Migraine...and Stroke:
Is there a link?

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Jenna's case

- Jenna, 36, presents with visual aura, which started in the upper temporal quadrant affecting the right eye.
- Later, the left eye became affected and evolved into complete right homonymous hemianopsia and persisted for more than 60 minutes.
- Her visual symptoms were followed by a left frontal temporal throbbing headache with autonomic features.
- Her past medical history is only significant for migraine with visual aura.
- She has smoked for several years and was on oral contraceptives at the time of her symptoms.
- Her general exam was normal.
- Her neurologic exam revealed right homonymous hemianopsia.
- In addition, she had alexia without agraphia.
- An MRI of the brain revealed left medial temporal and occipital stroke in the posterior cerebral artery distribution (Figure 1).
- A detailed stroke work up was negative.
- She was left with visual deficit, but her reading improved. She was advised to discontinue her oral contraceptives and quit smoking.
- She was started on acetylsalicylic acid, 81 mg, daily.

Migrainous stroke

Migrainous stroke is caused when a migraine fulfills the following:

1. The index attack. A migraine patient with aura is attacked as before, except one or more aura symptoms are present or the neurologic defect does not resolve within seven days.
2. The neuroimaging demonstrates ischemic infarction in a relevant area.
3. The symptoms are unattributed to another disorder.[1,2]

What is the incidence of migrainous stroke?

In the general population, the incidence of migrainous stroke is 3.36/100,000 per year and 1.44/100,000 after controlling for other risks factors (*i.e.,* hypertension, smoking).[3] The Mayo Clinic study cited an incidence rate of 1.7/100,000.[4]

Is migraine a stroke risk factor?

Migraine is an independent risk factor for stroke in young patients. A history of migraine was more frequent in the transient ischemic attack (TIA)/stroke patient group.[5,6]

One US study showed a doubled risk of stroke in patients with migraine after adjusting for all confounding variables,

compared to patients with non-migraine headache (relative risk [RR] 2.0 of ischemic stroke, RR 1.8 of all strokes).[7] Broderick and Swanson, in the Rochester Study, reported a 1% annual risk of stroke in patients with migraine.[4]

Q What are the risk factors for migrainous stroke?

A There are several risk factors for stroke, which have been identified in several studies, in patients suffering from migraines. These risk factors include:

1. Smoking is the number one risk factor for migrainous stroke. Tzourio *et al*, found that young women who smoke were 10 times more likely to suffer a migrainous stroke than patients in the control group.[8]
2. Oral contraceptives (OC) increase the risk. In most women, initiation of OC does not cause or worsen existing migraine headache. Of concern, is the possibility that OC use with migraine (both of which are potential risk factors for ischemic stroke) has an additive effect on stroke risk. A review of the available evidence suggests that OC prescribing practices with migraine should be based on a consideration of the patient's age, type of migraine and the presence or absence of other risk factors for stroke. The existence of a complex or prolonged migraine aura, or of additional stroke risk factors, such as increased age, smoking and hypertension, is likely to enhance the risk of stroke in women with migraine when OCs are prescribed (a meta-analysis of 16 studies: RR of 1.93 [1.4-2.7], controlling for smoking and hypertension).
3. Patients that are older than 35 and female patients are at greater risk.[5]
4. The presence of aura, high frequency rates and long duration migraine headache also increase a patients risk of stroke (WHO Collaborative Study: Increased risk of stroke with:
   > 12 attacks per year, > 12 years of migraine history).

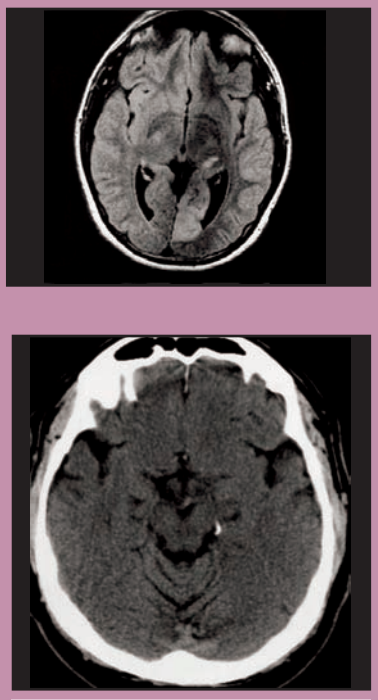

Figure 1. Head CT and MRI of the brain. Head CT showed dense left posterior cerebral artery clot and slight effacement of the left occipital lobe. MRI of the brain showed left posterior cerebral artery stroke.

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Q What is the mechanism of stroke in migraine?

A The exact mechanism of migrainous stroke is not known, but the following associations have been found:

1. Arterial causes: vasospasm (during acute attack), spontaneous arterial dissection, or small vessel vasculopathy.
2. Blood causes: hypercoagulability, antiphospholipid syndrome.[11]
3. Cardiac causes: patent foramen ovale (PFO) is a common finding in the general population (25% to 30%). It is more common in young stroke patients with migraine (45%). The causal relation between PFO and migrainous stroke is not established yet.

Q What investigations should be done?

A A complete workup for stroke should be performed looking for lipid panel, fasting glucose, homocysteine, antiphospholipid antibodies and lupus anticoagulant. Other procoagulants may be tested where indicated.

In young patients, cervical arterial dissection is an important cause for stroke and, therefore, appropriate neuroimaging (*e.g.,* MRI/MRA or conventional catheter angiogram) must be performed in consultation with radiology. Trans cranial doppler (TCD) may be a useful quick screening tool for microbubble studies that identify possible intracardiac right to left shunt. Cardiac investigations include ECG, transesophageal echocardiogram and, if indicated, Holter monitor for 24 to 48 hours.

Q Are triptans contraindicated in a migraine with aura?

A There is no absolute contraindication. However, triptans should be avoided in patients with ischemic or hemorrhagic stroke, coronary artery disease, poorly controlled hypertension, hemiplegic migraine and basilar migraine.

Karen's case

- Karen, 47, presents with a three day history of left frontal headache.
- She developed expressive speech difficulty and right-side weakness for one hour.
- Afterwards, she had residual difficulty finding words, which lasted for several days.
- Her medical history is significant for migraine with aura.
- Her general exam revealed left Horner syndrome and word finding difficulty.
- Her head CT revealed left middle cerebral artery stroke and her CT angiography showed left cervical internal carotid arterial dissection.

Table 1

Characteristics of headache in different types of ischemic and hemorrhagic stroke and migraine

	SAH	ICH	Ischemia	Migraine
Onset	Sudden	Acute to subacute	Acute to subacute	Subacute
Intensity	Severe	Variable	Variable	Variable
Duration	Hours	Hours to days	Hours to months	Minutes to hours
Location	Diffuse	Location	Location	Unilateral
Nausea/ Vomiting	At onset	Variable	Unusual	Frequent
Prior HA	+	+/-	-	+++
Neurologic Finding	+/-	+	+	-

SAH: Subarachnoid hemorrhage ICH: Intracerebral hemorrhage

Comments

Migraine patients are at higher risk than others for extra cranial cervical artery dissection because of the increase serum elastase activity (such enzymes are involved in matrix degradation).

The clinical history and physical exam are very crucial in distinguishing between migraine headache and headache as a manifestation of hemorrhagic or ischemic stroke (Table 1). Dx

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Take-home message

- Migraine is a risk factor for stroke.
- Treat all stroke risk factors in patients suffering from migraines aggressively.
- Strokes can mimic migraine and vice versa (Table 1).
- Triptans should be avoided in patients with stroke, coronary artery disease, poorly controlled hypertension, migraine and stroke mimics.