Migraine Stroke: A Possible Complication of Both Migraine With and Without Aura

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We describe four migraine patients who developed an ischemic stroke during their typical migraine attacks.

Cerebral infarction as a possible complication of migraine without aura is discussed.

We propose a review of the migraine stroke definition of the International Headache Society.

Key words: migraine, ischemic stroke, complication

Abbreviations: IHS international Headache Society, PFO patent foremen ovale

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In 1988, the International Headache Society (IHS) classified migrainous infarction under the complications of migraine with aura. Several recent reports have also described migrainous infarction in patients affected by migraine without aura.

We relate the onset of migrainous infarction in four patients; two with migraine with aura and two with migraine without aura.

The aim of our study was to review the definition of migrainous infarction as proposed in the IHS classification.

CASE HISTORIES

The four patients were admitted to our clinic between 1989 and 1994 because of the onset of an ischemic stroke documented by cerebral computed tomography (CT) scan and/or magnetic resonance imaging (MRI). Each patient had migraine according to the diagnostic criteria of the IHS classification and underwent the diagnostic protocol used in the study of cerebrovascular diseases in our clinic. This protocol included hematologic laboratory tests (plasma glucose, serum creatinine, urea and electrolytes, erythrocyte sedimentation rate, complete blood cell count, hematocrit, serum cholesterol and triglycerides, low and high density lipoprotein, β-thromboglobulin and platelet factor 4 plasma levels, prothrombin time, partial thromboplastin time, fibrinogen, protein C and S, plasminogen, antithrombin III, antiphospholipid antibodies, lupus anticoagulant, anti-ENA, anti-DNA and antinuclear antibodies, and lactic acid), electrocardiogram, two-dimensional transthoracic and transesophageal echocardiography, and echo-Doppler of the upper aortic branches.

Patient 1.—A 37-year-old woman was seen in September 1989. She had no family history of migraine nor cerebrovascular disease. She had never smoked.

In 1982, she began to take oral contraceptives. After 1 year, she started to suffer from attacks of migraine with typical aura, consisting of speech difficulty and right hemiparesthesias and weakness, lasting about 15 minutes; these attacks recurred once a year. In 1987, the patient underwent a cerebral CT scan, which was normal.

In 1989 during a typical migraine attack, she developed mental confusion and drowsiness. Furthermore, her neurologic aura became persistent. ACT scan revealed an ischemic lesion near the left basal ganglia. Cerebral angiography showed a thrombus in the left middle cerebral artery.

Our standardized investigations disclosed no abnormal findings.

Patient 2.—A 34-year-old woman was seen in November 1992. She had no family history of migraine, but there was a family history of cerebrovascular disease. She had never smoked.

Since menarche she had suffered attacks of migraine without aura, which recurred once or twice a month during her menstrual cycle.
When she was 31 years old, she began to take oral contraceptives; after some months her headaches became more severe and more frequent. In November 1992, during a typical migraine attack, she had the sudden onset of motor aphasia and a severe right hemiparesis.

The CT scan and MRI revealed an ischemic lesion near the left basal ganglia.

Our standardized diagnostic protocol showed a significant increase of β-thromboglobulin and platelet factor 4 plasma levels and the presence of a patent foramen ovales (PFO). All the other evaluated parameters were normal.

**Patient 3.**—A 29-year-old man came to our attention in May 1993.

He had no family history of migraine nor cerebrovascular disease. His history disclosed the onset in infancy of partial epileptic seizures, promptly controlled by carbamazepine. The patient had never smoked.

When he was 25 years old, he began to suffer from basilar migraine attacks, which recurred twice a year.

In 1991, during a typical migraine attack, he had left hemiparesis and the sudden onset of decreased level of consciousness, which lasted 12 hours. On this occasion the CT scan was normal, while the MRI detected an ischemic lesion in the right cerebellar hemisphere. Cerebral angiography was normal.

In May 1993, the patient was hospitalized to undergo our standardized diagnostic protocol for cerebrovascular disease. A muscle biopsy was also obtained to rule out a mitochondrial disease. A moderate increase of the plasma levels of cholesterol and triglycerides was the only pathologic finding.

**Patient 4.**—A 27-year-old woman was seen in February 1994. She had a family history of migraine, but there was no family history of cerebrovascular disease. She smoked about 20 cigarettes per day.

She reported having had frequent attacks of migraine without aura since adolescence.

In February 1994, during a typical migraine attack, she complained of left-sided hemi-paresthesias followed by a left hemiparesis.

The CT scan was normal, while the MRI detected a right pontine ischemic lesion.

Because of the finding of an exercise-induced lactic acidosis, we performed a muscle biopsy, which was normal. Echocardiography revealed only the presence of a PFO.

The Table summarizes the stroke risk factors and other details of the four patients.

**COMMENTS**

In our opinion, all four patients came under the definition of migrainous stroke, as proposed in the IHS classification. Each experienced an ischemic stroke during a typical migraine attack. Other causes of stroke were ruled out by appropriate investigations. Although oral contraceptives (patients 1 and 2), hyperlipidemia (patient 3), and smoking (patient 4) are recognized stroke risk factors, the possible relationship between the presence of a PFO (patients 2 and 4) and the onset of a stroke has still to be defined.

However, two of the patients (Nos. 2 and 4) did not fulfill the first required diagnostic criterion; ie a previous diagnosis of migraine with aura.

In earlier years, the onset of an ischemic stroke had only been reported as a possible complication of classic migraine. In 1980, Prendes described the first case of complicated migraine in a patient with classic migraine during propranolol therapy; similar associations were later suggested by Gilbert and Bardwell and Trott. Bogousslavsky et al collected 22 patients with classic migraine who developed a migraine-related stroke; 10 were on an oral contraceptive and 7 were smokers.

It was only in 1988 that Rothrock et al described the onset of an ischemic stroke in 5 patients with common migraine; the same complication was reported in 9 patients with classic migraine and 8 patients with complicated migraine. Of the 22 patients overall, 6 were smokers and 3 were taking oral contraceptives or estrogen replacement.

Six further cases of migrainous infarction were reported in 1989 by Sacquegna and co-workers: five patients with common and one with classic migraine. Cigarette smoking and oral contraceptives were again considered the main associated risk factors of cerebral infarction.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Migraine Type</th>
<th>Stroke Risk Factors</th>
<th>Stroke Causes</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>With aura</td>
<td>Oral contraceptives</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>Without aura</td>
<td>Oral contraceptives</td>
<td>—</td>
<td>Patent foramen ovale</td>
</tr>
<tr>
<td>3</td>
<td>With aura</td>
<td>Hyperlipidemia</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>Without aura</td>
<td>Smoking</td>
<td>—</td>
<td>Patent foramen ovale</td>
</tr>
</tbody>
</table>
Within 1 year, Welch and Levine, in their review on migraine-related stroke, reported some examples of migraine-induced stroke; one was a patient with migraine without aura and two were affected by migraine with aura; one of whom was taking oral contraceptives.

Systematic cardiac investigations have only been obtained in the later studies, and the presence of a PFO was not described.

It is unquestionable that the onset of an ischemic stroke has been, until now, described more often in patients affected by migraine with aura, as underlined by Rothrock et al., but the same authors raised doubts on the correct interpretation of the data.

In fact, several variables can justify these results: (1) a truly more frequent association between migraine with aura and migraine stroke, (2) a natural cerebral link between the aura of migraine and the focal neurologic deficits of stroke, (3) the possibility that a previous migraine without aura goes unnoticed.

It appears also that both migraine with and without aura usually need additional stroke risk factors to result in cerebral infarction; in this connection oral contraceptives and smoking seem to be the major culprits.

On the basis of the literature and our data, we believe both migraine with and migraine without aura can potentially result in cerebral infarction, mainly in those with additional stroke risk factors. When this complication develops during an otherwise typical migraine attack and other recognized causes of stroke can be ruled out, a migrainous stroke exists.

In agreement with Welch, we propose that migrainous infarction should be redefined in the IHS classification as a possible complication of both migraine with and migraine without aura.

REFERENCES