

Severe diffuse intracranial vasospasm as a cause of extensive migrainous cerebral infarction

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We report on a 47-year-old white female with a long history of recurrent episodes of migraine with aura, who progressed to develop a continuous intractable headache during the course of which cortical blindness and quadriplegia occurred due to extensive and bilateral hemispheric cerebral infarction. Severe diffuse intracranial major arterial vasospasm was demonstrated by arteriogram. All studies were negative for CNS vasculitis, including cerebral biopsy. The arterial spasm reversed itself, but the patient did not improve. Smoking was the only additional risk factor. Vasospasm is an important cause to be considered in migrainous infarctions. The use of vasoconstrictor agents such as DHE in patients with migraine with prolonged aura has to be carefully re-evaluated. • *Cerebral infarction, migraine, vasospasm*

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Migrainous stroke could result from cerebral vasospasm (1-7), arterial dissection (8), persistent dilatation, stasis and thrombus formation (9), associated mitral valve prolapse and consequent cerebral embolism (10), or prolongation of the migraine process itself (11). Solomon et al. (12) reported cerebral vasospasm in a patient with prolonged refractory migraine without associated neurological symptoms. Isolated cerebral vasculitis is usually considered in the differential diagnosis of vasculopathy associated with migraine (12-15).

We report on a patient with a history of migraine with aura who developed stroke associated with diffuse cerebral vasospasm without evidence of cerebral vasculitis.

Case report

A.S., a 47-year-old white female, presented to us with a long history of migraine with visual aura since the age of 14. Initially the headache was occasional, but in the past three years it had worsened, occurring three to five times a week and sometimes daily. Headache was always on the right side, throbbing in character, associated with nausea and vomiting, photophobia and sonophobia and preceded by scintillating scotoma lasting for 30 min to an hour in both visual fields. The attacks were worsened during menstrual periods.

The patient had a hysterectomy but was not receiving hormonal replacement. There were no specific triggers for the attacks. She was treated previously with tricyclic antidepressants, beta-blockers, calcium channel blockers, sodium valproate, methysergide, indomethacin, ergotamine, isometheptene, narcotics and simple analgesics, without any improvement. The patient smoked approximately 30 cigarettes a day.

When she was initially seen by us one year ago, she had had a severe continuous headache for two weeks. She was admitted to the hospital, at which time no neurological deficit was found. An MRI of the brain and all laboratory studies done at that time, including sedimentation rate and tests for collagen vascular disease, were negative. She was treated with

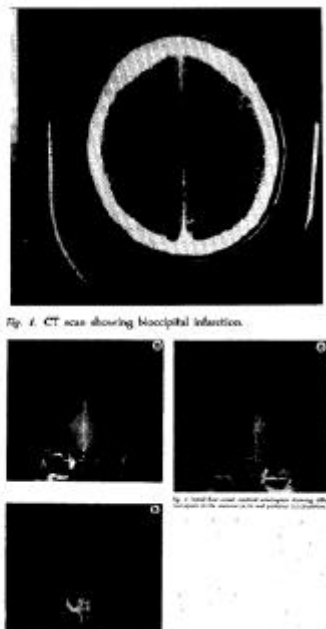


Fig. 1. CT scan showing bioccipital infarction.

repeated injections of intravenous dihydroergotamine in therapeutic dosages in the hospital and was discharged on a combination of methysergide and nortriptyline as prophylactic agents. She improved greatly and during the following three months had only occasional headaches. At the end of three months, methysergide was changed to sodium valproate and she was well for another three months until May 1992 when the headache again became very frequent. A SPECT scan which was done in May 1992 while the patient was having moderate headache showed bilateral diffuse perfusion reduced in the cerebral cortex. Sodium valproate was replaced by methysergide and papaverine hydrochloride was added. The patient again improved for a three-month period. Soon after, however, her condition worsened with continuous headache. A repeat SPECT scan done on 20 August 1992 showed normal perfusion, indicating improvement compared to the previous study even though her headaches were worse. As there was no improvement, she was readmitted to the hospital for a repeat course of intravenous dihydroergotamine and prochlorperazine. Sodium valproate, indomethacin, and chlordiazoxipoxide/amitriptyline combination were also started on admission. The laboratory examinations on admission showed normal routine laboratory values, a sedimentation rate of 27, a negative ANA, normal C3 and C4, negative anticardiolipin antibody profile and negative lupus anticoagulant. The patient continued to complain of severe excruciating headache after admission to the hospital. Ketorolac and verapamil were added. A lumbar puncture revealed clear fluid with an opening pressure of 220 millimeters of H₂O (the pressure was borderline high, no cells, a glucose of 64 mg% and protein of 29 mg%). A repeat sedimentation rate the next day was 20 millimeters per hour. Sjögren antibodies were negative.

Because there was no improvement after the initial doses of intravenous dihydroergotamine, IV dexamethasone was started on the second day of admission. She continued to complain of severe headache and towards the end of the second day developed cortical blindness and left-sided hemiparesis and hemineglect. An MRI of the brain showed bilateral occipital infarctions. DHE was stopped immediately and dexamethasone was continued. On the third day she developed quadriplegia. A CT scan of the brain showed infarctions of the parietal and frontal regions as well as of occipital areas (Fig. 1). Methylprednisolone was started in place of dexamethasone. EKG was normal. Echocardiogram was unremarkable.

The headache continued. A four-vessel cerebral arteriogram performed on the third day after a stroke showed a diffuse decreased caliber of the arteries with collateral vessels to the occipital area that originated from the posterior inferior and superior cerebellar arteries (Fig. 2a, b and c). Vasospasm was noted in all intradural vessels, including the branches of the anterior cerebral artery bilaterally. The pattern was similar to the vasospasm seen in acute subarachnoid hemorrhage. The differential diagnosis at that time was considered to be migrainous vasospasm or diffuse vasculitis of the CNS.

A lumbar puncture was repeated. The fluid was clear with an opening pressure of 190 millimeters of H₂O, two cells, a glucose of 86 mg% and a protein of 28 mg%. Bilateral carotid ultrasound showed a high resistance pattern in the right internal carotid compared to the external carotids. As isolated vasculitis of the CNS could not be excluded, methyl-prednisolone and cyclophosphamide were started. Temporal artery biopsy as well as meningeal and brain biopsies from the temporal lobe were normal. Brain biopsy was from non-infarcted brain. Both the meningeal and brain biopsies contained arterial segments and they were normal. The patient did not improve in spite of steroids and cyclophosphamide and continued to complain of continuous severe headache. Because of the intense vasospasm nimodipine was also started. The pain was controlled only by meperidine injections. Intense physical therapy was also instituted.

A repeat MRI four weeks later showed definite infarction of the frontal lobes, especially on the left side, as well as the changes noted previously (Fig. 3). A cerebral arteriogram repeated five weeks after the first showed normal caliber of all the blood vessels (Fig. 4a and b).



Fig. 3. MRI of the brain showing bilateral occipito-parietal infarction with extension to the frontal areas, especially on the right side.



Fig. 4a, b. Repeat cerebral arteriogram five weeks after the first, showing resolution of the vasospasm.

The patient continued to complain of severe persistent headache even with frequent use of meperidine, methylprednisolone, cyclophosphamide and ketorolac. Her quadraparesis and cortical blindness remain.

Discussion

Diffuse and focal or segmental cerebral vasospasm occurs with complicated migraine and migrainous infarction (1-7, 11-14). On the other hand, angiographic findings of segmental vasospasm may also be due to isolated vasculitis of the brain (15-17). Our patient had a long history of migraine with aura and subsequently developed migrainous infarction associated with diffuse cerebral vasospasm. The

question is whether this patient had migraine alone or had associated vasculitis of the CNS. Moore et al. (16) proposed the following criteria for the diagnosis of isolated CNS vasculitis: (a) patients usually present with acute headache without previous history of headaches, (b) the condition is associated with multiple neurological deficits, encephalopathy and seizures, (c) angiography demonstrates focal segmental narrowing, (d) there is usually no evidence of any systemic inflammatory, infectious or collagen disease, and (e) leptomeningeal or brain biopsy may demonstrate vascular inflammation. In a report of 11 cases by Crane et al. (17) isolated vasculitis of the CNS was diagnosed by arteriogram and in the only case where biopsy was performed, it was negative. All the patients presented with headache of acute onset and multifocal neurological deficits without a previous history of headache. All patients, except one who died, improved with steroids and cyclophosphamide. The investigation of our patient, including negative brain biopsy, failed to identify vasculitis and she did not clinically improve with steroids or cyclophosphamide.

Transient or vanishing cerebral vasculopathy during pregnancy has been reported (18). Experimentally, vasculopathy has been reported following estrogen stimulation (19). Our patient had a hysterectomy and was not on hormonal replacement. Thus, estrogen could not have played a role in the reversible vasculopathy she developed.

Smoking is well documented as a risk factor for stroke. In a large study of risk factors, Bonita et al. found a threefold increase in the risk of stroke in smokers compared to non-smokers (20). Smoking was associated with migrainous infarctions in a previous case report (9). It is difficult to prove smoking acted as a risk factor for cerebral vasospasm and stroke in our patient.

Our patient was receiving dihydroergotamine intravenously at the time she developed cerebral infarction. A similar case was reported by Ganji et al. (21). Ergotamine compounds cause vasospasm (22, 23), but it is usually generalized and mostly affects the medium-sized muscular arteries of the extremities. It is not clear whether dihydroergotamine acted as an additional factor in triggering vasospasm in our patient. This leads to the question of the advisability of using dihydroergotamine in patients with status migrainosus with a history of migraine with prolonged aura. It is also possible that the intractable headache was due to persistent vasospasm. Further observations and research are needed to answer these questions.

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