 1. On sagittal SE T1-weighted sequence **(a)**, open-lip schizencephaly cleft *(arrows)* in the right inferior frontal gyri is seen. On transverse T2-weighted Propeller sequence **(b)**, the cleft is again shown by arrows. Coronal SPGR IR sequence **(c)** shows thickened gray matter along the cleft *(arrows)*. On coronal SPGR IR image through the brainstem **(d)**, contralateral periventricular heterotopia is seen.

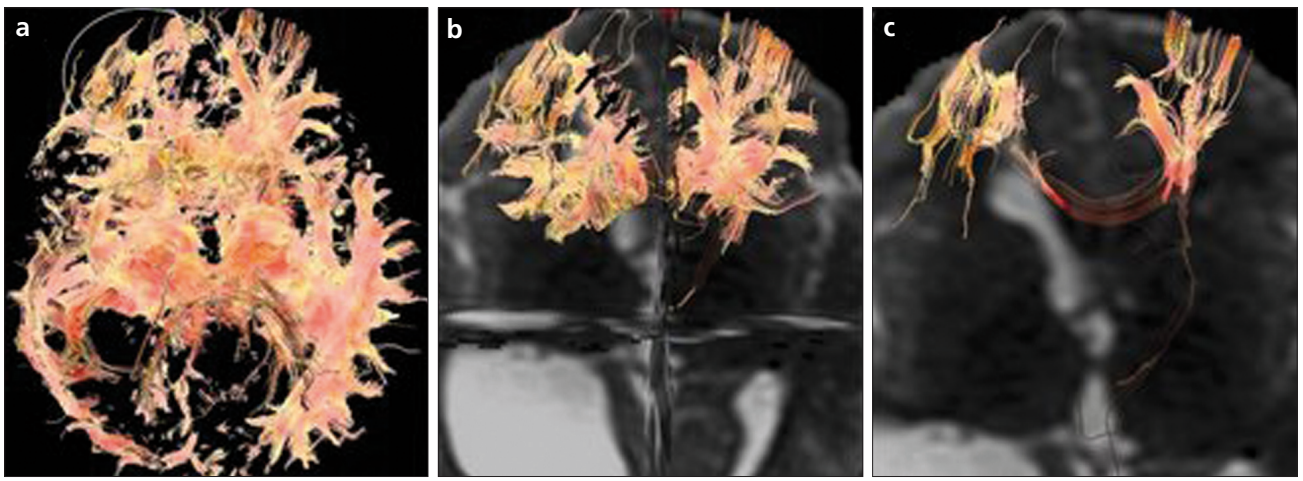

Figure 2. a–c. Tractography images of Case 1. Whole brain tractography *(view from below)* **(a)** shows the white matter tracts in the cleft vicinity *(encircled)* to be irregular and distorted when compared with the contralateral side. With localized seed ROIs **(b, c)**, arrows show the cleft **(b)**. Note the normal appearing genu of the corpus callosum **(c)**.

tween the hemispheres. There was loss of volume and disruption of the subcortical fibers in the right frontal lobe (Fig. 2). In addition, the right occipital lobe demonstrated loss of volume in the white matter tracts because of marked dilatation of the right lateral ventricular occipital horn. The superior longitudinal fascicle, cingulum, and uncinate fascicle were not involved because of the inferomedial location of the cleft.

Case 2

A 41-year-old male with congenital epilepsy, nystagmus, and ataxia underwent neuroimaging for the first time. Imaging showed a vertical closed-lip schizencephaly at the medial occipitotemporal sulcus, starting from the anterior left temporal lobe and extending posteriorly. The left lateral ventricle was asymmetrically dilated. Another striking finding was

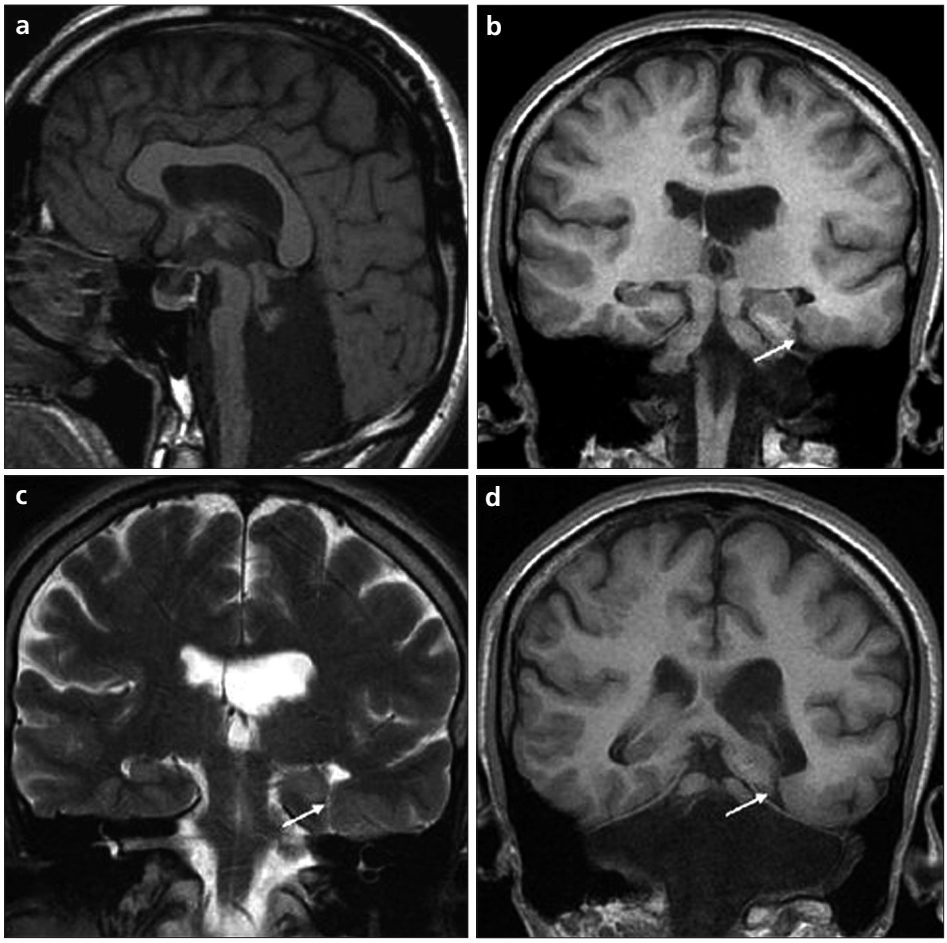

Figure 3. a–d. Conventional MRI of Case 2. On midsagittal SE T1-weighted image **(a)**, severe cerebellar and brainstem hypoplasia is seen. On coronal T1-weighted SGPR IR **(b)** and T2-weighted **(c)** images, schizencephaly cleft is indicated in the left parahippocampal gyrus *(arrow)*. On coronal T1-weighted SPGR IR image more posteriorly **(d)**, the cleft is seen extending to the posterior temporal and temporooccipital areas *(arrow)*.

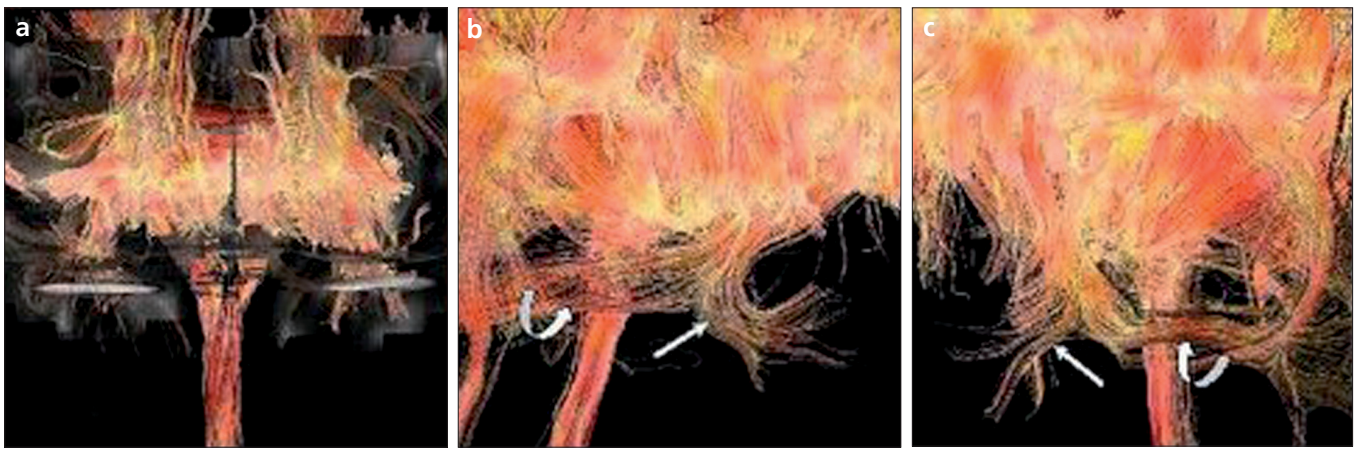

Figure 4. a–c. Tractography of Case 2. On whole brain tractography anterior view **(a)**, the cleft is not seen; however, severe brain stem hypoplasia with almost absence of cerebellar peduncles are evident. Right view **(b)** demonstrates the normal right uncinate fascicle *(straight arrow)* and inferior longitudinal fascicle *(curved arrow)*. Left view **(c)** for the visualization of the affected side shows the uncinate fascicle to be fanned out and distorted *(straight arrow)* and asymmetry of the inferior longitudinal fascicle *(curved arrow)*.

severe cerebellar and brainstem hypoplasia leading to an almost "empty posterior fossa" (Fig. 3). Tractography showed disruption of subcortical fibers in the left temporal lobe as well as involvement of the uncinate fascicle and inferior longitudinal fascicle (Fig. 4).

Case 3

An 80-year-old male patient with a history of remote epilepsy and stroke history presented with recent onset progressive cognitive impairment. He had a wide open-lip horizontal schizencephaly in the right frontal lobe with absence of the right frontal operculum and orbital gyri. An arachnoid cyst filled the defect at the right frontal lobe. The schizencephaly cleft extended to the frontal horn of the right lateral ventricle, consequently leading to an asymmetry in the ventricular size in favor of the right one. Cortical dysplasia was present in the vicinity of the

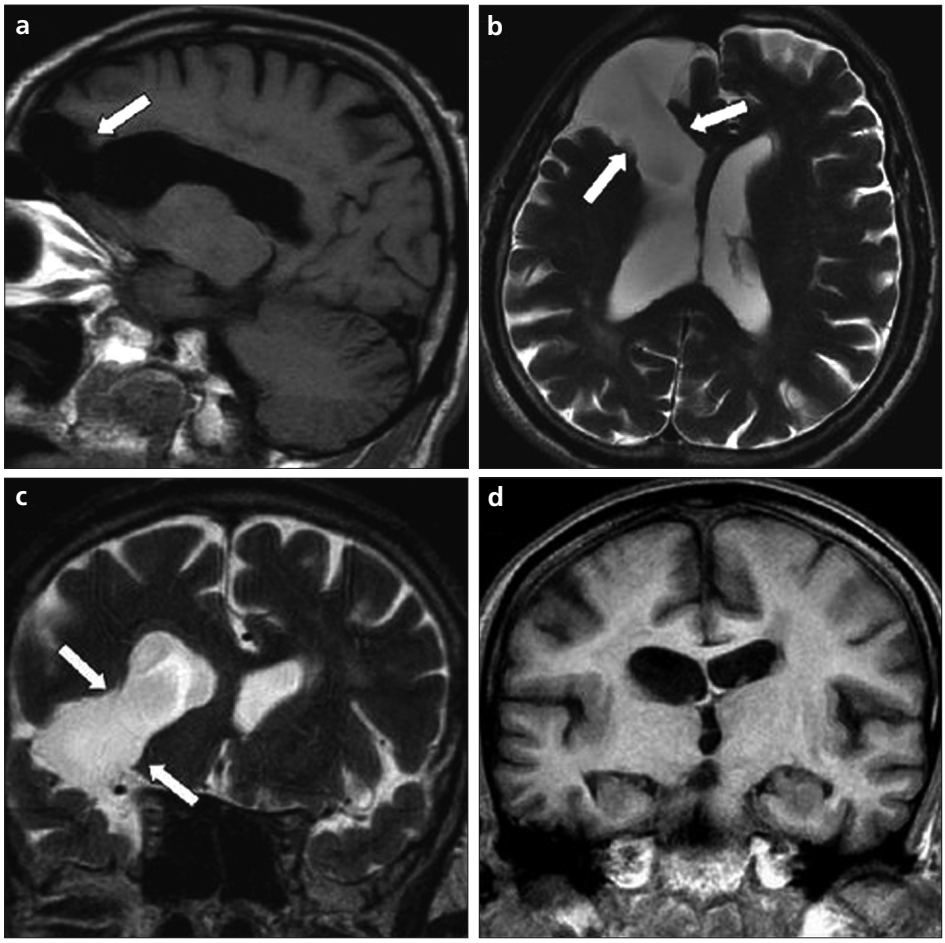

Figure 5. a–d. Conventional MRI of Case 3. On sagittal SE T1-weighted image **(a)**, a schizencephaly cleft involving the right inferior orbital gyri and frontal operculum with an arachnoid cyst anteriorly *(arrow)* is seen. Transverse **(b)** and coronal **(c)** T2-weighted images show the open-lip schizencephaly *(arrows)*. More posterior coronal T1-weighted image **(d)** shows uninvolved parietal and temporal lobes. White matter ischemic changes are noted in the bilateral posterior periventricular white matter.

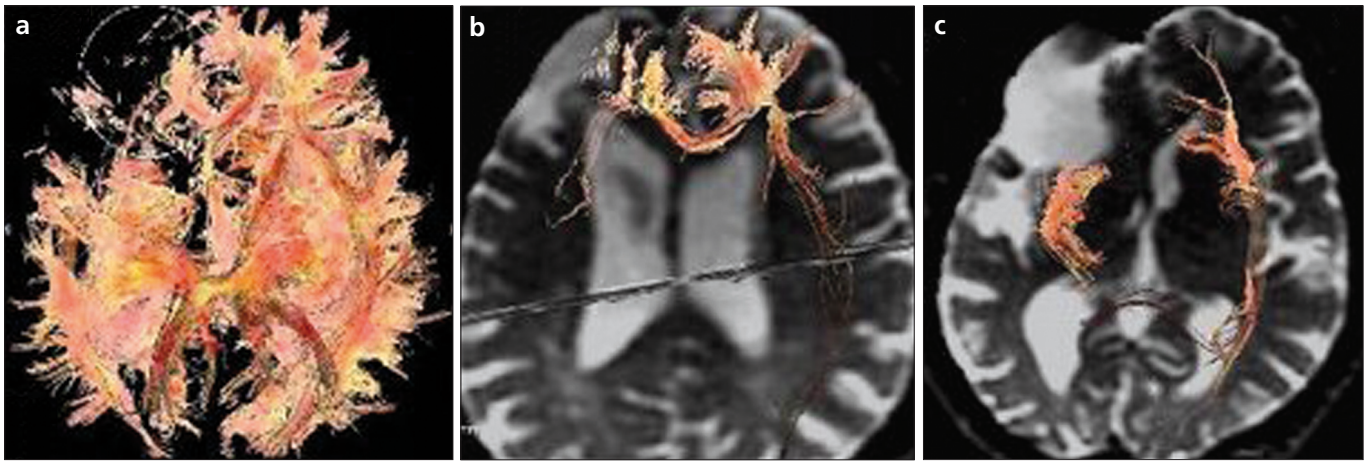

Figure 6. a–c. Tractography of Case 3. Whole brain tractography **(a)** shows the white matter changes in the right frontal lobe *(encircled)*. The involved right side features disrupted subcortical fibers whereas the left side and genu of the corpus callosum appear totally normal **(b)**. Projector fibers, namely the corticoclaustral fibers, are shown bilaterally **(c)**. The normal appearance is seen on the left. Note the clumped appearance of the right fibers.

cleft, including the parietal operculum and insular cortex (Fig. 5). Tractography showed disruption of subcortical fibers in relatively normal appearing parts of the frontal lobe. The uncinate fascicle was also affected on the right side, with involvement of the projecting fibers, such as the corticospinal and corticoclaustral fibers (Fig. 6).

Case 4

A 44-year-old male patient with recent onset cognitive impairment was incidentally shown to have a closed-lip schizencephaly in the left temporal lobe, which was best identified with the high resolution volumetric sequence (3D SPGR) (Fig. 7). The cleft was recognized in the left fusiform gyrus, without appreciation of major tract involvement.

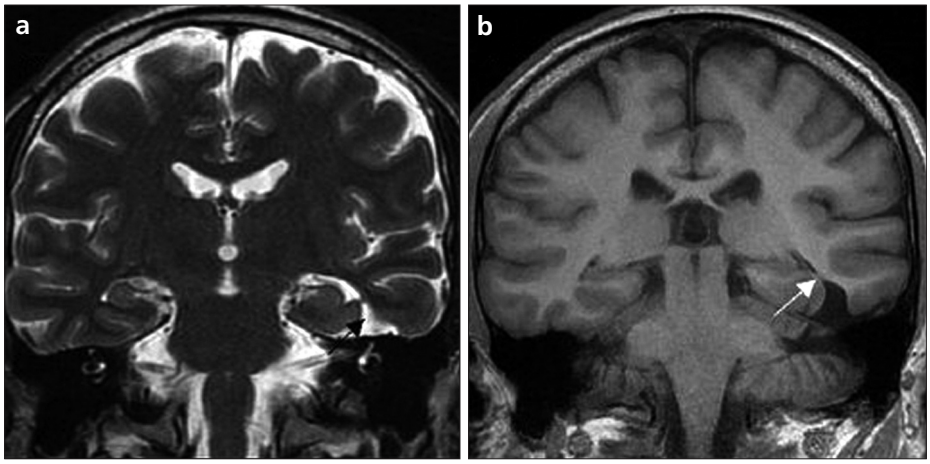

Figure 7. a, b. Conventional MRI of Case 4. On coronal T2-weighted image **(a)**, the defect in the left fusiform gyrus is seen *(arrow)*. On the 3D sequence (SPGR) **(b)**, the cleft is better shown *(arrow)*. Tractography of the patient (not shown) was unremarkable.

Discussion

Schizencephaly refers to a gray matter lined cleft through which pia covering the cerebral hemisphere contacts with the ependymal lining of a lateral ventricle creating the "pial-ependymal seam", a term first defined by Yakovlev and Wadsworth (2, 3). Histologically, pial ependymal seam is crucial in differentiating schizencephaly from a deep infolding of a dysplastic gyrus (4). Schizencephaly can be roughly classified into "open-lip" and "closed-lip" categories, depending on the width of the cleft or the amount of the missing tissue. When tissue loss is minimal, leading to a narrow cleft and apposition of the walls, it is called closed-lip schizencephaly. If there is greater amount of tissue loss with a cerebrospinal fluid filling space extending through the cleft towards the ventricle, the designation is open-lip schizencephaly. In either form it is common to find gyral anomalies within the cleft or in its vicinity (4–6). Although schizencephaly can be seen in any lobe, in a study of 20 patients by Barkovich and Kjos, 44% occurred in the frontal lobes, 30% involving the frontal and parietal lobes together, 19% parietal and occipital lobes, and only 7% in the temporal lobes (6). This distribution was found to be similar with other cortical malformations (7). Barkovich and Kjos also noted that 7 of their 20 patients had bilateral clefts (6). The exact incidence of bilaterality is unknown. All patients in our series had unilateral involvement—two with frontal lobe involvement and two with temporal lobe involvement.

None of our patients exhibited callosal anomalies or absence of septum pellucidum. Nevertheless, association of schizencephaly with absence of septum pellucidum with or without more extensive anomalies, such as septooptic dysplasia and callosal dysgenesis, is well known (5).

The pathogenesis of schizencephaly is not fully understood. Based on the findings of Takashima and Tanaka that watershed zones exist between the ventriculopetal arteries situated along the ventricular walls before the third trimester, Barkovich and Norman proposed that these clefts develop after a hypotensive episode at around 7th week of gestation, causing infarction in the watershed zone, which can also account for its association with septooptic dysplasia, since it is also presumed to be secondary to an ischemic attack in the 7th week (5, 8).

A wide range of clinical severity and neurologic involvement is seen in schizencephaly, depending on the amount of the missing tissue, unilateral or bilateral involvement, location of the cleft (e.g., perisylvian location), and coexisting anomalies. All of our patients had unilateral clefts—two open-lip and two closed-lip—and the clinically most severe case (Case 2) had associated severe anomalies. The incidentally diagnosed patient (without seizures, Case 4) had subtle imaging findings.

Case 2 is worth special emphasis, with severe cerebellar and brainstem hypoplasia accompanying schizencephaly. Little is known about the association of cerebellar hypoplasia with cerebral cortical malformations except for lissencephaly with cerebellar dysplasia, in which mutations of the reelin gene, crucial for cell positioning in the brain, or VLDLR (very low-density lipoprotein receptor) for reelin signalling pathway, are responsible (9). Genetic studies for this patient are in progress. However, detailed information about this coexistence is beyond the scope of this text.

Not only with schizencephaly but with all cortical malformations, dysgenesis or disruption of white matter tracts may contribute to epileptogenicity as well as functionality (10). Prior studies have shown reduced white matter in cerebral hemispheres, often with reduced diffusion (4, 11, 12). Lim et al. presented a case with bilateral schizencephaly with radiating gray matter signal extending from the ventricle to the cortex; DTI was also used in that report (10). However, there is no published DTI study of a group of patients with schizencephaly.

The purpose of this report was to show the feasibility of MR tractography in providing additional information in schizencephaly and to emphasize its potential for future studies correlating white matter tract integrity with clinical severity and impairment. The results are inconclusive in this study because of the small number of cases with lesions involving different sites. The major drawbacks of this study are the lack of quantitative assessments of white matter tracts, and the use of MRI equipment of a relatively low magnetic field (1.5 T). Today 3T MRI equipment is state-of-the-art and is superior to 1.5 T, especially in advanced methods. Functional MRI, when performed, may be complementary to DTI in providing more detailed information.

In conclusion, DTI appears to be beneficial in identification and evaluation of schizencephaly. In the future, imag-

ing of the white matter tracts should be crucial in determining the severity of neurologic involvement in patients with schizencephaly at a rather early age, and our increased knowledge about schizencephaly may aid our understanding of functions of individual white matter tracts.

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