Microinfarction in Classic Migraine? A Study With Magnetic Resonance Imaging Findings

A. Ferbert, MD; D. Busse; and A. Thron, MD

By means of magnetic resonance imaging we investigated a total of 45 patients suffering from classic migraine; 25 patients had been treated in our department for classic migraine over the past 2 years (group A), and 20 other patients investigated between 1976 and 1984 were reexamined for this study (group B). Thirty-two age- and roughly sex-matched healthy volunteers underwent magnetic resonance imaging and served as controls (group C). There was a trend for patients with classic migraine to have more subcortical patchy lesions on T2-weighted magnetic resonance imaging. In a comparison of our control subjects and patients with a history of >20 attacks of classic migraine taken from groups A and B, this difference in number of lesions was significant (p = 0.02). The results suggest that patchy lesions in patients with classic migraine should be interpreted with particular caution before diagnosing a demyelinating disease since the lesions could be ischemic in origin. (Stroke 1991;22:1010–1014)

Despite major efforts, the cause of migraine is still unknown. However, some important mechanisms involved in the pathophysiology of classic migraine have been elucidated. Investigations of cerebral blood flow (CBF) have demonstrated a “spreading oligemia” beginning at the occipital lobe and moving slowly anteriorly. Those authors found substantial evidence that this spreading oligemia is secondary to a primary neural process generally thought to be equivalent to Leao’s spreading depression. Thus, reduced CBF could be an adaptive mechanism to reduced demand that leaves the coupling mechanism between electrical activity of the nervous tissue and regional CBF intact. This interpretation does not explain the permanent tissue damage known to be an infrequent event in patients suffering from migraine.

Because magnetic resonance imaging (MRI) is more sensitive to ischemic lesions than computed tomography (CT), it may be possible to detect small lesions in more patients by using MRI than CT. Since spreading oligemia may be present in classic but not common migraine, we studied patients with classic migraine.

Subjects and Methods

We investigated 45 patients with classic migraine. The diagnosis was established according to recommendations of the Headache Classification Committee of the International Headache Society. In this classification, “migraine with aura” is preferred to “classic migraine.” However, we did not include patients who experienced only visual symptoms, such as fortification scotomas, except for homonymous hemianopsia. Thus, most of our patients having migraine with aura had sensory, motor, or aphasic symptoms in addition to visual symptoms. We therefore investigated a subset of migraine with aura, usually referred to as migraine accompagnée. We introduced this bias in consideration of the fact that these patients were suffering from more severe attacks of classic migraine. We excluded three patients with migrainous infarction who exhibited a permanent clinical deficit and an extensive low-density lesion on CT. All patients were examined neurologically and had an MRI study. Frequency of the attacks, as well as quality and duration of the aura symptoms, were assessed retrospectively in most patients while some patients with frequent attacks kept personal records of the attacks. All patients of group B (see below) had been asked about the frequency of the attacks on their first examination several years before this study. Patients with hypertension, diabetes mellitus, or other systemic diseases were excluded.

The 45 patients consisted of two groups. Group A (n = 25, age range 14–53 years, mean age 30.5 years) comprised 17 females and eight males. These patients came to our department between January 1987 and May 1989 because of an attack of classic migraine, 17 as inpatients and eight as outpatients. Nineteen patients had an electroencephalogram and 17 had routine laboratory studies including complete
TABLE 1. Incidence, Number, and Size of Small Subcortical Lesions on Magnetic Resonance Imaging in Patients With Classic Migraine (Groups A and B) and Controls (Group C)

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Yes</th>
<th>Number</th>
<th>Size</th>
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<tbody>
<tr>
<td></td>
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<td>&lt;3 mm</td>
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<tr>
<td>Group</td>
<td>n</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>A</td>
<td>25</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>B</td>
<td>20</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>C</td>
<td>32</td>
<td>25</td>
<td>7</td>
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Group B (n=20, age range 20-48 years, mean age 30 years) comprised 11 women and nine men. From the hospital records, we found 78 patients who had been treated for migraine accompagnée in our department between 1976 and 1984. Twenty of these fit our inclusion criteria and were reexamined clinically and with MRI between October 1988 and May 1989 as outpatients. Four of eight patients with hyperintense lesions on MRI also had visual evoked potential studies (visual, n=4; somatosensory, n=6; and brain stem auditory, n=1) performed in some patients with patchy hyperintense lesions on MRI were normal.

A third group, group C, consisted of 32 healthy subjects without migraine who had an MRI study. This group was of the same age and sex composition as groups A and B (age range 20-50 years, mean age 31 years; 15 women, 17 men). Exclusion criteria were arterial hypertension, diabetes, and systemic diseases as in groups A and B. Subjects with only occasional tension headaches were not excluded. Patients from the neurological department exhibiting nonspecific symptoms did not serve as control subjects.

**TABLE 2. Incidence, Number, and Size of Small Hyperintense Lesions on Magnetic Resonance Imaging of Patients With History of >20 Attacks of Migraine Accompaniee and Controls**

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Yes</th>
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<tr>
<td></td>
<td></td>
<td>1-3</td>
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<tr>
<td>Patients</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>Controls</td>
<td>32</td>
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*p=0.02 different from control by Fisher's exact test.

The MRI studies were performed on a 1.5-T unit, and 18 T2-weighted horizontal slices were obtained (repetition time=2,200 msec; echo time=90 msec; 256×256 matrix). No flow compensation was used to improve image quality in the posterior fossa. All MRI films were reviewed in a blinded fashion, with a random sequence for patients and control subjects. The number of hyperintense lesions was classified as none, 1-3, or >3. The size of the largest lesion was classified as <3 mm or ≥3 mm. The lesions were assigned to the following anatomic structures: subcortical white matter, deep white matter, periventricular white matter, basal ganglia, and brain stem/cerebellum. Small "lesions" in the caudal rim of the basal ganglia near the substantia perforata were not recorded.

We used Fisher's exact test for statistical analysis. As an additional analysis, we compared group C with the 22 patients from groups A and B who had a history of >20 attacks of classic migraine. The mean age of this subgroup was 32.4 years, not significantly different from the mean age of the controls.

**Results**

Table 1 shows the incidence of hyperintense lesions for groups A, B, and C. More patients with classic migraine had more lesions on MRI than did the control subjects, but this difference was not significant (p=0.138). The subgroup of patients with a history of 20 attacks of migraine accompagnée had significantly (p=0.02) more hyperintense lesions on MRI than the control group (Table 2). The correlation between frequency of migraine attacks in the history and incidence of lesions is shown in Figure 1.

Most lesions appeared as small, patchy hyperintense areas in the subcortical and deep white matter (Figures 2 and 3). Confluent lesions, such as one sees in patients with multiple sclerosis (MS), were rare. Despite the periventricular site of some lesions (Figure 3), a periventricular preponderance as exists in MS patients was more the exception than the rule.
Statistical analysis of the anatomic location was not possible due to the small numbers.

A single lesion observed in a control subject could not per se be distinguished from a lesion in a migraine patient. However, the lesions tended to be larger in the migraine patients than in the controls.

All electrophysiological studies in groups A and B showed normal results. Of 11 patients in group A who had CT, five showed lesions on MRI. In only one of the five could a small lesion also be identified on CT. Nine patients in group B had CT, all with normal results. However, the CT studies in group B were performed following the first admission to our hospital between 1976 and 1984 and were not repeated.

To find a possible correlation between side of the signs and side of the lesions, we selected nine of 18 migraine patients with MRI lesions in whom neurological signs during different attacks were exclusively attributable to the same hemisphere. No correlation could be found. In five patients the lesions did not show a preponderance in one hemisphere, in three patients the lesions were predominantly in the hemisphere contralateral to the signs, and in one subject the lesions were mainly in the ipsilateral hemisphere.

Of the 21 patients who had attacks of migraine accompagnée exclusively, eight had lesions on MRI. Of the 20 patients who also had common migraine attacks, nine had such lesions. In these nine patients, common migraine attacks occurred more often than migraine accompagnée attacks in six and less often in three. In four patients, sufficient data concerning additional common migraine attacks were not available. An increased frequency of migraine accompagnée attacks per time was associated with a higher incidence of MRI lesions. However, in general, patients with an increased frequency of attacks per time also had a higher absolute number of attacks. Intake of ergotamine or oral contraceptives had no influence on the frequency of MRI lesions.

**Discussion**

We found an increased frequency of small hyperintense lesions on MRI in patients with >20 attacks of migraine accompagnée than in age- and sex-matched controls. In both our patient groups combined, comprising several patients with only one attack of classic migraine, the difference was not significant. Thus, the hyperintense lesions in our patients might be related to the severity of the disease.

Three arguments speak against an interpretation that the lesions could be plaques of MS. Results of all tests that could be indicative of MS (visual, somatosensory, and brain stem auditory evoked potentials as well as cerebrospinal fluid studies) were normal.

Second, we had two patient groups, one of which (group B) comprised patients who were diagnosed as having migraine accompagnée 5–12 years previously.
and whose further clinical course favored this diagnosis. Finally, the location of the lesions in our patients did not show a periventricular preponderance as in most MS patients.

Hyperintense lesions on MRI have been described in 11 of 24 migraine patients. However, patients with common migraine and those with classic migraine were regarded as one group, although the two types of migraine may have different pathogenetic mechanisms. Spreading oligemia can be found in classic migraine but not in common migraine. Whether the incidence of the described lesions is also higher in patients with common migraine than in controls remains to be answered. In two more recent studies, spots in the white matter with increased T2-weighted signal intensity have been found in “a few subjects” with basilar artery migraine and in 39.6% of patients with either common, classic, or complicated migraine.

Small, patchy hyperintense lesions on T2-weighted images are often observed in normal individuals. These lesions have been studied extensively in elderly subjects and appear to be common even in healthy elderly subjects. Studies concerning the incidence of such lesions in young adults are controversial, and the incidence ranges from 0% to 35%. We also found hyperintense lesions in 22% of young, healthy volunteers, including patchy lesions <3 mm in diameter.

The pathological correlates of small subcortical lesions on MRI have been studied by comparing postmortem MRI of elderly patients who died of nonneurological causes with histological examinations. Incidental MRI lesions were noted in all brains. Those authors regard vascular ectasia leading to dilated perivascular spaces as the most likely explanation for most of the lesions, whereas other authors regard mild vascular insufficiency leading to atrophy of the perivascular tissue as the underlying mechanism. Small lacunar infarcts and dilated Virchow-Robin spaces (état criblé) cannot be distinguished by MRI characteristics; both are strongly associated with hypertension. All these studies refer to elderly patients, and the pathological basis of the lesions described in our patients may or may not be different, especially because hypertension was not present in our patients.

The nature of the lesions in our patients cannot be determined by this study. Since a persistent neurological deficit in patients with complicated migraine is due to ischemic infarction, the lesions in our patients may also be ischemic in nature.

The fact that angiography is often normal is not contradictory to this hypothesis since ischemia may result from constriction of arterioles. Only rarely does migrainous infarction resemble ischemic events in well-established territories, mostly of the posterior cerebral artery. One might speculate then that spreading depression is not the primary event in migraine accompagnée. In fact, the oligemia may be even more pronounced than described in earlier studies.

The main practical implication of our study is that small patchy hyperintense lesions on MRI in young adults presenting with neurological symptoms and signs compatible with classic migraine should not be automatically interpreted as plaques of MS. Even in young healthy adults who undergo MRI for some other reason, the occurrence of hyperintense lesions is not rare.

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Ferbert et al MRI in Classic Migraine 1013


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