

Ischemic Stroke: Evaluation, Treatment, and Prevention

Matthew Brandon Maas, MD, and Joseph E. Safdieh, MD

QUESTIONS

Questions 1–3 refer to the following case.

A 72-year-old man presents to the emergency department complaining of weakness and lightheadedness. The patient reports having passed out twice earlier in the day. He has no history of cardiac symptoms. On initial evaluation, the patient is hypotensive and tachycardic. A gastrointestinal hemorrhage is identified and treated appropriately. Two days later, despite normal hemoglobin level and volume repletion, the patient still complains of weakness. On examination, his grip strength and distal leg strength are normal, but he is found to have proximal weakness, especially in the arms. The possibility of myopathy is entertained, but creatine kinase levels are normal. A diffusion-weighted magnetic resonance imaging (MRI) sequence of the brain is obtained (**Figure**).

1. The diffusion-weighted MRI (DWI) in the **Figure** shows areas of hyperintensity. What other MRI finding would help confirm that the findings seen on DWI likely represent acute infarction?

- (A) Corresponding hyperintensity on apparent diffusion coefficient (ADC) maps
- (B) Corresponding hyperintensity on fluid attenuation inversion recovery imaging
- (C) Corresponding hypointensity on ADC maps
- (D) Corresponding hypointensity on T2-weighted images

2. What is the most likely etiology of this DWI finding?

- (A) Bilateral middle cerebral artery (MCA) stroke
- (B) Chronic microvascular ischemic changes
- (C) Internal watershed distribution infarcts
- (D) Multiple embolic infarcts

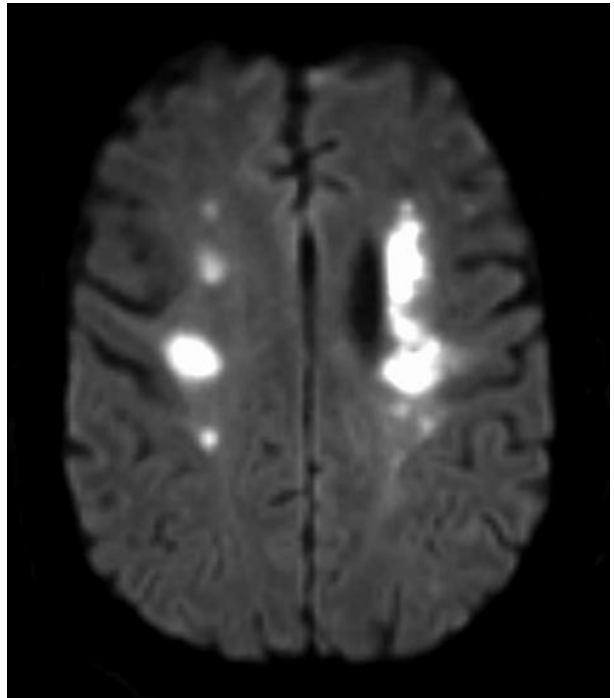


Figure. Diffusion-weighted image of the patient in questions 1 to 3.

3. Which diagnostic step is least relevant to the evaluation of stroke in this patient?

- (A) Echocardiogram to assess for low ejection fraction or aortic stenosis
- (B) Holter monitoring to assess for arrhythmia
- (C) Imaging of the carotid arteries
- (D) Imaging of the intracranial arteries to assess for proximal MCA stenosis

Dr. Maas is a fellow in Stroke and Neurocritical Care, Harvard Medical School, Departments of Neurology, Massachusetts General and Brigham and Women's Hospitals, Boston, MA. Dr. Safdieh is an assistant professor of neurology, Department of Neurology and Neuroscience, Weill Medical College of Cornell University, New York, NY.

Questions 4–8 refer to the following case.

A 72-year-old man is brought to the hospital after being found on the floor by his wife at 5 PM. His wife reports that he had been normal before taking a nap in his recliner chair. When she found him, he was unable to stand up due to weakness in his right arm and leg, so she called 911. He arrived at the hospital 30 minutes after his wife initially discovered him on the ground. The patient has a history of hypertension, dyslipidemia, and atrial fibrillation. His medications are warfarin, lisinopril, metoprolol, and atorvastatin. He has not had a stroke or transient ischemic attack (TIA) in the past. A rapid initial survey shows that his vital signs are stable. He is breathing comfortably and his airway sounds clear. A general physical examination shows no evidence of significant trauma. The rhythm monitor and electrocardiogram (ECG) show atrial fibrillation with a rate near 70 bpm. The ECG also shows ST-segment depression in the precordial leads. A standardized National Institutes of Health Stroke Scale (NIHSS) examination is performed. The patient's deficits are as follows: partial right visual field hemianopsia; paralysis of the lower face sparing the brow; no movement in the right arm or leg; severe sensory loss over the right face, arm and leg; and mild dysarthria. The total NIHSS score is 14. The patient is right handed.

- 4. This patient's clinical syndrome is most consistent with an occlusion of which artery?**
- (A) Left superior division of the MCA
 - (B) Left inferior division of the MCA
 - (C) Left anterior choroidal artery (AChA)
 - (D) Left anterior cerebral artery
 - (E) Left recurrent artery of Heubner
 - (F) Left lenticulostriate artery
- 5. Emergent noncontrast head computed tomography (CT) scan and CT angiography are performed. The time is currently 6:30 PM. Which piece of clinical data would deter administration of intravenous tissue plasminogen activator (tPA)?**
- (A) The patient's NIHSS is greater than 12
 - (B) The patient's platelet count is 87,000 cells/mm³
 - (C) The patient's international normalized ratio (INR) is 1.65
 - (D) The patient had knee surgery 20 days ago
 - (E) The patient was last seen normal by his wife at 4 PM
- 6. Due to thrombocytopenia, the patient does not receive intravenous tPA. Because no large proximal vessel occlusions are identified on CT angiography, revascularization interventions are not pursued. MRI is performed, which shows a DWI hyperintense lesion of relatively small volume in the posterior limb of the internal capsule and posterior corona radiata. The patient is admitted for further evaluation and management. The ECG abnormalities are pursued by drawing a repeat panel of cardiac enzymes, which are reported as elevated. The patient is seen by a cardiologist, who emphasizes the need for antithrombotic therapy. Which of the following statements regarding heparin therapy is most accurate?**
- (A) Administration of heparin in the acute phase is likely to prevent deterioration of the patient's neurologic condition
 - (B) Administration of heparin is contraindicated in the acute phase due to an unacceptable risk for hemorrhagic conversion
 - (C) Administration of heparin is unlikely to benefit the patient's neurologic condition but is reasonable in the context of an acute myocardial infarction
 - (D) Administration of heparin must be delayed for 24 hours to mitigate the risk of hemorrhagic complications
- 7. Further cardiac evaluation shows stenotic lesions in 2 coronary arteries. Coronary artery bypass grafting (CABG) is recommended. A decision is made to allow the patient time for rehabilitation and to reassess whether he remains a good candidate for CABG based on his functional status 3 months later. His cardiologist recommends treatment with an antiplatelet medication for his coronary artery disease in the meanwhile. Which of the following treatment regimens is best for this patient?**
- (A) Warfarin with a goal INR of 2–3
 - (B) Warfarin with a goal INR of 2–3 and aspirin 81 mg daily
 - (C) Warfarin with a goal INR of 1.7–2.5 and aspirin 81 mg daily
 - (D) Aspirin 325 mg daily
 - (E) Clopidogrel 75 mg daily and aspirin 81 mg daily

8. The patient returns for an outpatient appointment where the results of a recent lipid profile are reviewed. His low-density lipoprotein (LDL) level is 90 mg/dL. He continues to take atorvastatin 20 mg daily. What is the most appropriate intervention based on this patient's LDL level?

- (A) Continue atorvastatin 20 mg daily
- (B) Continue atorvastatin and add niacin
- (C) Continue atorvastatin and add gemfibrozil
- (D) Increase atorvastatin to 40 mg daily

Questions 9 and 10 refer to the following case.

A 52-year-old man presents to the emergency department complaining of a 5-minute episode of left-sided numbness. He reports that on the previous day he experienced a 10-minute episode of blindness in his right eye.

9. Presuming the episode of left-sided numbness was a TIA, which of the following localizations is least probable?

- (A) Posterior limb of the internal capsule
- (B) Postcentral sulcus
- (C) Subcortical corona radiata
- (D) Thalamus

10. The patient reports no significant past medical history. He is physically active and works out at a gym twice a week. On review of systems, the patient notes that he has had a moderate intensity, constant left-sided headache for the last 48 hours. He believes the headache is due to a neck strain because his right neck has been aching since he lifted weights the day the headache started. On examination, the left pupil is larger than the right pupil, and the left palpebral fissure is wider than the right. Which of the following tests will most likely lead to a diagnosis of the etiology of this patient's TIAs?

- (A) CT angiography of the neck
- (B) Magnetic resonance angiography (MRA) of the head
- (C) MRI of the brain
- (D) Transesophageal echocardiogram

ANSWERS

1. **The correct answer is (A), corresponding hyperintensity on ADC maps.** T2-weighted image hyperintensity can contribute substantially to DWI signal, causing DWI hyperintensity in areas of T2 hyperintensity that do not correspond to acute ischemia. This phenomenon is called "T2 shine through." ADC maps are useful in distinguishing between the

contribution of T2 signal and ischemia in DWI images because T2 effects do not impact ADC images. In areas of true restricted diffusion (eg, acute infarcts), the ADC map will be hypointense. This technique is particularly useful in patients with a substantial burden of chronic microvascular ischemic changes as these patients may have a new lacunar infarction located within an area of high T2 signal.

2. **The correct answer is (C), internal watershed distribution infarcts.** The DWI sequence demonstrates infarcts in the internal watershed distribution. The patient is experiencing signs of a well-described, although uncommon, stroke syndrome called "man-in-a-barrel." This syndrome consists of weakness in the proximal arms and legs with sparing of distal strength. The unique pattern is attributed to the somatotopic distribution of the corticospinal tract as it traverses the internal watershed territory.¹

Reference

1. Gottesman RF, Sherman PM, Grega MA, et al. Watershed strokes after cardiac surgery: diagnosis, etiology, and outcome. *Stroke* 2006;37:2306–11.

3. **The correct answer is (D), imaging of the intracranial arteries to assess for proximal MCA stenosis.** Imaging of the carotid arteries is necessary to assess for hemodynamically significant stenosis. Significant carotid stenosis can predispose patients to watershed infarction in conditions of diminished flow that would not otherwise cause ischemia. Flow limitation due to cardiac structural or functional abnormalities could also cause watershed infarcts. Holter monitoring can be useful in patients presenting with unexplained syncope. Stenosis of the MCAs would lead to infarction of the deep MCA distribution rather than watershed stroke.

4. **The correct answer is (C), AChA.** This stroke presentation is most consistent with an AChA occlusion. Although AChA strokes are much less common than MCA strokes, it would be unlikely to have an MI MCA stroke with infarction that is sufficiently widespread to produce profound motor, sensory, and visual deficits without causing aphasia. Likewise, an MCA stroke of the superior division can cause profound motor and sensory deficits, but in the left hemisphere it would be expected to cause expressive aphasia and to spare visual function. Stroke affecting the inferior division tends to spare motor and sensory function and produces receptive aphasia.

An anterior cerebral artery infarct could generate significant sensory loss and weakness, although arm weakness is often partial and visual deficits would not be expected. Occlusion of the recurrent artery of Heubner can cause a dense hemiparesis but often causes some expressive aphasia and spares visual and sensory functions. Thrombosis of a lenticulostriate artery can cause a dense sensorimotor lacunar syndrome but would not cause a visual field deficit. It should be noted that this syndrome can also be produced by strokes due to multiple emboli to discrete territories, which is not rare in cardioembolic events.

- 5. The correct answer is (B), the patient's platelet count is 87,000 cells/mm³.** There is no absolute NIHSS score or age threshold beyond which administration of intravenous tPA is contraindicated. Despite thrombolysis treatment, patients with a high NIHSS score (ie, > 22) and the elderly tend to experience poor outcomes. Nevertheless, analysis of the NINDS trial could not identify a threshold age or NIHSS score beyond which no benefit from tPA could be predicted.¹ Depending on the goals of treatment at the time the patient is being emergently evaluated, thrombolysis may be appropriate in some patients with high NIHSS scores. Because of the risk of hemorrhagic complications, a minimum platelet count of 100,000 cells/mm³ and an INR of 1.7 or less are stipulated by FDA indication. With a platelet count of 87,000 cells/mm³, IV thrombolysis treatment would be considered unsafe. Other conditions conferring prohibitive hemorrhage risk include surgery within the prior 15 days or central nervous system surgery, head trauma, or stroke within the prior 3 months.

Reference

1. Albers GW, Olivot JM. Intravenous alteplase for ischemic stroke. *Lancet* 2007;369:249–50.

- 6. The correct answer is (C), administration of heparin is unlikely to benefit the patient's neurologic condition but is reasonable in the context of an acute myocardial infarction.** Several trials have evaluated the role of heparin in acute stroke. Thus far, no trial has demonstrated efficacy in preventing early stroke recurrence, preventing neurologic deterioration, or improving overall outcomes, although 1 trial employing heparin early for patients with nonlacunar strokes found improved outcomes.¹ In general, heparin is avoided acutely because of the increased risk for hemorrhagic complications that are particularly

relevant for large-volume strokes. All antithrombotic treatments must be withheld for 24 hours following thrombolysis, which this patient did not receive. The use of heparin may be necessitated by the competing cardiac risks. Heparin is reasonable therapy when indicated for treatment of other concurrent medical conditions, such as this patient's cardiac pathology.² Although low-molecular-weight heparin is often used for non-ST elevation myocardial infarction, use of unfractionated heparin is preferred in this case to allow for the possibility of rapid reversal of anticoagulation in the case of a hemorrhagic complication.

References

1. Camerlingo M, Salvi P, Belloni G, et al. Intravenous heparin started within the first 3 hours after onset of symptoms as a treatment for acute nonlacunar hemispheric cerebral infarctions. *Stroke* 2005;36:2415–20.
 2. Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists [published errata appear in *Stroke* 2007;38:e38 and 2007;38:e96]. *Stroke* 2007;38:1655–711.
- 7. The correct answer is (B), warfarin with a goal INR of 2–3 and aspirin 81 mg daily.** The presence of atrial fibrillation is a strong indication for anticoagulation with warfarin. A large analysis has found that anticoagulation intensity below an INR of 2 is insufficient for stroke prevention.¹ Another clinical trial has demonstrated that anticoagulation intensity below an INR of 2 remains insufficient for stroke prevention even with the addition of aspirin.² Aspirin alone is recommended as an alternative only for patients unable to take oral anticoagulation. The combination of clopidogrel and aspirin increases the risk of hemorrhage with little increased efficacy. This treatment was specifically evaluated in the ACTIVE W trial³ comparing clopidogrel and aspirin versus warfarin with a target INR of 2 to 3 for patients with atrial fibrillation. The study was terminated early as the superiority of warfarin was significantly demonstrated by the midpoint with lower rates of vascular events and a lower rate of major bleeding complications compared with the clopidogrel and aspirin combination. The most recent

guidelines recommend adding aspirin (in doses up to 162 mg daily) to warfarin at a target INR of 2 to 3 for patients with atrial fibrillation and concurrent ischemic coronary artery disease.⁴

References

1. Hylek EM, Skates SJ, Sheehan MA, Singer DE. An analysis of the lowest effective intensity of prophylactic anticoagulation for patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1996;335:540–6.
2. Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. *Stroke Prevention in Atrial Fibrillation Investigators. Lancet* 1996;348:633–8.
3. Connolly S, Pogue J, Hart R, et al. ACTIVE Writing Group of the ACTIVE Investigators. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet* 2006;367:1903–12.
4. Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;37:577–617.

- 8. The correct answer is (D), increase atorvastatin to 40 mg daily.** There is mounting evidence that intensive statin therapy reduces the risk of ischemic vascular events, even in disproportion to the degree of cholesterol lowering. The results of the recent SPARCL trial¹ of atorvastatin in patients with a recent stroke or TIA but no known coronary artery disease have reemphasized the cumulative evidence in this direction. Although an LDL below 100 mg/dL is the goal for all patients with a history of ischemic cerebrovascular events, a stricter goal of an LDL level below 70 mg/dL has emerged as the recommendation for high-risk patients with multiple risk factors.¹ Given this patient's overall medical condition and recently diagnosed advanced coronary artery disease, further lowering of his LDL cholesterol level is indicated. He is currently on low-dose atorvastatin. The dose of the statin should be raised in an attempt to optimize his lipid profile. Because the efficacy of niacin and gemfibrozil is less established, there is no rationale for adding a second-line agent unless his lipid profile remains suboptimal on high-dose statin therapy.

Reference

1. Adams RJ, Albers G, Albers MJ, et al; American Heart Association, American Stroke Association. Update to the AHA/ASA recommendations for the prevention of stroke in patients with stroke and transient ischemic attack. *Stroke* 2008;39:1647–52.

- 9. The correct answer is (D), thalamus.** All of the above brain regions contain sensory pathways that can produce hemisensory loss. The postcentral sulcus obtains its blood supply from cortical branches of the MCA. The posterior aspect of the corona radiata lies in the watershed of the deep and superficial MCA territories, and the inferior aspect derives some supply from the AChA.^{1,2} The posterior limb of the internal capsule obtains its blood supply from the AChA and lateral lenticulostriate arteries.³ All of these vascular territories are supplied by the internal carotid artery. Strokes in the thalamus that produce sensory impairment occur in the territory of the inferolateral arteries, specifically the medial geniculate or principal inferolateral artery. The inferolateral arteries branch from the P2 segment of the posterior cerebral artery.^{4,5} Given this patient's temporally-associated transient monocular blindness, ischemia in an ipsilateral carotid territory is more likely than a posterior circulation lacunar syndrome.

References

1. van der Zwan A, Hillen B. Review of the variability of the territories of the major cerebral arteries. *Stroke* 1991;22:1078–84.
2. Nakano S, Yokogami K, Ohta H, et al. CT-defined large subcortical infarcts: correlation of location with site of cerebrovascular occlusive disease. *AJNR Am J Neuroradiol* 1995;16:1581–5.
3. Mohr J, Steinke W, Timsit S, et al. The anterior choroidal artery does not supply the corona radiata and lateral ventricular wall. *Stroke* 1991;22:1502–7.
4. Schmammann J. Vascular syndromes of the thalamus. *Stroke* 2003;34:2264–78.
5. Hayman LA, Berman SA, Hinck VC. Correlation of CT cerebral vascular territories with function: II. Posterior cerebral artery. *AJR Am J Roentgenol* 1981;137:13–9.

- 10. The correct answer is (A), CT angiography of the neck.** Neck pain, headache, and Horner's syndrome ipsilateral to symptoms of hemispheric and retinal ischemia provoke high suspicion for the presence of a carotid dissection. A CT angiogram of the neck is the most appropriate examination in this case. MRI and MRA of the neck using fat suppression

techniques are alternatives.¹ MRI/MRA has the benefit of identifying signs of dissection other than lumen irregularity but may overestimate the degree of stenosis.

Reference

1. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. *N Engl J Med* 2001;344:898–906.

Copyright 2009 by Turner White Communications Inc., Wayne, PA. All rights reserved.