RESIDENT & FELLOW SECTION

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Clinical Reasoning: A 42-year-old man who developed blurred vision and dropped his iPod while jogging

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SECTION 1

A 42-year-old man noted sudden onset of blurriness in his left eye and dropped his iPod from his right hand while jogging. In the emergency room, it was noted that visual blurring resolved with right eye closure, but his ophthalmologic examination was otherwise normal. He had subtle right nasolabial fold flattening and right arm pronator drift. His examination was otherwise normal. He reported no headache, neck pain, prior trauma, prior transient neurologic deficit, or palpitations. He took no medications and did not smoke, drink alcohol, or use illicit drugs.

Question for consideration:

1. What is the localization and differential diagnosis of the patient's deficits?

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SECTION 2

The differential diagnosis for acute-onset neurologic deficits includes vascular causes, seizures, and migrainous phenomena. There was no history to suggest seizure, and the monocular visual deficit and lack of headache would be atypical (albeit not impossible) for complex migraine. Extraocular muscle weakness causing ocular misalignment can cause the phenomenon of blurred vision resolving with closure of one eye, but no extraocular muscle weakness was detected on examination. Abrupt onset of unilateral blurred vision with contralateral face and arm weakness suggests simultaneous retinal and ipsilateral frontal hemispheric ischemia. Potential etiologies include embolism or hypoperfusion due to pathology of the internal carotid artery, aortic arch, or heart. In a series of 1,008 patients age 15–49 with first stroke, cardioembolism and cervical artery dissection were the 2 most common causes of stroke, causing 19.6% and 15.4% of strokes, respectively.[1] Under age 45, dissection was even more common (18.6%). In our patient, initial CT and MRI revealed no evidence of infarction, but CT angiogram demonstrated dissection of the left internal carotid artery (figure, A). On further questioning, there were no identifiable inciting events for the dissection.

Question for consideration:

1. How should the patient's carotid dissection be managed?

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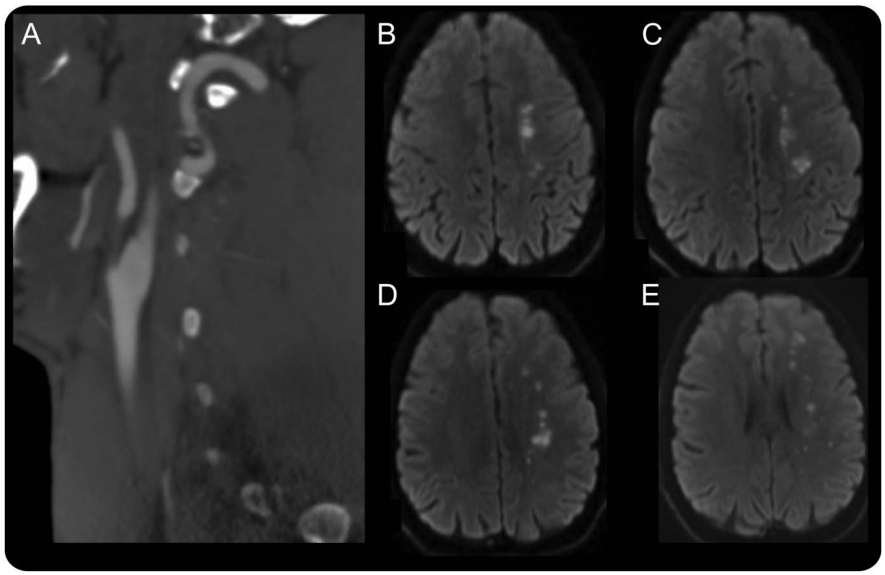
Figure CT angiogram and MRI



(A) CT angiogram demonstrates "flame-shaped" tapering of the left internal carotid artery consistent with dissection. (B–E) MRI diffusion-weighted imaging demonstrates infarction in the middle cerebral artery–anterior cerebral artery (B–C) and internal (D, E) borderzone territories.

SECTION 3

There are no randomized trials comparing antiplatelet agents and anticoagulation for stroke prevention in cervical artery dissection. The most recent meta-analysis of nonrandomized data included 1,636 patients from 39 studies in which 1,137 patients were anticoagulated (with unfractionated heparin, low-molecular-weight heparin, or warfarin) and 499 received antiplatelet agents (with aspirin, clopidogrel, or dual therapy with aspirin and clopidogrel or aspirin and dipyridamole).[2] Thirty-three patients had strokes across both groups (2.6% in the antiplatelet group, 1.8% in the anticoagulation group) and 14 patients died (1% in the antiplatelet group, 0.8% in the anticoagulation group). There were no statistically significant differences in rates of stroke or mortality between the 2 treatment strategies. However, it has been noted that most studies of carotid dissection failed to capture patients during the acute period when stroke risk is highest.[3] In patients with cervical artery dissection–related strokes who could pinpoint the precise onset of their initial prestroke symptoms (e.g., headache, Horner syndrome, or TIA), 82% had a stroke within 1 week, and 44% of those strokes were within the first 24 hours.[4] Based on the presumed artery-to-artery embolic mechanism of stroke in cervical dissection and until more definitive data are available, it is reasonable to consider anticoagulation in such patients,[5] though this decision must be individualized, weighing the risks of intracranial hemorrhage, especially in cases of large stroke or intradural extension of dissection.

Given that our patient had clinical evidence of cerebral ischemia and had neither intradural extension of his dissection nor a large stroke, the benefits of anticoagulation were believed to outweigh the risks, and he was initiated on IV heparin.

Approximately 24 hours after his presentation and 12 hours after initiation of anticoagulation, he developed worsening right arm weakness and aphasia. His blood pressure was 100/60 mm Hg. An MRI was repeated (figure, B–E).

Question for consideration:

1. What does the pattern of infarction suggest with respect to stroke mechanism?

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SECTION 4

The MRI reveals cerebral infarction in the watershed or borderzone regions between the middle cerebral artery (MCA) and anterior cerebral artery territories (figure, B and C) and in the internal borderzone at the juncture of the superficial (leptomeningeal) and deep (lenticulostriate) perforating branches of the MCA (figure, D and E). While borderzone infarction is classically attributed to hypotension, there is evidence that embolism may also play a role. The end-arterial territories are potential sites for the smallest emboli, and patients with borderzone infarction due to carotid disease have been noted to have evidence of ongoing embolization on transcranial Doppler high-intensity transient signal studies.[6] Hypoperfusion and embolism may therefore interact in the pathophysiology of borderzone infarction through impaired clearance of emboli in states of hypoperfusion.[6]

Carotid dissection can cause stroke through both embolism and hypoperfusion: artery–artery embolism of intraluminal thrombus or cerebral hypoperfusion due to carotid occlusion from enlarging intramural hematoma. In our patient, radiologic evidence of carotid occlusion and a blood pressure of 100/60 mm Hg suggested hypoperfusion as the mechanism of his new strokes.

Question for consideration:

1. How can ongoing cerebral ischemia attributable to hypoperfusion be managed?

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SECTION 5

Induced hypertension can increase cerebral blood flow to maximize collateral circulation and decrease brain ischemia. The largest prospective trial of induced hypertension included only 13 patients,[7] and the largest retrospective study only 46 treated patients.[8] Existing studies are heterogeneous with respect to methodology, duration of induced hypertension, and concurrent use of anticoagulation with induced hypertension. However, several important observations emerge from these studies. Patients with acute ischemic stroke most likely to benefit from induced hypertension are those with large-vessel occlusion or stenosis (e.g., of the carotid or MCA stem) and those with a demonstrable blood pressure threshold, i.e., a specific blood pressure above which a neurologic deficit is reversed and below which the deficit is present. There appears to be no increased incidence of hemorrhagic complications or other adverse outcomes in patients undergoing induced hypertension after acute ischemic stroke, even in patients who have been simultaneously anticoagulated. While larger controlled trials are necessary, preliminary data suggest that induced hypertension may be both safe and beneficial in selected patients.

It is unclear whether any of the patients in studies of induced hypertension reported as having large-vessel stenosis or carotid stenosis/occlusion may have had carotid artery dissection as the etiology. However, because our patient had new strokes while receiving anticoagulation in the setting of flow-limiting carotid dissection and a low blood pressure, phenylephrine was initiated. At systolic blood pressures of 130 mm Hg and above, he was able to maintain his right arm against gravity, but below this threshold, he could not lift this arm from the bed. His aphasia persisted even at systolic blood pressure of 180. This blood pressure threshold for his right arm strength persisted for several days, and oral midodrine and fludrocortisone were initiated in order to wean him from phenylephrine. He was discharged to rehabilitation on warfarin, midodrine, and fludrocortisone. At follow-up 1 month later, he had full right arm strength, and his aphasia had begun to improve. Midodrine and fludrocortisone were tapered without recurrence of symptoms.

Questions for consideration:

1. How long should anticoagulation be maintained?
2. Should the patient undergo repeat imaging to aid in this decision?

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SECTION 6

Current guidelines recommend antithrombotic treatment for 3–6 months after dissection, acknowledging that this duration is "arbitrary."[9] The recommended duration of 6 months is based in part on the largest study of stroke recurrence after cervical artery dissection (459 patients followed for mean 31 months, 384 of whom had carotid dissections).[10] In this study, there were 4 recurrent strokes: 2 within the first 6 months of follow-up in patients with incompletely healed dissections and 2 at around 2 years due to recurrent dissection contralateral to the original dissection. Some practitioners recommend repeat vascular imaging as early as 6 weeks following initiation of anticoagulation, with discontinuation of anticoagulation if the artery remains occluded, and continuation of anticoagulation if arterial patency has returned but with persistent significant stenosis.[5] In patients with no recurrent stroke or TIA, we typically anticoagulate patients with cervical artery dissection for 6 months and then convert from anticoagulation to an antiplatelet agent at that time. We also obtain vessel imaging at 6 months. Although our decision to discontinue anticoagulation and initiate an antiplatelet agent at 6 months is not influenced by findings on vascular imaging, this imaging establishes a new radiologic baseline for the patient, should a subsequent new ischemic event occur. Six months following his initial presentation, our patient had made substantial progress in his speech with speech therapy. CT angiogram revealed persistent occlusion of his left internal carotid artery, anticoagulation was discontinued, and aspirin was initiated.

DISCUSSION Cervical artery dissection is a common cause of stroke in the young.[1] Predisposing factors include trauma, chiropractic manipulation, and connective tissue diseases, although many patients have no clear predisposing factor. Patients may present with ischemic symptoms (i.e., TIA or stroke) or local symptoms such as headache, neck pain, Horner syndrome, or cranial nerve palsies (most commonly IX, X, XI, or XII, though III, V, VI, and VII have rarely been reported in carotid dissection[11]). Up to 43% of patients with cervical artery dissection presenting with local symptoms alone may ultimately have strokes,[4] so discovery of dissection warrants stroke preventative therapy, even if initial symptoms are nonischemic in nature. There are no data from randomized controlled trials to guide therapeutic decision-making. Therefore decisions about the use of antiplatelet agents or anticoagulants, optimal duration of therapy, and when or if to repeat cervical arterial imaging must be individualized for each patient. The Cervical Artery Dissection in Stroke Study (CADISS) is currently recruiting patients into a randomized trial of anticoagulation vs antiplatelet therapy. This will hopefully yield answers to long-controversial questions in the management of cervical artery dissection.

AUTHOR CONTRIBUTIONS

Dr. Berkowitz conceived of, wrote, and revised the manuscript; created the figure; and cared for the patient. Dr. Voinescu revised the manuscript and cared for the patient. Dr. Feske revised the manuscript and cared for the patient.

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REFERENCES

1. Putaala J, Metso AJ, Metso TM, et al. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: the Helsinki young stroke registry. Stroke 2009;40:1195–1203.
2. Kennedy F, Lanfranconi S, Hicks C, et al. Antiplatelets vs. anticoagulation for dissection: CADISS nonrandomized arm and meta-analysis. Neurology 2012;79:686–689.
3. Caplan LR. Antiplatelets vs. anticoagulation for dissection: CADISS nonrandomized arm and meta-analysis. Neurology 2013;80:970–971.
4. Biousse V, D'Anglejan-Chatillon J, Toubol P, Amarenco P, Bousser M. Time course of symptoms in extracranial artery dissections: a series of 80 patients. Stroke 1995;26:235–239.
5. Caplan LR. Dissections of brain-supplying arteries. Nat Clin Practice Neurol 2008;4:34–42.
6. Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. Arch Neurol 1998;55:1475–1482.
7. Rordorf G, Koroshetz WJ, Ezzeddine MA, Segal AZ, Buonanno FS. A pilot study of drug-induced hypertension for treatment of acute stroke. Neurology 2001;56:1210–1213.
8. Koenig MA, Geocadin RG, de Grouchy M, et al. Safety of induced hypertension therapy in patients with acute ischemic stroke. Neurocrit Care 2006;04:3–7.
9. Furie KL, Kasner SE, Adams RJ, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011;42:227–276.
10. Touze E, Gauvrit J-Y, Moulin T, et al. Risk of stroke and recurrent dissection after a cervical artery dissection: a multicenter study. Neurology 2003;61:1347–1351.
11. Sturzenegger M, Huber P. Cranial nerve palsies in spontaneous carotid artery dissection. J Neurol Neurosurg Psychiatry 1993;56:1191–1199.

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