MR Imaging Findings of Cortical Dysplasia of the Brain: Correlation with Pathologic Grades and Subtypes

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Purpose : Cortical dysplasia is known to be of variety of MR imaging findings. We attempted to classify MR imaging findings of cortical dysplasia into several types and to correlate those with histopathologic grades and subtypes.

Materials and Methods : Preoperative MR images of 97 patients with pathologically-proven cortical dysplasia were retrospectively reviewed with knowledge of the diagnosis and operative sites. The patients were divided into MR- positive and MR-negative groups based on the presence or absence of MR imaging abnormalities. In MR-positive group, MR imaging features were arbitrarily classified into four types (atrophic, cortical-band, inward-rounding, and nonspecific types) on the basis of size of the gyrus and adjacent CSF space, cortical thickness, signal intensity of the subcortical white matter, and blurring of the gray-white matter junction. The pathologic findings were also retrospectively reviewed without knowledge of MR imaging findings and divided into three grades (mild, moderate, and severe) and two subtypes (nonballoon-cell and balloon-cell). Pathologic grades and subtypes were compared between MR-positive and MR-negative groups. Four MR types of the MR-positive group were correlated with the pathologic grades and subtypes.

Results : MR-positive and MR-negative groups consisted of 39 (40%) and 58 (60%) patients, respectively . Of the MR-positive group, atrophic type was seen in 13 patients (33%), cortical-band type in 9 (23%), inward-rounding type in 9 (23%), and nonspecific type in 8 (21%). There was no significant difference in the pathologic grades between MR-positive and MR-negative groups, although MR-positive group tended to have higher pathologic grades than MR-negative group did. Balloon-cell subtype was found significantly higher in MR-positive group than in MR-negative group ($p < 0.05$): 21% (8/39) versus 5% (3/58). The inward-rounding type corresponded to the pathologically severe grade and balloon-cell subtype in 78% (7/9) and 56% (5/9) of the patients, respectively, while the atrophic type to the mild grade and nonballoon-cell subtype in 77% (10/13) and 100% (13/13), respectively.

Conclusion : A variety of MR imaging abnormalities were found in 40% of the patients with cortical dysplasia and those were classified into four types (atrophic, cortical-band, inward-rounding, and nonspecific types), of which the inward-rounding type correlated well with the pathologically severe grade and balloon-cell subtype, whereas the atrophic type with the mild grade and nonballoon-cell subtype.

Index words : Brain, abnormalities, Brain, MR

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Introduction

Focal cortical dysplasia (CD) has been thought to be a discrete disease entity since Taylor' s histologic description in 1971 (1). Although pathologic criteria for the focal CD was well established, it may also be overlapped in a variety of cortical malformation such as microdysgenesis, heterotopia, polymicrogyria, and agyria/pachygyria regardless of unique morphology in each entity (2-4). Therefore, CD, in the broadest sense, is defined as a neuronal migration disorder or malformative lesion of the neocortex which exhibits a spectrum of pathologic changes reflecting a disturbance in the process of its development. The earlier insult, the more abundant stem cells such as balloon cells, and the later insult, the more destructive patterns in histologic examination (4).

It is well known that CD is associated with the development of epilepsy and may derive some benefit from surgical excision of the lesion (5-7). With the advances of MR equipments and imaging techniques, detection or characterization of MR imaging abnormalities has become easier and the outcome has improved with appropriate surgical excision (8). In the previous studies, MR images in patients with CD showed abnormalities such as nodular or bandlike thickening of the cortex, abnormal signal intensity in the white matter, blurring of the gray-white matter junction or macrogyria (2, 9, 10). But, it is unclear whether those MR imaging findings would be consistently shown in all patients with CD or not. Additionally, there were poor pathological definition of cortical dysplasia and inconsistent inclusion criteria of the cases in the previous reports. To our knowlegde, there have been no reports regarding any correlation

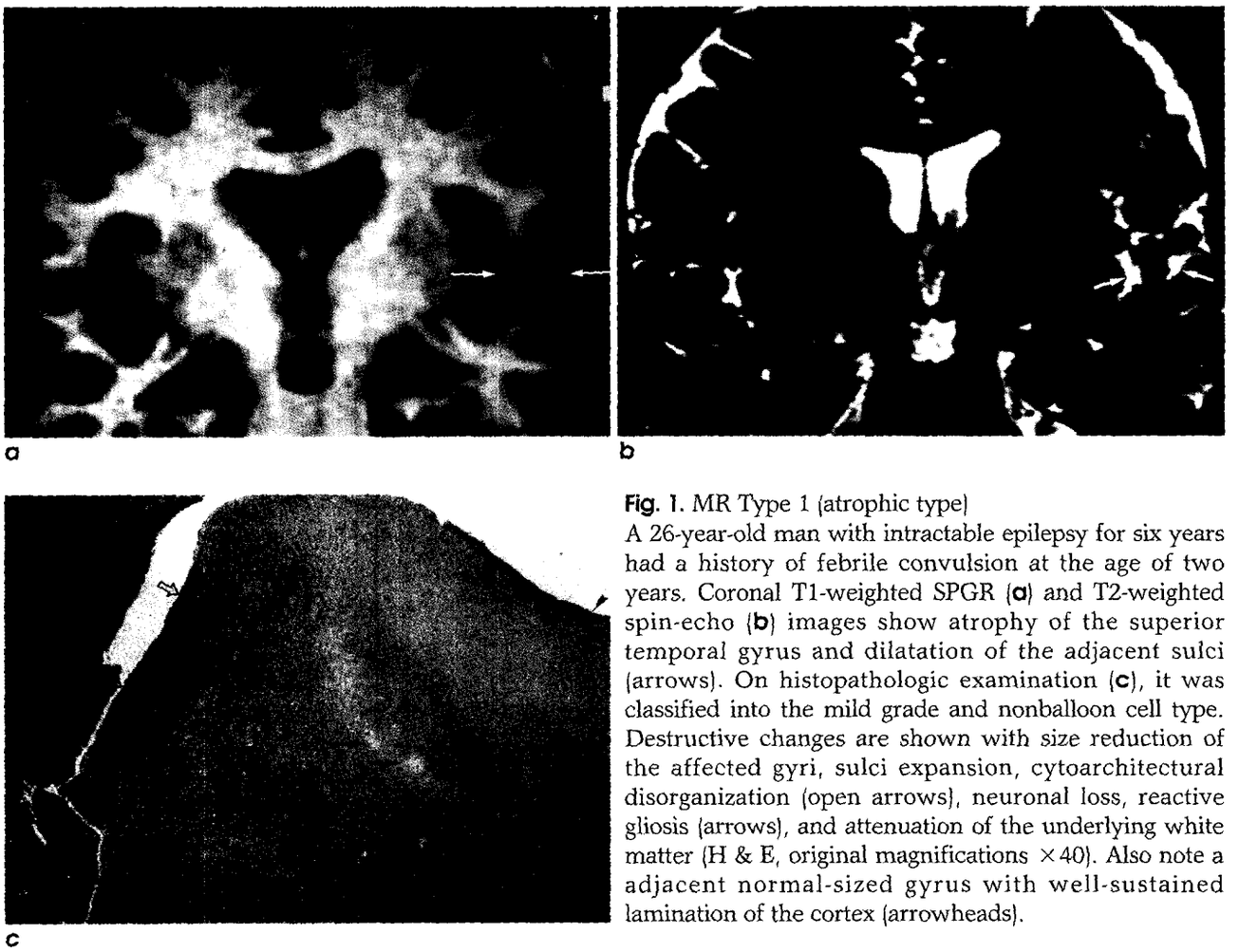


Fig. 1. MR Type 1 (atrophic type)
A 26-year-old man with intractable epilepsy for six years had a history of febrile convulsion at the age of two years. Coronal T1-weighted SPGR (**a**) and T2-weighted spin-echo (**b**) images show atrophy of the superior temporal gyrus and dilatation of the adjacent sulci (arrows). On histopathologic examination (**c**), it was classified into the mild grade and nonballoon cell type. Destructive changes are shown with size reduction of the affected gyri, sulci expansion, cytoarchitectural disorganization (open arrows), neuronal loss, reactive gliosis (arrows), and attenuation of the underlying white matter (H & E, original magnifications ×40). Also note a adjacent normal-sized gyrus with well-sustained lamination of the cortex (arrowheads).

between MR imaging types and histopathologic grades and subtypes of CD that might be related with prognosis. In this study, we tried to classify MR imaging abnormalities of patients with CD in relatively large series of our institution, in order to correlate those imaging abnormalities with pathologic grades and subtypes.

Materials and Methods

We retrospectively reviewed brain MR images and pathologic slides of 97 patients (64 male, 33 female) with pathologic diagnosis of CD. The patients ranged in age from 1.5 to 47 years old (mean, 25.7 years). All patients had medically intractable seizures and underwent surgery. We did not include the cases with coexistent tumor, hippocampal sclerosis, tuberous sclerosis, or other pathologies.

All MR examinations were performed with 1.5T imagers: Magnetom or Magnetom Vision Plus (Siemens, Erlangen, Germany), or Signa (General Electric, Milwaukee, WI). MR sequences and parameters were as follows: (1) T2-weighted fast (turbo) spin echo (SE) (T2WI) axial and/or coronal sequences (TR, 3500-4000 msec; TE, 90-104 msec; section thickness, 3-5 mm; matrix, 256×192), (2) proton density-weighted axial sequence (TR, 3500 msec; TE, 19 msec; section thickness, 3-5 mm; matrix, 256×192), (3) T1-weighted 3D spoiled gradient-echo (SPGR) or magnetization-prepared rapid acquisition gradient-echo (MP-RAGE) coronal and/or sagittal sequence (TR, 9.7-14 msec; TE, 3.4-4 msec; flip angle, 12-20; section thickness, 1.5-2 mm; matrix, 256× 256), (4) conventional T1-weighted SE (T1WI) sequence (TR, 500-600 msec; TE, 14-20 msec; section thickness, 3-5 mm; matrix, 256×192), (5) fluid-attenuated inversion recovery (FLAIR) axial and/or coronal sequence (TR, 10002 msec; TE, 133 msec; inversion time, 2200 msec; section thickness, 3-5 mm).

Two neuroradiologists (BJK, KHC), with knowledge of the diagnosis and operative site, together retrospectively reviewed preoperative brain MR images with regard to gyral size of a lesion relative to the contralateral side, cortical thickness, signal intensity of the subcortical white matter, blurring of the gray-white matter junction, and abnormal orientation of the sulci. Presence or absence of these MR abnormalities were determined by a consensus of the two neuroradiologists. Thus, all patients were divided into MR-positive and MR-negative groups. In MR-positive group we arbitrarily classified MR abnormalities into four types (Figs. 1-4): type 1 (atrophic type), in which the gyral size was decreased and the adjacent sulcus dilated; type 2 (cortical-band type), in which the cortical ribbon was

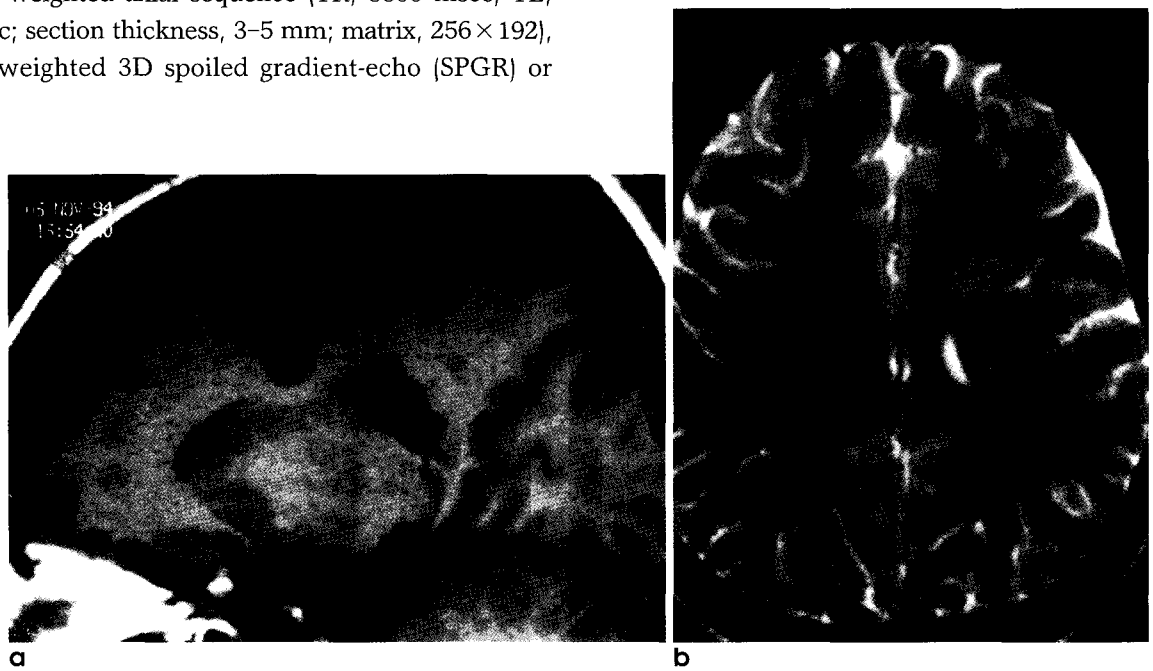


Fig. 2. MR Type 2 (cortical-band type)
T1-weighted spin-echo sagittal (**a**) and T2-weighted spin-echo axial (**b**) images show a thickened cortical ribbon extending to the periventricular portion with isointense signal relative to the normal cortex (arrows).

thickened with signal intensity isointense to the normal gray matter; type 3 (inward-rounding type), in which the thickened cortex was associated with discrete subcortical white matter hyperintensity and inward-rounding shape on T2WI; type 4 (nonspecific type), in which a lesion did not belong to above types and had only some abnormal white matter signal intensity or blurring of the gray-white matter junction.

A neuropathologist (YLC) retrospectively reviewed pathologic slides of the 97 cases without knowledge of MR imaging findings. Checklists in review of the pathologic slides were as follows: cortical laminar disorganization, single heterotopic neuron in the white matter, neurons in the molecular layer, persistent remnants of the subpial granular cell layer, marginal glioneuronal heterotopia, polymicrogyria, white matter neuronal heterotopia, neuronal cytomegaly, and balloon cells. Based on these features, histopathologies of all cases were graded into mild (at least presence of cortical laminar disorganization and two other findings of the first five), moderate (at least presence of

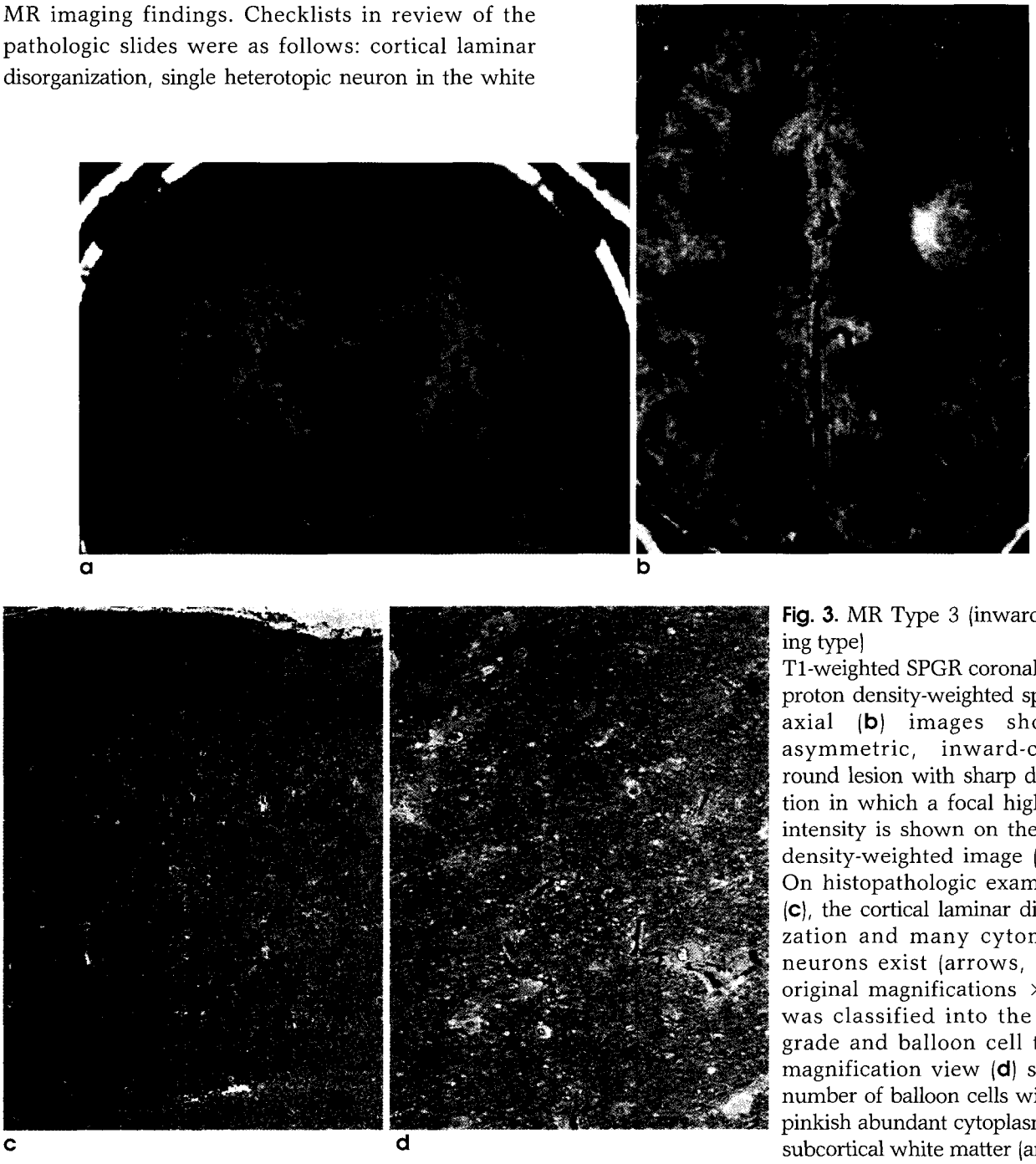


Fig. 3. MR Type 3 (inward-rounding type)
T1-weighted SPGR coronal (**a**) and proton density-weighted spin-echo axial (**b**) images show an asymmetric, inward-convex, round lesion with sharp demarcation in which a focal high signal intensity is shown on the proton density-weighted image (arrow). On histopathologic examination (**c**), the cortical laminar disorganization and many cytomegalic neurons exist (arrows, H & E, original magnifications ×40). It was classified into the severe grade and balloon cell type. A magnification view (**d**) shows a number of balloon cells with pale-pinkish abundant cytoplasm in the subcortical white matter (arrows).

polymicrogyria or heterotopia in the white matter), or severe grade (at least presence of neuronal cytomegaly or balloon cells) according to the grading system proposed by Mischel et al (4), and divided into two subtypes depending on absence (nonballoon-cell subtype) or presence (balloon-cell subtype) of balloon cells (Fig. 3D). In addition to these, destructive changes including atrophy, reactive gliosis, or calcification were checked on.

Any differences of pathologic grades and subtypes between MR-positive and MR-negative groups were assessed. The four MR types of the MR-positive group were also correlated with the pathologic grades and subtypes. Additionally, we evaluated relationship between increased T2 signal of the subcortical white matter and the balloon-cell subtype. The x^2 test was performed using SPSS 7.5 Windows software for the statistical evaluation.

Results

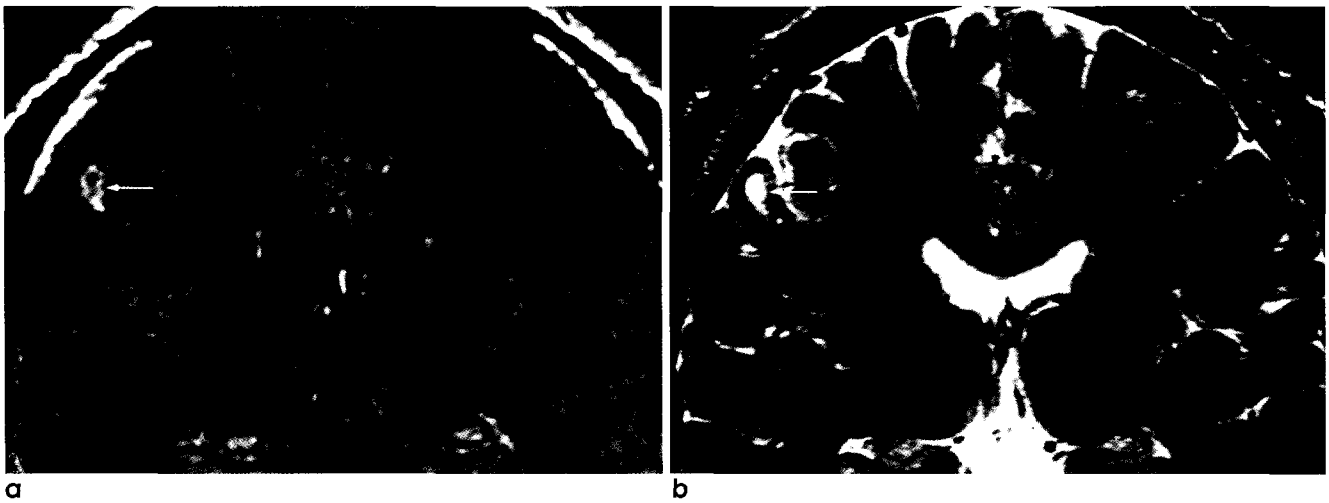
MR abnormalities were detected in 40% (39/97) of all patients, of which type 1 (atrophic type) was seen in 33% (13 patients), type 2 (cortical-band type) in 23% (9 patients), type 3 (inward-rounding type) in 23% (9 patients), and type 4 (nonspecific type) in 21% (8 patients).

A variety of MR imaging findings and their frequency are summarized in Table 1. The frequency of each MR imaging abnormality was ranged from 10% to 28%. Of these abnormalities the most frequent feature was increased T2 signal of the subcortical white matter (28%, 27/97) followed by blurring of the gray-white matter junction (27%, 26/97) and increased cortical thickness (21%, 20/97).

In the pathologic examinations the mild grade was the most common (61%, 59/97) regardless of MR-positive and MR-negative groups, compared with the frequency of the moderate (12%, 12/97) and severe grade (27%, 26/97). MR-positive group included 34% (20/59) of patients with the pathologically mild grade, 58% (7/12) of the moderate grade, and 46% (12/26) of the severe grade. There was no significant difference in pathologic grades between MR-positive and MR-negative groups ($p > 0.05$), although MR-positive group generally tended to have higher pathologic grades than MR-negative group did (Table 2). The frequency of the mild grade was particularly higher in both MR-negative

Table 1. MR Imaging Features of 97 Patients with Cortical Dysplasia

MR Features	case numbers (%)	
Abnormal gyral size		23 (23)
Decreased	13 (13)	
Increased	10 (10)	
Abnormal cortical thickness		32 (33)
Decreased	12 (12)	
Increased	20 (21)	
Increased T2 signal of subcortical white matter		27 (28)
Blurring of the gray-white junction		26 (27)
Abnormal orientation of sulci		13 (13)



a b

Fig. 4. MR Type 4 (nonspecific type)
FLAIR (**a**) and T2-weighted spin-echo (**b**) coronal images show a teardrop-shaped, well-demarcated high signal intensity in the subcortical white matter (arrow) mimicking a small benign surface-located tumor.

group and MR type 1 (atrophic type) of the MR-positive group. MR-positive group included 73% (8/11) of the balloon-cell subtype and 36% (31/86) of the nonballoon-cell subtype patients. The frequency of the balloon-cell subtype was significantly higher in MR-positive group than in MR-negative group ($p < 0.05$) : 21% (8/39) vs. 5% (3/58). The balloon-cell subtype and pathologically severe grade were more frequently seen in MR type 3 (inward-rounding type) (56% [5/9] and 78% [7/9], in respect) than the other three MR types (Table 3). The balloon-cell subtype was noted in 19% (5/27) of patients with increased T2 signal of the subcortical white matter, whereas it was seen in 9% (6/70) of patients with normal T2 signal in the subcortical white matter. But this difference was not statistically significant ($p > 0.05$).

Destructive changes including gyral atrophy, reactive gliosis, and calcification were seen in the only MR atrophic type (7/13) (Fig. 1C).

Table 2. Relationship between MR-positive/-negative Groups and Pathologic Grades/Subtypes

Pathologic grades	MR-positive (n = 39)	MR-negative (n = 58)	Total (n = 97)
Mild	20 (51%)	39 (67%)	59 (61%)
Moderate	7 (18%)	5 (9%)	12 (12%)
Severe	12 (31%)	14 (24%)	26 (27%)
Pathologic subtypes	**MR-positive (n = 39)**	**MR-negative (n = 58)**	**Total (n = 97)**
Nonballoon-cell	31 (79%)	55 (95%)	86 (89%)
Balloon-cell	8 (21%)	3 (5%)	11 (11%)

p-value: 0.223 and 0.025 in upper and lower table each in Chi-Square test

Discussion

Histopathological examination of resected brain tissue after surgery for neocortical epilepsy has increasingly recognized focal CD as a cause of intractable seizures. CD, pathologic term, means a spectrum of pathologic changes injured from genetical or environmental etiologies at different time windows of neuronal migration. Although there has not been generally acceptable classification for CD, morphology-based classification such as agyria/pachygyria or schizencephaly, if possible, should be described and the histological description with grades or subtypes, otherwise, is now in common use to describe CD. Pathogenetical terms such as neuronal migration disorder, cortical malformation, or cortical developmental disorder are representative of those kinds of diseases (10).

CD can be histologically classified by two- or three-tiered system (4, 8, 10). These system used balloon cells or neuronal cytomegaly as a marker of a distinct higher subtype or grade which was negatively correlated with surgical outcome (8). The surgical outcome is also known to be positively correlated with the extent of removal of the visible structural lesion in MR images (5, 8). Major or complete removal of the visible lesions leaded the surgical outcome to the more favorable one than minor or partial resection in postoperative seizure control. Therefore, MR detection and accurate determination of extent of CD is one of the most important for the preoperative studies.

We could detect MR imaging abnormalities in only 40% of the patients with CD, although CD has been reported to be detected in majority on MR images.

Table 3. Relationship between MR Types and Pathologic Grades/ Subtypes N = 39

	MR types			
Pathologic grades	Atrophic (n = 13)	Cortical-band (n = 9)	Inward-rounding (n = 9)	Nonspecific (n = 8)
Mild	10 (77%)	4 (44%)	2 (22%)	4 (50%)
Moderate	3 (23%)	3 (33%)	0 (0%)	1 (13%)
Severe	0 (0%)	2 (22%)	7 (78%)	3 (38%)
Pathologic subtypes	**Atrophic (n = 13)**	**Cortical-band (n = 9)**	**Inward-rounding (n = 9)**	**Nonspecific (n = 8)**
Nonballoon-cell	13 (100%)	7 (78%)	4 (44%)	7 (88%)
Balloon-cell	0 (0%)	2 (22%)	5 (56%)	1 (12%)

p-value: 0.009 and 0.015 in upper and lower table each in Chi-Square test.

Previous studies for MR imaging features of CD reported 60-100% rate of detection for cortical thickening with blurring of gray-white junction and 20-60% rate for abnormal white matter signal intensity (8-11). But these rates of detection seem to be not accurate because of limited materials comprised of only balloon-cell subtypes or without histologic inclusion criteria for the studies. Our study included pathologically-proven cortical dysplasia of any grades or subtypes. Therefore, the frequencies of each MR imaging feature were much lower in our study (10-28%) than in other studies. Increased T2 signal of the subcortical white matter was slightly more frequent than increased cortical thickness or blurring of gray-white junction in our study. This result might be caused by different inclusion criteria of the materials including low grade CD, atrophic type of CD or strict application of increased cortical thickness to the lesion isointense relative to the normal cortex even in deeper portion in our study.

We classified MR lesions of CD by several factors. Type 1 (atrophic type) showed decreased size of the gyrus and cortical thickness, and dilatation of the adjacent sulci, which appeared distinctive from the other three types. Type 2 (cortical-band type) or type 3 (inward-rounding type) was different from the other types in view of the presence of the thickened cortex with or without change of the subcortical white matter signal intensity. Presence of only a less inconspicuous finding, either blurring of gray-white junction or increased white matter signal intensity, was categorized into the nonspecific type. Of these four MR types, type 2 and 3 (cortical-band and inward-rounding type) are similar to 'focal thickened gyrus' and 'transmantle dysplasia' which pathologically revealed classical findings and were pointed out as a kind of cortical malformation by Barkovich and Kuzniectky (12).

For the histopathologic review we followed the histologic grading system proposed by Mischel et al. (4). But this system has some intrinsic problems in the mild grade. While features of the mild grade were considered to belong to CD by Prayson et al.(13), others have judged most of them as normal variants (14, 15). Some cases of CD proven as the mild grade with Mischel' s criteria may not be true CD but normal variants or other kinds of diseases. Marin-Padilla (16) suggested that progressive postinjury reorganization of undamaged cortex resulted from acquired perinatal injury represents the main underlying mechanism in the pathogenesis of ensuing neurological sequelae. In his study there were common features of the microscopic findings in undamaged cortex adjacent to destructive white matter: cytoarchitectural disorganization, partial obliterations of laminations, gray and white matter attenuation, and some degree of reactive gliosis, and atrophic/hypertrophic neurons, and he called these 'acquired cortical dysplasia' collectively. Lombroso (17) reported that closed head trauma in perinatal period might also induce microdysplasia in which the pathogenesis would be a regional disorder of postmigrational intrinsic cortical remodeling. These reports suggest that perinatal brain injury might result in evolving cortical reorganization with the parenchymal volume loss morphologically, and CD histologically. The cases of MR type 1 (atrophic type) in our study are similar to these acquired lesions morphologically and histologically. Thus, we suppose this type might result from late developmental or perinatal injury although only a half of the cases classified as the atrophic type had the significant traumatic or febrile histories. Pathologically, there is no clear-cut criteria to differentiate the mild grade features of CD from the secondary changes of traumatic, inflammatory, or ischemic events. Previous studies described about 10-18 % rate of infarct or remote ischemic damage as a cause of extratemporal lobe epilepsy (18, 19). Frater et al. (18) reported 11 cases with coexistent CD histologically shown as cortical laminar disorganization, and infarct or remote ischemic damage as a cause of epilepsy. Therefore, it is not unexpected that atrophic or cerebromalatic lesions on MR images of children or adults with epilepsy would prove cortical dysplasia histopathologically, although we cannot know the exact time when the injuries were struck, that is, developmental or acquired origin.

It was revealed for MR detectability of CD (numbers of MR-positive cases) not to be significantly correlated with the pathologic grades, and only inward-rounding type showing the subcortical white matter hyperintensity in all cases corresponded well with the severe grade which was histologically assigned to presence of the neuronal cytomegaly or balloon cells. Kuzniecky et al (10) reported the positive correlation of presence of the balloon cells with the white matter

hyperintensity, and Gomez-Anson et al (20) proposed single heterotopic neurons or poor myelination as a factor which may be related to the hyperintensity on pathologic correlation of a few cases. In our study, balloon-cell subtype was found in only 11% (11/97) of all patients, five of which showed increased T2 signal in the subcortical white matter. We could not find significant correlation between the balloon cells and the increased T2 signal, and discover which factors caused the high association of the inward-rounding type with the severe grade. Further prospective studies with quantification of several histologic features would be needed to evaluate any histologic difference between the inward-rounding type and others, and to determine the factors to cause the association.

In conclusion, MR imaging detected abnormal findings in only 40% (39/97) of patients with pathologically-reported CD. A variety of MR imaging features of CD were classified into four types (atrophic, cortical-band, inward-rounding, and nonspecific types), of which the inward-rounding type well correlated with the pathologically severe grade and balloon-cell subtype, while the atrophic type well correlated with the mild grade and nonballoon-cell sub type.

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대한자기공명의과학회지 7:47-55(2003)

뇌피질 이형성증의 자기공명영상소견: 병리적 등급 및 유형과의 연관성에 대하여

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목적: 뇌피질 이형성증의 다양한 자기공명영상소견을 유형별로 분류하고 병리적 등급 및 유형과의 연관성을 분석한다.

대상 및 방법: 수술 후 병리적으로 뇌피질 이형성증이 확진된 97명을 대상으로 하였다. 수술 전 MR 영상을 후향적으로 분석하였으며, 이상 소견의 유무에 따라 MR 양성군과 MR 음성군으로 나누었다. MR 양성군에서는 뇌회와 인접 지주막하 공간의 크기, 뇌피질 두께, 피질하 백질의 신호 강도, 뇌피질과 백질 경계부의 명확성에 의하여 MR 이상 소견을 분류하였다. 병리적 소견 역시 영상 소견을 모르는 상태에서 후향적으로 분석하였으며, 경도, 중등도, 고도와 비풍선세포형, 풍선세포형 으로 나누었다. MR 양성군과 음성군 사이에서 그리고 MR 양성군의 네가지 유형 내에서 각각 병리적 등급 및 유형의 차이가 있는지 분석하였다.

결과: MR 양성군과 음성군은 각각 39 (40%) 명, 58 (60%) 명이었다. MR 양성군 중 위축형은 13 (33%) 명, 피질떠형은 9 (23%) 명, 내측 만곡형은 9 (23%) 명, 그리고 비특이적 형태는 8 (21%) 명이었다. MR 양성군과 음성군 사이에서 병리적 등급은 의미있는 차이가 없었으나, MR 음성군에 비하여 MR 양성군에서 고도의 병리적 등급의 빈도가 높은 경향을 보였으며 또한 풍선세포형의 빈도 역시 유의하게 높았다 (5% Vs 21%, $p<0.05$). 특히 MR 양성군 중에 내측 만곡형은 고도의 병리적 등급과 풍선세포형의 빈도가 각각 78% (7/9), 56% (5/9) 인 반면에, 위축형은 경도의 등급과 비풍선세포형의 빈도가 각각 77% (10/13), 100% (13/13) 이었다.

결론: 뇌피질이형성증 환자의 MR 영상에서 반 이하에서만 이상 소견을 발견할 수 있었고, 특히 내측 만곡형은 병리적으로 고도의 등급 및 풍선세포형, 그리고 위축형은 경도의 등급 및 비풍선세포형과 높은 연관성을 보여 주었다.

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