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Perils in Diagnosing a Stroke

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The Case

A 75-year-old man with a history of hypertension, diabetes, chronic back pain, and opioid use disorder was brought to the emergency department after being found unresponsive. The patient's wife had been driving him back from the store when she noticed he was very lethargic. After he became unresponsive, she called 911. In the emergency department, the physician suspected a stroke given the patient's risk factors and the relatively acute onset of symptoms. A CT scan revealed no bleeding into the brain. After consulting with a neurologist, the decision was made to give systemic thrombolytics (drugs to dissolve a blood clot).

After the thrombolytic was administered, the patient's nurse noticed multiple patches on the patient's back. She realized that they were fentanyl patches—a potent opioid medication. She spoke with the patient's wife, who said that the patient was prescribed the patches for his chronic back pain and that she had placed two fentanyl patches on the patient earlier that morning. The patient's wife stated his physician had recently increase the dose due to his pain level. The nurse asked a pharmacy technician to perform medication reconciliation, which revealed that the patient's fentanyl patch had recently been increased from 100 micrograms per hour to 150 micrograms per hour. However, his wife had accidentally applied two 150 microgram patches that morning—instead of one—as she assumed the two patches would be his new regimen. Therefore, the patient had inadvertently received three times his previous dose of fentanyl.

The nurse alerted the physician, who realized that the opioid overdose probably explained the patient's symptoms. He quickly ordered administration of naloxone (an opioid reversal agent). Although the patient initially became more responsive, shortly thereafter he had a generalized seizure. A repeat CT scan showed intracranial hemorrhage—an adverse consequence of the thrombolytics. His neurologic status deteriorated, and he required urgent surgery to drain the bleeding. The patient had a long, complex hospital course, but eventually he was discharged to a rehabilitation facility with substantial (though not complete) recovery of his functional status.

The Commentary

Commentary by Joseph L. Schindler, MD

The case above represents a known complication from intravenous (IV) thrombolytics, a potentially avoidable one if the patient indeed was not having a stroke. Intracerebral hemorrhage is the most feared complication of IV thrombolytics. In the early National Institute of Neurological Disorders and Stroke trial, the rate of symptomatic hemorrhage was 6.4%; it has fallen to as low as 2.4% in subsequent trials.(1,2) Even with the improvement, the complication is a source of angst among practitioners administering thrombolytics for patients that are having a stroke. The angst, of course, would be far greater if administered to a patient who has been incorrectly diagnosed as having a stroke. A recent study reviewed about 9000 patients treated with IV thrombolytics and 392 patients were identified as not having strokes. The rate of intracerebral hemorrhage in this population was 0.5%, far lower than in patients with stroke.(3) The primary reason for the low risk of lytic complications in stroke mimics is that this population does not have ischemic, friable brain tissue that can transform into hemorrhage. In addition, they may not have cerebrovascular disease characteristics such as white matter disease and microhemorrhages that may increase a patient's risk for a coagulopathy-related intracerebral hemorrhage. Nevertheless, when this complication occurs it is devastating for both patients and providers, and this case thus challenges us to review potential system and cognitive factors that could have contributed to this outcome.(4)

In this case, the first step is to determine whether there were process factors or deviations from the standard of care set by the policies and protocols of the institution. The development of primary stroke centers was recommended by the Brain Attack Coalition in 2000, a group of multidisciplinary specialists, partly in response to the underutilization and poor outcomes from the administration of IV thrombolytics.(5) The focus of a primary stroke center is the adoption and implementation of evidence-based protocols to safely and effectively deliver IV thrombolytics, which requires a highly coordinated effort among multiple disciplines and locations within the hospital.

In thinking about this case, the communication among the nurse, ED physician, and the neurologist as it pertains to the history, examination, and test results must be scrutinized. Each practitioner should have well-defined tasks within the stroke evaluation process, and these can be reviewed by assessing the documentation within the medical record. In this case, the patient's history of taking excessive pain medications was not elicited in a timely manner. This directly impacted the practioners' clinical assessment and decision to treat with thrombolytics as opposed to administering naloxone first.

Because IV thrombolytics have a narrow therapeutic window, practitioners must provide rapid assessments and make swift decisions to deliver the medication within the time window of 4.5 hours. Studies have demonstrated that earlier treatment with thrombolytics leads to better functional outcomes.(6) In response, stroke centers and practitioners have adopted the mantra "time is brain."(7) Additionally, the American Heart Association has endorsed quality-improvement initiatives such as "Target: Stroke," which also emphasizes fast administration of IV thrombolytics.(8) These factors have led stroke care systems to favor expeditious treatment over a confirmatory diagnosis, citing the relatively low risk of complications when thrombolytics are given to nonstroke patients.

Accordingly, stroke centers have emphasized increasing the sensitivity of evaluations by recognizing and treating all possible stroke candidates in the emergent setting. To date, acute ischemic stroke remains a clinical diagnosis formed by the history and neurological examination. The 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke state that for most patients, a noncontrast head CT

will provide the practitioner the requisite information for acute stroke management.(9) However, the noncontrast head CT is not a sensitive study (7%–14%) to diagnose ischemic stroke (at least within the window for thrombolytics), and it is therefore used to exclude a hemorrhage or a stroke mimic such as a brain mass.(10) Unlike myocardial infarction, there is no serum test or biomarker to diagnose stroke. In consequence, the burden is on the practitioner to expeditiously and accurately identify the stroke patient.

Diagnosing stroke can be challenging for primary responders and nonneurologists. Many reviews of the difficulty and pitfalls in stroke recognition focus on uncommon presentations, such as posterior circulation strokes, the young stroke patient, and subarachnoid hemorrhage. Recently, groups that have studied diagnostic accuracy have focused more on the missed diagnosis. One meta-analysis of studies between the years 1995–2016 concluded that 9% of cerebrovascular events are missed in the ED.(11) Our group randomly abstracted charts of patients with a discharge diagnosis of stroke in both our academic medical center and a large community hospital. We concluded that 20% of stroke patients at our medical center did not receive a diagnosis of stroke during their evaluation in the ED. The same was true of 25% of patients at the community hospital.(12)

Neurological presentations are varied and complex. Up to 30% of patients with a suspected stroke in the ED may be experiencing a stroke mimic.(13) Common mimics include acute vestibular neuritis, migraine, seizure, metabolic or toxic encephalopathy, seizure, and conversion disorder. Given the necessary rapid evaluation and emphasis on failure to recognize patients, the rates of thrombolytic administration in mimics has increased. MRI has a much higher sensitivity (88%–100%) for acute ischemic stroke, and its routine use would substantially increase diagnostic accuracy and reduce the treatment of mimics.(14) However, most hospitals do not have the infrastructure or resources to obtain MRI studies in a timely manner. Current guidelines do not recommend MRI since it has not been shown to be cost-effective.(9)

This case represents the treatment of a stroke mimic or misdiagnosis that contributed to an adverse outcome. There may have been several cognitive errors among the practitioners related to gathering the appropriate history, examination, clinical reasoning, and formation of the assessment. It is reasonable to preliminarily suspect stroke in a patient with risk factors and an acute change in mentation. However, the clinicians should have considered other diagnoses in the setting an unresponsive patient and a head CT that excludes hemorrhage, since few strokes without hemorrhage will render a patient completely unresponsive. Exam findings on a patient with a narcotic overdose that might have been clues include pinpoint pupils, an intact brainstem, absence of focality on the motor examination, and a plantar flexor response. Had there been continued concern for stroke after the examination, a CT angiogram of the neck and head could have excluded a basilar artery thrombosis, one of the few ischemic strokes that leads to a severely depressed mental status. Given the likelihood that the nonspecialist clinicians were unaware of some of these diagnostic clues, educational interventions should review common stroke mimics, stroke identification tools, and the neurological examination.

The nature of the consultation between the ED physician and neurologist in this case is uncertain. One potential way of increasing diagnostic accuracy and reducing the treatment of mimics when neurological expertise is not available at the bedside is the use of telemedicine. Telestroke (the use of high-definition video-conferencing to perform consultations on a suspected stroke patient) has been shown to increase the accuracy of diagnosis and appropriateness of treatment compared to telephone communication between

the ED and the neurologist.(15)

Diagnostic errors in stroke patients can be due to both system and cognitive factors. Implementing evidence-based protocols in the evaluation of the acute ischemic stroke patient, ensuring reliable and effective communication among practitioners, selective use of MRI, and bedside access to stroke expertise through telemedicine can increase diagnostic accuracy. Traditionally, the focus has been on missed diagnosis that results in *failure* to treat with IV thrombolytics. However, the downstream consequences of inappropriately treating stroke mimics with thrombolytics should be further evaluated. This can potentially promote wasteful testing, drain intensive care resources, foster the unnecessary administration of medications, and, as in this case, expose patients to risks such as hemorrhage, which can be devastating.

Take-Home Points

- Acute ischemic stroke remains a clinical diagnosis despite modern advances in neuroimaging.
- Diagnostic errors in stroke can be related to systems and cognitive factors.
- While the emphasis to date has been on reducing underdiagnosis of stroke, overdiagnosis can also be problematic, particularly when it leads to the administration of potentially toxic medications such as thrombolytics.
- Defined tasks during the stroke evaluation process, improved communication among practitioners, utilization of validated identification and screening tools, selective use of MRI, and rapid accessibility to neurological expertise can improve diagnostic accuracy in stroke.

Joseph L. Schindler, MD
Acting Chief, Division of Vascular Neurology
Associate Professor of Neurology and Neurosurgery
Yale School of Medicine
Director, Yale New Haven Comprehensive Stroke Center
Yale New Haven Hospital
New Haven, CT

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