

# Hemiplegic Migraine Induced by Exertion

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**Background:** It is known that exertion can aggravate migraine headache. However, the relationship between exertion and migraine aura is unknown.

**Objective:** To study the relationship between exertion and migraine aura.

**Design:** Case report.

**Setting:** Tertiary care hospital.

**Patient:** A 67-year-old man presented with recurrent attacks of exertion-induced hemiplegic migraine. Since the hemiparetic attacks were exertion induced, they were initially ascribed to recurrent transient ischemic attacks. However, the clinical picture, normal findings on cerebral angiography and neuroimaging (during the

period of hemiparesis), lack of response to treatment with antiplatelets and anticoagulants, and successful treatment with verapamil suggested that the hemiparesis was not due to ischemia, but was indeed a migraine aura. We suggest that exertion induced the aura of hemiparesis by lowering the threshold for the development of cortical spreading depression. Even though our patient had no family history of hemiplegic migraine, a mutation in an ion channel gene (eg, the *CACNA1A* gene on chromosome 19) might account for his episodic attacks.

**Conclusion:** Migraine aura should be included in the differential diagnosis of exertion-induced focal neurologic deficit.

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**M**IGRAINE is defined as a unilateral, throbbing headache that (1) is associated with nausea, vomiting, and photophonophobia; (2) lasts 4 to 72 hours; and (3) may be accompanied by an aura.<sup>1,2</sup> Migraine aura is a reversible focal neurologic deficit that appears shortly before or during the development of migraine attack, and the findings of neuroimaging are normal.<sup>1,2</sup> While the usual duration of a migraine aura is less than an hour, it can last up to a week (prolonged aura).<sup>1</sup>

It is known that exertion can aggravate migraine headache. However, the relationship between exertion and migraine aura is unknown. Exertion can induce visual aura in migraineurs,<sup>3</sup> but, to our knowledge, aura of hemiparesis provoked by exertion has not been reported. We describe a patient who had recurrent attacks of hemiplegic migraine that were induced by exertion.

## REPORT OF A CASE

A 67-year-old right-handed man presented with recurrent attacks of exertion-induced hemiparesis associated with headache. Right-sided throbbing headaches with photophonophobia started at the age of 24 years. He did not have nausea, vomiting, or autonomic symptoms. The headaches occurred at a frequency of once a month and lasted a few hours to a few days. They were initially accompanied by scintillating scotomas that lasted 5 to 60 minutes. At the age of 50 years, the visual symptoms were replaced by episodes of left hemihypesthesia and hemiparesis that would start in the left hand and travel to the left side of the face and the left leg over a few minutes. The symptoms would reach maximum severity (3/5 strength and 50% sensory loss) within 20 minutes, last from half an hour to a day, and resolve spontaneously within an hour. They were not associated with any obvious provocation. When the

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patient was 65 years old, the episodes of hemiparesis switched to the right side, accompanied by a mild non-fluent aphasia, but then occurred only after exertion. The patient's medical history was significant for pulmonary embolus, chronic lymphocytic leukemia, hypercholesterolemia, and major depressive disorder. His medications included warfarin sodium, simvastatin, and venlafaxine hydrochloride (Effexor). His mother had migraine without aura.

After a period of severe exertion (moving furniture for 30 minutes), he had a typical attack and was admitted to the hospital. During the examination, he complained of excruciating right-sided throbbing headache and photophonophobia. His blood pressure was 129/81 mm Hg; his heart rate was 72 beats/min; and he was afebrile. The results of his general medical examination were normal. On neurologic examination, his mental status was normal. He had mild nonfluent aphasia, right-sided central facial paresis, hemiparesis (3/5), hemihyesthesia (50%), hyperreflexia, and extensor plantar response. Headache and neurologic deficits lasted for 1 day and resolved spontaneously within 1 hour. The results of the following laboratory tests and determinations were normal: complete blood cell count, general chemistry profile, coagulation studies, protein C, protein S, antithrombin III, anticardiolipin antibody, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, serum pyruvate, serum lactate, thyroid function test, urinalysis, urinary drug screen, radiography of the chest, electrocardiography, transesophageal echocardiography, electroencephalography, computed tomography of the brain, magnetic resonance imaging with contrast (during the period of hemiparesis), and cerebral angiography. A typical attack was provoked by 20 minutes on a cardiac treadmill, but the results of the patient's cardiac and blood pressure monitoring were unremarkable. He had a mild headache, mild nonfluent aphasia, right-sided central facial paresis, hemiparesis (4/5), hemihyesthesia (75%), hyperreflexia, and extensor plantar response. His headache and neurologic deficits lasted for a few hours and resolved spontaneously within half an hour. He was treated with a combination of warfarin, aspirin, pentoxifylline, phenytoin sodium, and amitriptyline hydrochloride for 2 years, but continued to have recurrent attacks (about 10). Subsequently, all his medications were discontinued, and he was treated with sustained-release verapamil (240 mg/d). He had complete relief of headache and hemiplegic attacks and remained asymptomatic for the following year.

#### COMMENT

Our patient's initial presentation fulfilled the criteria for migraine with aura.<sup>1,2</sup> His headache was unilateral, throbbing, associated with photophonophobia, and accompanied by an aura of scintillating scotoma and lasted for at least 4 hours.

Subsequently, the visual aura was replaced by longer-lasting episodes of hemiparesis that occurred only after exertion. Since the hemiparetic attacks were exertion induced, they were initially attributed to recur-

rent transient ischemic attacks.<sup>4,5</sup> However, the clinical picture, normal findings on cerebral angiography and neuroimaging (during the period of hemiparesis), lack of response to treatment with antiplatelets and anticoagulants, and successful treatment with verapamil suggested that the exertion-induced hemiparesis was not due to ischemia, but was in fact a migraine aura. We believe that our patient fulfilled the criteria for hemiplegic migraine, which, according to the International Headache Society, is classified under migraine with prolonged aura of hemiplegia (as opposed to familial hemiplegic migraine).<sup>1,6</sup> While our patient as well as others with hemiplegic migraine had normal findings on neuroimaging during the aura (a defining feature of a migraine aura),<sup>1,2,6</sup> a recent case report of abnormal gyri enhancement demonstrated on magnetic resonance imaging scans during hemiplegic migraine is intriguing and merits further investigation.<sup>7</sup>

Migraine aura is thought to result from cortical spreading depression (CSD).<sup>2</sup> It is not clear, however, whether additional mechanisms, such as ischemia, are required for a prolonged aura (as occurred in our patient). Although in our patient a superimposed ischemic process cannot be excluded, the clinical picture, the normal findings on cerebral angiography and neuroimaging (during the period of hemiparesis), and the lack of response to antiplatelet and anticoagulant treatment suggested that ischemia was not a major contributory factor to his prolonged aura of hemiparesis.

In our patient, exertion seemed to precipitate the aura of hemiparesis. Thus, we suggest that there is a relationship between exertion and CSD, the pathophysiological correlate of migraine aura. Exertion is associated with hyperventilation and hypocapnea, which are known to cause cerebral vasoconstriction. Hyperventilation can also cause respiratory alkalosis and hypomagnesemia.<sup>8</sup> Since hypomagnesemia can also cause vasoconstriction,<sup>9</sup> the transient hypomagnesemia induced by hyperventilation, combined with the primary magnesium deficiency seen in migraineurs,<sup>9</sup> may lead to the known exaggerated vascular response to hypocapnea in migraineurs with aura.<sup>10</sup> The combination of exertion-induced hyperventilation, hypocapnea, and hypomagnesemia predisposes these patients in particular to have even further cerebral vasoconstriction during exertion. In fact, frontal hypoperfusion has been observed in patients with exertional headache.<sup>11</sup> Both hypomagnesemia and hypoperfusion have been reported to lower the threshold for the development of CSD or aura in migraineurs.<sup>2,12</sup> We suggest that in our patient exertion induced the aura of hemiparesis by lowering the threshold for the development of CSD in the frontal lobe, possibly through exertion-induced frontal hypoperfusion and hypomagnesemia. This hypothesis is consistent with previous reports showing that CSD in hemiplegic migraine starts in the frontal lobe of the affected hemisphere and spreads posteriorly,<sup>13</sup> unlike in typical migraine with aura, in which CSD starts in the occipital lobe and spreads anteriorly.<sup>3,12-14</sup>

Familial and sporadic hemiplegic migraine are genetically heterogeneous conditions that have been

mapped to 3 different chromosome loci so far: 1 on chromosome 19 and 2 on chromosome 1.<sup>7,15-17</sup> Fifty percent of familial (17 families) and 2 cases of sporadic hemiplegic migraine are linked to at least 8 missense mutations within *CACNA1A*, a gene on chromosome 19 that encodes the  $\alpha 1A$  subunit of a neuronal P/Q-type calcium channel.<sup>7,15-17</sup> Currently, investigation is underway to screen our patient's DNA for mutation in the 47 exons of the *CACNA1A* gene. Even though our patient had no family history of hemiplegic migraine, this ion channel gene mutation might account for his episodic attack.

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