

Aberrant fissure in polymicrogyria

Polimikrogiride aberran fissür

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SUMMARY

Objective: Polymicrogyria (PMG) is the most common malformation of the brain cortex. There is an impaired migration and proliferation of neuronal cells leading to a thickened cortex with multiple small (micro) gyri. It can be focal or diffuse. The aim of this study is to delineate the MRI properties of an aberrant fissure (AF) associated with PMG.

Method: MR images of 34 patients were retrospectively investigated for the features of PMG, the presence of an AF and its properties along with the clinical findings.

Results: Thirty-one patients (91.2%) showed focal PMG, whereas 3 patients (8.8%) had diffuse involvement of the brain. None of the diffuse PMGs showed an AF, whereas 30 patients (88%) with focal PMG showed an associated AF. Only one patient with a focal PMG did not display an AF, however, he had an arachnoid cyst adjacent to the PMG. AFs were related to or in continuity with major fissures of the brain in 27 subjects.

Conclusions: An AF is present in the vast majority of patients with a focal PMG, however, there is no significant relation between the presence of AF and clinical findings.

Keywords: Aberrant fissure, magnetic resonance imaging, polymicrogyria

ÖZET

Amaç: Polimikrogi (PMG) beyin korteksinin en sık görülen malformasyonudur. Beyin gelişimi sırasında nöronal migrasyonun son evresinde ve migrasyon sonrası korteks organizasyonunda bozukluk mevcuttur. PMG fokal veya diffüz olabilir. Bu çalışmanın amacı PMG’de görülen aberran fissürün (AF) MR özelliklerini ortaya koymaktır.

Yöntem: PMG tanısı alan 34 hastanın manyetik rezonans görüntüleme (MRG) bulguları ve dosya bilgileri PMG özellikleri, AF varlığı ve özellikleri ile klinik bulguları yönünden retrospektif olarak değerlendirildi.

Bulgular: 34 hastanın 31’inde (% 91.2) fokal, 3’ünde (% 8.8) diffüz PMG görüldü. Diffüz PMG’li 3 olguda AF izlenmedi. Fokal PMG li 30 olguda AF saptandı. AF saptanmayan bir fokal PMG olgusunda PMG komşuluğunda araknoid kist mevcuttu. 27 hastada AF beyin bilinen majör fissürleri ile ilişkiliydi ya da onlarla devamlılık gösteriyordu.

Sonuç: Fokal PMG li olguların büyük çoğunluğunda AF izlenmekle birlikte klinik bulgular ile anlamlı ilişkisi yoktur.

Anahtar sözcükler: Aberran fissür, manyetik rezonans görüntüleme, polimikrogi

INTRODUCTION

Polymicrogyria (PMG) is the most common malformation of the brain cortex¹. It is caused by an alteration in the neuronal migration or the organization of the brain cortex after migration². Congenital infections, intrauterine ischemia, metabolic disorders and gene mutations are suspected in the etiology of PMG³⁻⁶. Pathogenesis of PMG is still not fully understood. Clinical findings vary depending on the location and size of PMG and most common symptoms include partial epilepsy, refractory epilepsy, growth retardation, hemiparesis and quadriplegia⁷.

PMG can be unilateral or bilateral, symmetric or asymmetric, focal, multifocal or diffuse topographically. The site of predilection is the posterior perisylvian area⁸.

PMG can either be isolated or associated with other brain malformations. The most common malformations accompanying PMG are corpus callosum dysgenesis/agenesis/hypogenesis, cerebellar hypoplasia and gray matter heterotopia⁹⁻¹¹.

Histologically, there are multiple abnormal small gyri, shallow sulci and fusion of the first molecular layer in PMG^{12,13}. Pial defects and abnormal vascular structures were also reported in PMG^{14,15}. In addition, cortical infoldings formed by the malformed cortex were also described, however, the MRI properties of these cortical infoldings and undulations have not yet been studied¹². We prefer to refer to these poorly-defined infoldings or undulations as 'aberrant fissures' (AFs), since they are oriented similar to the major fissures and, most of them extend as the continuity of the Sylvian fissure, rather than being only a deep or shallow recess. The aim of this study is to delineate the MRI properties of AFs associated with PMG and discuss their clinical and pathological relevance.

MATERIAL AND METHODS

This retrospective study was approved by the institutional ethics committee.

The study enrolled 36 patients diagnosed with PMG between January 2000 through May 2015. MRI images and clinical data of these patients were examined and evaluated. Patients who had low-quality MR images such as MRIs with motion artifacts were excluded from the study.

MR examinations were performed with two 1.5 Tesla scanners (Magnetom Aera, Siemens, Erlangen, Germany and Exelart, Toshiba, Tokyo, Japan) using 20-channel phased-array head coil and standard head coil, respectively. The imaging protocols for two vendors, respectively, were as follows: Axial and sagittal T1-weighted spin echo (SE) (TR: 520 and 550 ms; TE: 5.6 and 15 ms; FA: 150° and 70/180°; NEX: 3 and 1.2; FOV: 220×84 and 220×180 mm; matrix: 256×100 and 256×160; slice thickness: 5 and 5 mm; interslice gap: 1.7 and 1 mm); axial and coronal, T2-weighted fast SE (TR: 4400 and 5000 ms; TE: 102 and 94 ms; FA: 150° and 90/180°; NEX: 2 and 2; FOV: 220×97 and 220×180 mm; matrix: 320×90 and 320×224; slice thickness: 5 and 5 mm; interslice gap: 1.7 and 1 mm) and axial FLAIR (TR: 8000 and 7500 ms, TE: 86 and 94 ms, TI: 2384 and 2200 ms; FA: 150° and 90/160°; NEX: 1 and 1; FOV: 220×97 and 220×180 mm; matrix 256×100 and 256×160; slice thickness 5 and 5 mm; interslice gap: 1.7 and 1mm). For selected patients, axial and coronal T1-weighted SE intravenous contrast-enhanced images were obtained with a 0.1 mmol/kg intravenous paramagnetic agent (gadolinium-DTPA or gadodiamide). A dedicated axial and coronal T1-weighted fluid-attenuated inversion recovery sequence was added to the protocol in patients with epilepsy with the following parameters: TR: 5390 and 4800 ms; TE: 15 and 18 ms; TI: 500 and 800; FA: 150° and 160°; NEX: 1 and 1.2; FOV: 200×100 and 220×180 mm; matrix: 256×100 and 256×160; slice thickness: 3 and 5mm; interslice gap: 1.7 and 1mm);

MR images were examined for the following parameters by two radiologists:

1. Location of PMG,
2. PMG being unilateral or bilateral,
3. Symmetry of PMG,
4. Being focal, multifocal or diffuse,
5. Presence of accompanying brain anomalies,
6. Presence of an AF
7. Association of the AF, if present, with major sulci such as Sylvian fissure, interhemispheric fissure, central sulcus or calcarine sulcus.

Data obtained from this study were analyzed with an SPSS software (version 22.0). Descriptive statistics were used to assess the frequency of variables. Chi-square test was used

to test the association between the MRI findings and the clinical data. The level of significance was assumed as $p < 0.05$.

RESULTS

Sixty-two percent (n: 21) of 34 patients enrolled in the study were men and 38% (n: 13) were women. The ages ranged from 1 to 81, the median age being 13. Demographic, clinical and MRI findings of patients are briefly summarized in Table 1.

Table 1. Demographic, clinical and MRI findings of patients

No	Age	Gender	Location of PMG	Symmetry	Involvement	Relation of AF	Associated anomalies	Clinical Findings
1	37	M	Right parietal	NA	Focal	Sylvian continuity	Cavum septum pellucidum	Epilepsy
2	21	M	Left occipital	NA	Focal	Calcarine continuity	No	No
3	14	M	Right frontal	NA	Focal	No AFs	CC agenesis+ arachnoid cyst+ heterotopia	No
4	8	F	Bilateral perisylvian	Symmetric	Focal	Sylvian continuity	CC dysgenesis	Epilepsy, bilateral hemiparesis
5	2	M	Diffuse	Symmetric	Diffuse	No AFs	CC dysgenesis+ cavum septum pellucidum+ dilated Virchow-Robin spaces	Developmental disorder, epilepsy
6	81	F	Bilateral frontal	Symmetric	Diffuse	No AFs	No	Mental retardation
7	42	M	Left parietal	NA	Focal	Sylvian continuity	CC hypoplasia + Heterotopia	Right hemiparesis
8	3	M	Bilateral perisylvian	Symmetric	Focal	Sylvian continuity	CC dysgenesis	Epilepsy, developmental disorder
9	7	F	Bilateral frontal	Symmetric	Focal	Sylvian continuity	No	Epilepsy
10	13	M	Right parietal	NA	Focal	Interhemispheric continuity	No	Left hemiparesis
11	16	F	Bilateral perisylvian	Symmetric	Focal	Sylvian continuity	No	Epilepsy, developmental disorder, bilateral hemiparesis
12	36	M	Right occipital	NA	Focal	Interhemispheric continuity	No	No
13	43	M	Left temporal	NA	Focal	Isolated AF	No	Epilepsy
14	18	M	Left parietal	NA	Focal	Central sulcus continuity	No	No
15	26	F	Left occipital	NA	Focal	Interhemispheric continuity	No	No
16	2	F	Right perisylvian	NA	Focal	Sylvian continuity	CC dysgenesis+ arachnoid cyst	Epilepsy

17	5	M	Left perisylvian	NA	Focal	Sylvian continuity	No	Right hemiparesis
18	11	M	Left occipital	NA	Focal	Interhemispheric continuity	No	No
19	10	F	Right frontal	NA	Focal	Interhemispheric continuity	Cavum septum pellucidum	No
20	8	M	Bilateral perisylvian	Symmetric	Focal	Sylvian continuity	CC hypoplasia	Epilepsy
21	5	F	Right perisylvian	NA	Focal	Sylvian continuity	No	Epilepsy
22	8	M	Left perisylvian	NA	Focal	Sylvian continuity	Cavum septum pellucidum	Developmental disorder
23	22	F	Right occipital	NA	Focal	Isolated	No	No
24	3	M	Bilateral perisylvian	Symmetric	Focal	Sylvian continuity	CC hypoplasia	Epilepsy
25	35	M	Left frontal	NA	Focal	Isolated	No	No
26	11	F	Left perisylvian	NA	Focal	Sylvian continuity	Arachnoid cyst	No
27	7	F	Right perisylvian	NA	Focal	Sylvian continuity	No	Epilepsy
28	43	M	Left occipital	NA	Focal	Interhemispheric continuity	Arachnoid cyst	No
29	4	M	Bilateral perisylvian	Asymmetric	Focal	Sylvian continuity	CC hypoplasia	Epilepsy, developmental disorder
30	1	M	Diffuse cerebral	Symmetric	Diffuse	No AFs	CC dysgenesis	Epilepsy, developmental disorder
31	43	M	Left parietal	NA	Focal	Interhemispheric continuity	No	No
32	36	F	Left frontal	NA	Focal	Sylvian continuity	No	No
33	55	M	Right perisylvian	NA	Focal	Sylvian continuity	Arachnoid cyst	No
34	13	F	Bilateral perisylvian	Asymmetric	Focal	Sylvian continuity	CC hypoplasia + Cavum septum pellucidum	Epilepsy, bilateral hemiparesis

CC: corpus callosum; NA: Not applicable

Thirty-one patients (91.2%) showed a focal involvement of the brain, whereas 3 patients (8.8%) had diffuse involvement. In 2 globally diffuse cerebral (Fig. 1) and in 1 lobar diffuse (Fig.2) PMG patients, that is, in all diffusely

involved patients, there were no AFs. There were no AFs in another patient with a focal PMG, either, but an arachnoid cyst was present adjacent to the PMG (Fig. 3). The rest of all PMG patients (n:30, 88%) showed an AF.

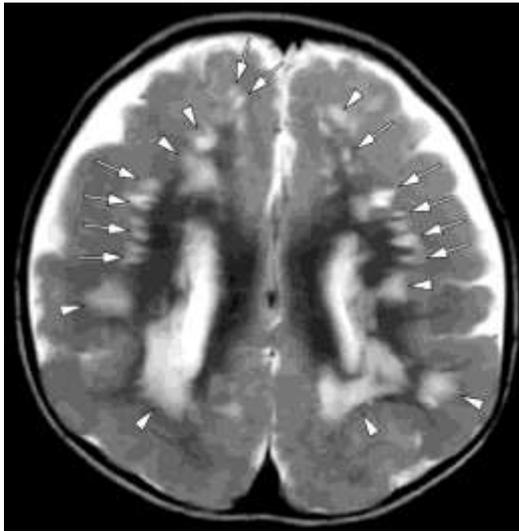


Figure 1. T2-weighted axial MR image displays global cerebral diffuse PMG. There are no AFs. Areas of hypomyelination (arrowheads), corpus callosum dysgenesis (not shown) and dilated Virchow-Robin spaces (arrows) are accompanying PMG.

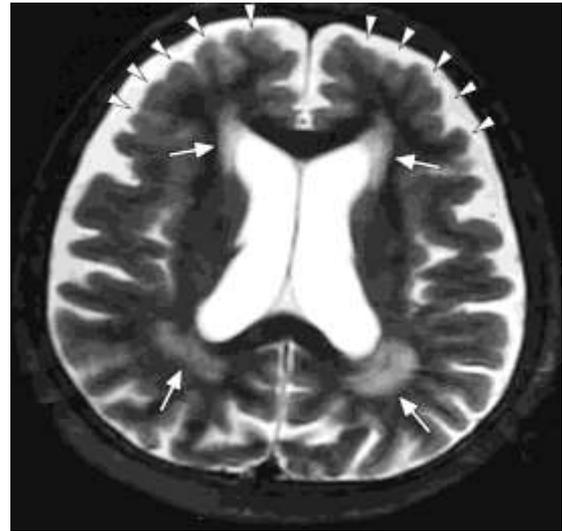


Figure 2. Bilateral frontal diffuse PMG (arrowheads) without an AF is demonstrated on T2-weighted axial MR image. Age-related (81-year-old patient) periventricular ischemic gliotic areas (arrows) are also present.

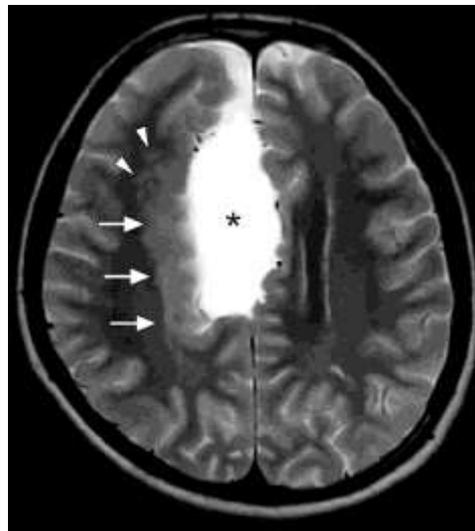


Figure 3. Axial T2-weighted image shows a right-sided frontal PMG (arrows), an adjacent arachnoid cyst (asterisk) and accompanying foci of heterotopia (arrowheads). AF is not present.

Focal PMGs were bilateral (Fig. 4) in 25.8% (n:8) and unilateral (Fig. 5) in 74.2% (n:23) of patients. AFs were associated with or extend as a continuation of normal fissures in 27 patients. In 3 patients AFs were formed independently apart from any known major fissures. Seventeen patients had AFs associated with the Sylvian fissure (Figs 6 and 7). Eight patients had AFs in association to interhemispheric fissure, 1 patient had AF in continuity with central sulcus and one with calcarine sulcus (Fig. 8).

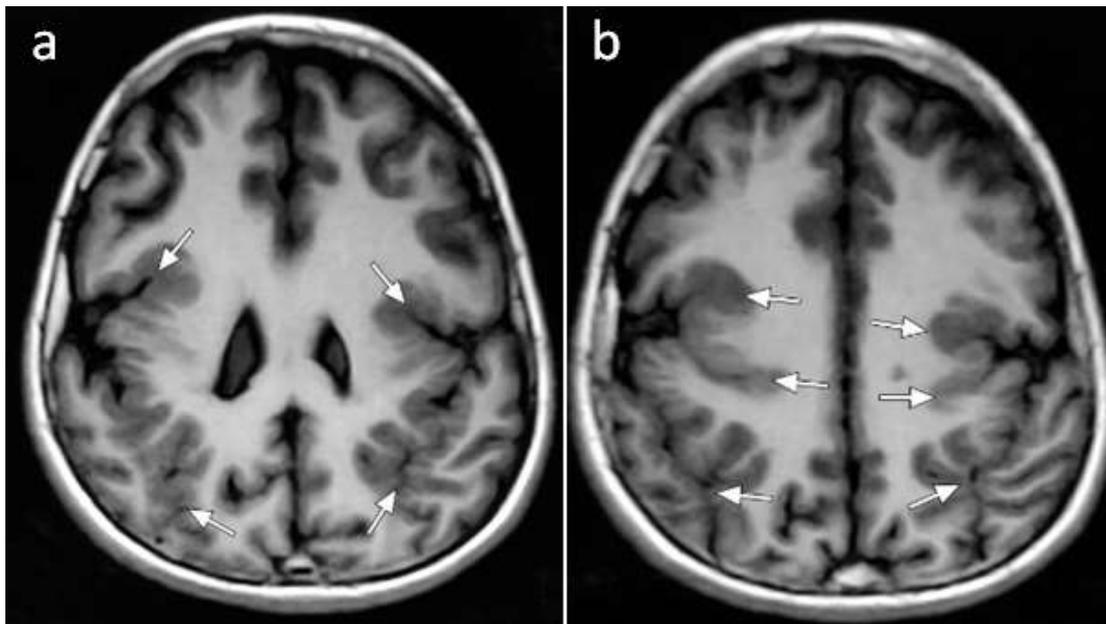


Figure 4. T1-weighted FLAIR images at the level of lateral ventricles (a) and at the level of centrum semiovale (b) reveal bilateral focal PMGs and multiple accompanying AFs (arrows).

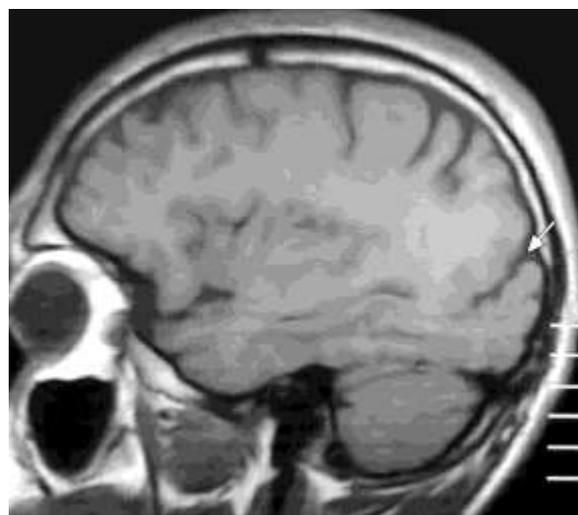


Figure 5. A unilateral focal PMG and accompanying AF (arrow) are seen on the sagittal T1-weighted image.

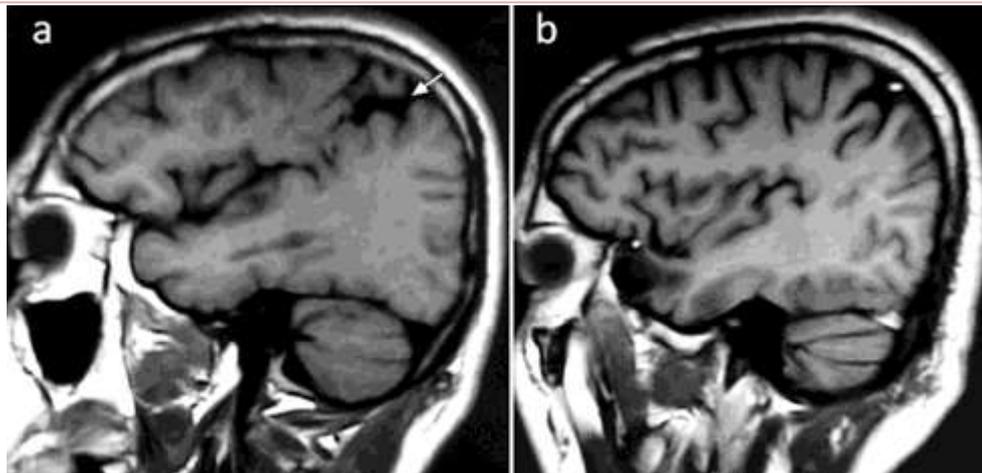


Figure 6. Sagittal T1-weighted images from both sides of the brain reveal an AF (arrow) continuous with the Sylvian fissure on the right (a) and a normal Sylvian fissure on the left (b).

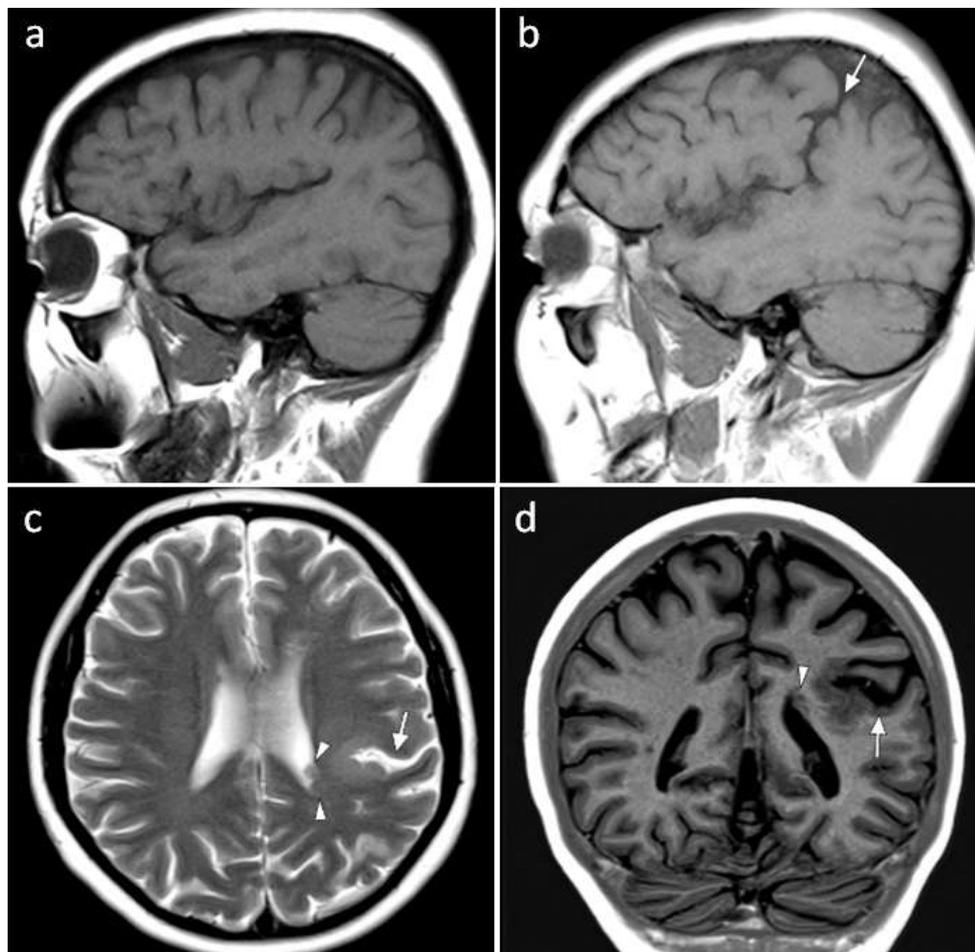


Figure 7. Sagittal T1-weighted images (a and b) of a patient reveal a normal Sylvian fissure on the right (a) and an AF (arrow) continuous with the Sylvian fissure on the left hemisphere (b). Axial T2-weighted (c) and coronal T1-weighted FLAIR (d) images of the same patient show an AF (arrows) and accompanying subependymal heterotopia (arrowheads).

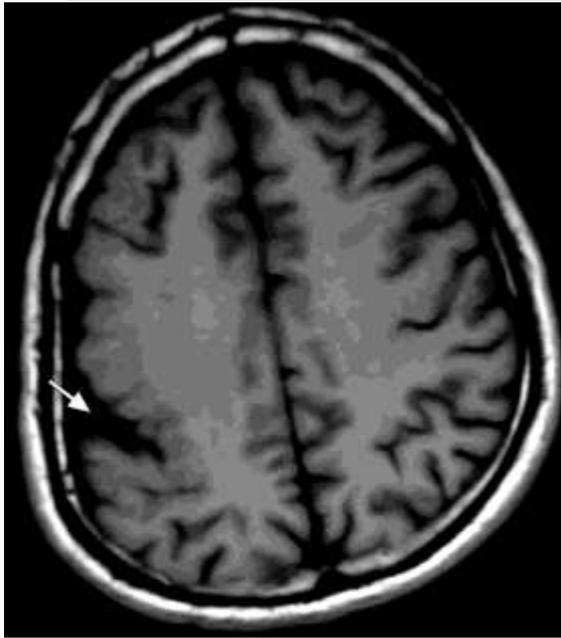


Figure 8. Axial T1-weighted image shows an AF in relation with the central sulcus in the right parietal lobe (arrow).

Bilateral PMGs were symmetric in 9 (26%) and asymmetric in 2 (6%) of the patients. Evaluation regarding the symmetry of the lesions was not applicable to 23 patients since they were unilateral (68%). In 4 of patients with focal PMG, there was multifocal involvement and multiple AFs were observed (Fig. 4).

Clinical findings are summarized in Table 1 and there was no significant difference between the clinical findings among different forms of AFs. Of all PMG patients, 50% showed an accompanying central nervous system anomaly. These anomalies included corpus callosum anomalies (in the form of agenesis, dysgenesis or hypoplasia, 17.7%), cavum septum pellucidum (8.8%), arachnoid cyst (8.8%) and multiple anomalies in combination (14.7%). Fifty percent of patients with PMG (n:17) did not exhibit any associated brain anomalies.

DISCUSSION

Some non-parenchymal alterations such as abnormal vascular structures, cortical infoldings, and pial defects are reported to be associated with PMG in addition to the malformed cortex^{12,14,15}. AF was first described as a cortical infolding by Barkovich, however, detailed features of this infolding have not been reported¹². Neither there exists a study on AFs associated with PMG

in the literature, to the best of our knowledge. The present study showed that 88% of PMGs are accompanied by an AF.

The pathophysiology of AFs or cortical infoldings in PMG remains to be unknown. Some researchers have suggested that there is a failure in the attachment of glial radial fibers to the pial limiting membrane and gaps are formed in the membrane¹⁵⁻¹⁷. PMG is postulated to occur as a result of incomplete migration and accumulation of neuronal cells to form dysmorphic cortical layers and small gyri close to the germinal matrix. We also think that pial defect and altered neuronal migration due to anomalous radial glial fiber may underlie the formation of AF in PMG. This might happen as a result of infolding of normal brain cortex towards the area of PMG to meet the abnormal cortex which cannot expand and stays deep in the brain. Our hypothesis is that, as a result of this cortical infolding an AF is formed. The presence of AF in all but one of the patients with focal PMG seems to support this hypothesis. We think that, since a large area is affected by the pathologic process in diffuse PMG cases and a deep-seated abnormal cortex relative to a normal cortex is absent, an AF is not formed in these patients with diffuse PMG. In our one patient with a focal PMG but no AF, we suggest that AF was not formed because of the mass effect resulting from the accompanying arachnoid cyst adjacent to the PMG.

Most of the PMGs that we have detected in this study were unilateral and located primarily in the perisylvian area in accordance with the existing literature.

We found other brain anomalies in association with PMG in 50% of our patients. This ratio is lower compared to a recent study by Jansen et al. in which they stated that PMG is almost always associated with other brain malformations¹⁵. This may be attributable to the smaller cohort in our study and the difference in that the above-mentioned study was a histopathologic one and our MRI study might not have been able to detect all malformations. Still, the current study shows that a radiologist should search for other central nervous system abnormalities in case of a detected PMG. Corpus callosum dysgenesis/agenesis/hypoplasia, heterotopia, and hypomyelination constituted the vast majority of these anomalies in our study. MRI examination revealed a few cases of cavum septum pellucidum and arachnoid cyst, however, since these

anomalies are relatively frequent in the normal population, it is hard to state whether they are coincidental or not. Widespread dilated Virchow-Robin spaces were present in a 5-year-old patient with PMG. Although they are common findings in the adult population, the presence of these spaces in a child is of note and may be of importance in leading new studies to investigate its association to PMG as an accompanying anomaly.

The presence of similar clinical findings in patients with and without an AF, as well as in AFs in association with different fissures (Sylvian fissure, interhemispheric fissure, etc) showed that there was no difference between these subgroups in terms of clinical picture, regardless of the existing PMG.

This study is mainly limited by its retrospective nature. The PMG area could have been visualized in more detail with very-thin-slice images and different imaging planes.

In conclusion, a great majority of focal PMGs are associated with an AF which does not affect the clinical picture directly, and the image interpreter should carefully search for other brain anomalies in cases with PMG.

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