Treatment of Patients With Suspected Ischemic Stroke of Undetermined Onset and Negative Head Computed Tomography Scan

Caution is Advised

Harold P. Adams Jr, MD

This case represents a difficult situation; by the description, this woman probably has a multilobar cerebral infarction that is most likely secondary to an occlusion of the internal carotid artery or the proximal segment of the middle cerebral artery. The computed tomography scan is normal, a finding somewhat surprising given the severity of her stroke; the presence of a dense artery sign suggesting occlusion of the internal carotid or middle cerebral artery or early ischemic changes in the insular cortex would be expected. The absence of early ischemic changes suggests that the stroke might be of recent onset and potentially treatable. Although the National Institutes of Health Stroke Scale score is not provided in the vignette, the description suggests that her score would be at =20; it may be higher. This information is important because it portends a poor prognosis; she is likely to die or be disabled as a result of the stroke. The natural reaction is to prescribe reperfusion therapy to alter this otherwise potentially dismal situation. Still, caution should be exercised because the risk of hemorrhagic complications is high in patients with multilobar infarction.

The lack of knowledge about the time of onset hampers decision-making. An effort to obtain information about the last time she was known to be in a usual state of health from relatives, friends, or acquaintances may help. At the same time, information about any recent medical illnesses or the use of medications that are a contraindication for reperfusion therapy may become available.

The use of results of brain imaging studies has been proposed as a surrogate method for estimating the time of onset of stroke. In this case, the normal computed tomography study implies that the stroke probably is recent—it might have happened in the past few hours and treatment might be given within the currently defined treatment windows. Still, the available computed tomography findings might not provide sufficient evidence to justify emergency reperfusion therapy. Perfusion computed tomography is a potentially useful diagnostic study for determining eligibility for reperfusion therapy. Another approach is the comparison of images found on diffusion-weighted (DWI) and fluid attenuated inversion recovery sequences obtained on MRI. The assumption is that a discrepancy (DWI shows the lesion, and fluid attenuated inversion recovery does not reveal the abnormality) would represent a stroke that is <4.5 to 6 hours old. Although this strategy holds promise, additional data are needed before it should be used to select patients who might be treated with intravenous recombinant tissue-type plasminogen activator (rtPA) or endovascular interventions. Another strategy would be to compare the findings on DWI and perfusion scans to determine the presence of potentially salvageable brain tissue. A relatively large DWI lesion probably would preclude treatment, but a small DWI lesion with a large perfusion defect (mismatch) might serve as an indication for an endovascular intervention. MR angiography or computed tomographic angiography could be used to confirm the presence of an arterial occlusion. This approach has been used in clinical trials to select patients who might be treated with endovascular interventions.

Regardless of the type of imaging findings used to select patients with stroke of unknown onset, limited data about the safety and potential efficacy of reperfusion therapy in the situation described in this case are available. The choices are intravenous administration of rtPA or use of an endovascular intervention. The large clinical trials of intravenous thrombolysis excluded patients in which the time of onset of stroke was not known, and currently available data about the safety and efficacy of intravenous thrombolysis are from small case series. Trials aimed at addressing this type of situation are planned or underway. Hopefully, the trials will give a clear answer. However, on the basis of the uncertainties about the safety of rtPA in this scenario and the modest efficacy of rtPA in patients with large artery occlusions, the most prudent course would be to not administer intravenous rtPA in this situation. An endovascular intervention is an alternative treatment option. Several devices have received regulatory clearance and their use potentially could be combined with pharmacological interventions, but the role of endovascular interventions in treatment of stroke has not been established. There are limitations of this treatment option because the expertise and resources to perform emergency
endovascular perfusion are available at a relatively small number of institutions, and the number of patients who could be treated may be less than anticipated. Because of the severity and type of neurological impairments, consent cannot be obtained from the patient and treatment options should be discussed with a next-of-kin or another authorized representative if available. Given the situation, the family should understand the risks of treatment, including hemorrhagic transformation of the infarction, and the likelihood that success might be limited.

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**References**

**Key Words:** stroke of undetermined onset ■ thrombolysis ■ endovascular treatment ■ brain imaging ■ vascular imaging
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