Crossing Diagnostic Borders: Herpes Encephalitis Complicated by Cultural and Language Barriers

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Background: **The patient who complains of vague mental status changes requires extra vigilance in that the underlying condition might itself affect the patient's ability to communicate well and relate a medical history. The differential diagnosis of delirium is broad, ranging from the benign to the potentially fatal. The diagnostic uncertainty inherent in primary care is compounded when language and cultural differences interfere with physician-patient communication.**

Methods: **We undertook a MEDLINE-assisted review of the medical literature concerning herpes simplex encephalitis. Additionally, we performed an Internet search of several government Web sites to find current legal and federal guidelines concerning the use of medical interpreters.**

Results and Conclusions: **We recount the case of a young Eastern European immigrant who complained initially of vague mental status changes and was found to have herpes simplex encephalitis. Diagnosis could have been made sooner had the physician been familiar with the patient's baseline mental status or had cultural and language barriers not stood between the physician and the patient and his mother. Herpes simplex encephalitis is a rare, but specific, cause of delirium for which prompt diagnosis and treatment with intravenous acyclovir can prevent death or serious sequelae. (J Am Board Fam Pract 2001;14:46–50.)**

A patient with an altered mental status can be a diagnostic dilemma, especially if the patient's baseline mental status is unknown or if there are cultural or language barriers. Effective communication is essential in establishing rapport with new patients and critical for diagnosing nonspecific symptoms. Despite having learned to communicate in their nonnative language, immigrant patients can have difficulty conveying the more subtle aspects of their medical history. Providers might miss nuances (in speech, body language, or cultural understandings) that would be intuitively understood when interacting with patients from their own cultural background.

We describe the case of a 17-year-old Eastern European patient with herpes simplex virus (HSV) encephalitis to emphasize four specific teaching points.

1. One must be very vigilant to recognize early signs and symptoms of delirium because of its fluctuating course.
2. HSV encephalitis is a rare specific cause of delirium. Mortality is 70% if left untreated, but morbidity and mortality are greatly reduced by early diagnosis and treatment.
3. Cultural and language barriers can add to diagnostic uncertainty, warranting additional time and investigation for potentially serious "zebras."
4. Qualified medical interpreters should always be used if there is any hint that language or cultural barriers are hindering a thorough understanding of the patient's problem.

Case Report

A 17-year-old Eastern European boy came with his mother to our outpatient clinic with an urgent appointment. Neither he nor his mother had ever been to our office. They had emigrated to the United States 3 years earlier. Although the mother spoke limited English, the patient spoke with near fluency, obviating the need for an interpreter. They both stated he had been ill for 2 days. He claimed

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he had initially developed right-sided neck pain while playing computer games, and although the pain had resolved the next day, he continued intermittently to feel weak and dizzy and have a low-grade fever. On the day of the appointment, he had one episode of emesis and one diarrheal stool. While his mother was trying to communicate in limited English that he was not acting and speaking normally, the patient stated he was now feeling better. A limited medical history was obtained. The patient had never been hospitalized or had any surgeries. He took no medications and denied illicit drug or alcohol use. He was a star tennis player on his high school team.

When examined at the office, the patient was an athletic-appearing teenager who generally was alert, oriented, and lucid, but he would occasionally pause between sentences and close his eyes until aroused. His temperature was 99.9°F, and his blood pressure, respirations, and heart rate were normal. The only notable findings on examination were evidence of a generalized upper respiratory tract infection with fluid behind his tympanic membranes and swollen, inflamed tonsils with exudates. Exudative tonsillitis was diagnosed. A blood specimen was drawn for a Monospot test, and the patient was given a prescription for amoxicillin. Not knowing his baseline mental status, the examining physician believed that the patient's mother's concerns about his "not acting normally" could be due to his febrile upper respiratory tract infection.

The next day the patient was brought back by his uncle, who was bilingual. They were seen by the office triage nurse. The uncle said the patient was "talking out of his head," and had high fevers at home. The patient himself was sleeping in the waiting room and had a temperature of 102.5F. He was easily aroused and lucidly told the nurse his history, that he had a headache, and that he just wanted to sleep. The nurse gave him acetaminophen and instructed him to continue with his treatment plan (amoxicillin).

He returned again on the third day with his mother and was seen by a different physician. He continued to have a fluctuating level of alertness but was generally too lethargic to communicate or walk. His mother tearfully stated he had had nothing to eat or drink that day. When examined, he was a moderately ill teenager who was slumped in a wheelchair and unable to speak or walk without assistance. His temperature was 100.0°F, his neck was supple, and there were no localizing signs. He was transported by ambulance to the emergency department.

In the emergency department, he was again more alert. He spoke with some prompting but did not always answer coherently. His temperature was 101.0°F, his heart rate 84 beats per minute, respirations 22/min, and blood pressure 140/102 mm Hg. Rales were noted in both lung bases. A complete blood cell count showed a white cell count of $15.9\times10^3/\mu L$ with 79% polymorphonuclear neutrophils, 7% band cells, 3% lymphocytes, and 11% monocytes. The emergency department physician noted that the patient clearly had an altered mental status but did not appear to have meningitis. She noted he acted as although intoxicated, but her formal assessment was sepsis, and he was transferred to the intensive care unit (ICU) in fair condition. Alcohol and drug screening tests were ordered.

In the ICU, he was again observed to have an altered mental status, giving nonsensical answers to questions other than his name. His fever now exceeded 104.0°F. At one point it was unclear whether he was having shaking chills or a generalized seizure, and he was given intravenous diazepam and phenytoin. His drug and alcohol screening tests were negative. The chemistry profile showed a sodium level of 125 mEq/L. An unenhanced computed tomographic (CT) brain scan was normal. A lumbar puncture resulted in normal opening pressure and clear fluid return. He began intravenous antibiotics for empiric treatment of meningitis and intravenous acyclovir at 10 mg/kg every 8 hours for possible HSV encephalitis.

On the morning after admission, enhanced magnetic resonance imaging (MRI) of his brain was ordered. Findings showed parenchymal abnormalities in the left medial temporal lobe, left insular cortex, and the subcortical white matter, which did not enhance with gadolinium. There was a mild mass effect. The radiologist commented that this distribution is characteristic of herpes simplex encephalitis (Figure 1).

For the next 2 days, the patient's high fevers gradually resolved, but his mental status continued to wax and wane. A second MRI 3 days after admission showed progression in the findings in the left temporal lobe with worsening edema and now slight similar findings in the right side.

On the third day after admission, the laboratory reported that the patient's cerebrospinal fluid poly-

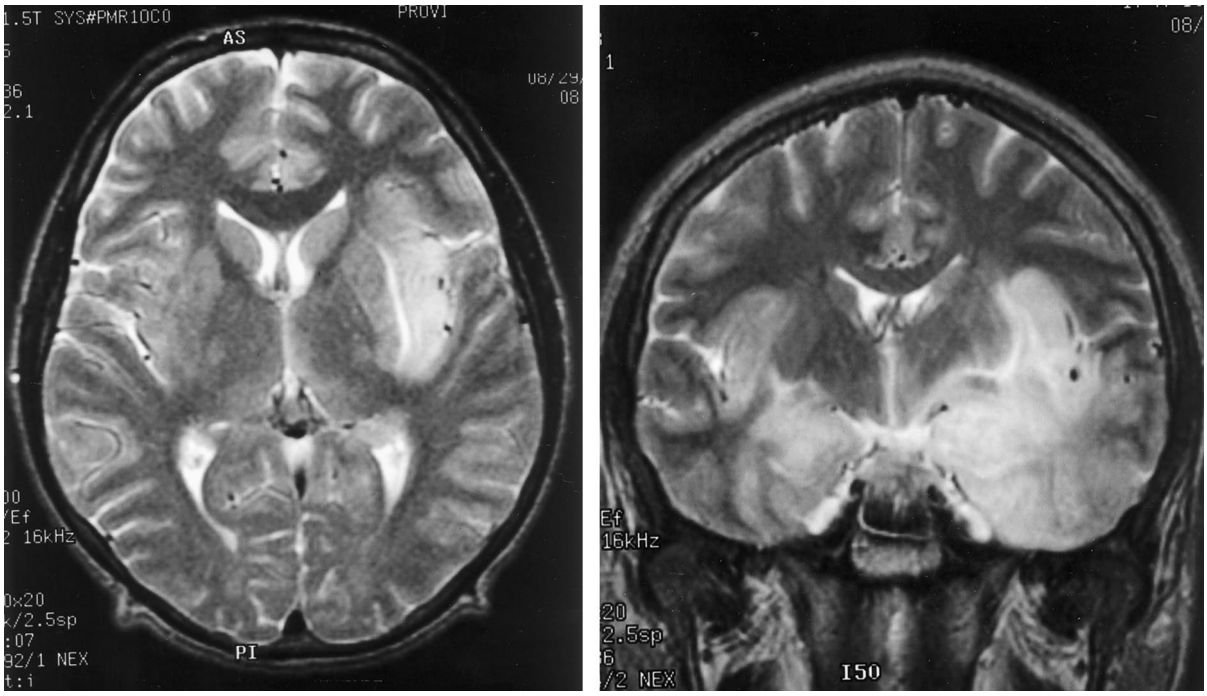

Figure 1. Magnetic resonance image of brain showing mild mass effect from abnormalities in the left medial temporal lobe, left insular cortex, and subcortical white matter that do not enhance with gadolinium. These findings are characteristic of early herpes simplex virus encephalitis.

merase chain reaction for HSV was positive. Empiric antibiotics were discontinued, and the acyclovir dosage was increased to 12 mg/kg every 8 hours. An electroencephalogram showed no seizure activity, but because of his high risk and the difficulty in clinically recognizing temporal lobe seizures, seizure prophylaxis with phenytoin was continued.

Six days after admission, with little improvement in his mental status, the patient had another MRI. The MRI changes now included enhancement of the lesions with gadolinium, small petechial hemorrhages, and worsening mass effect secondary to edema. High-dose intravenous steroids were begun.

During the next several days, the patient's mental status gradually improved. He continued to be very lethargic at times and consistently had a profound expressive aphasia in both English and his native language. Ten days after admission, he was transferred to the rehabilitation unit, where he continued to improve slowly. He completed the recommended 20-day course of intravenous acyclovir. At the end of that time, although his mental status was not back to baseline, he was sufficiently improved to be released from the hospital for outpatient therapy. He missed most of the first 3 months of his senior year of high school, but he was able to make up his work and graduate with his class. He returned to our office 10 months after his first visit for a college tennis preparticipation physical examination, feeling proud that he had been able to return to the tennis form he had achieved before his illness.

Discussion

Delirium

Delirium is a disturbance of consciousness or change in cognition that develops within a period of hours to days. Typically there is variability of symptoms during a 24-hour period, which necessitates obtaining a comprehensive history from a reliable patient or caregiver. The history, physical examination, and laboratory tests help initially to narrow the diagnosis into four categories: (1) delirium as a direct physiologic consequence of a general medical condition, (2) substance-induced delirium (caused by drug abuse, medication, or toxin exposure), (3) delirium resulting from multiple causes, or (4) delirium not otherwise specified (if no definite cause can be found).[1]

Changes in consciousness are manifested by difficulty focusing and sustaining attention. Questions must be repeated, and patients might perseverate

with an answer to a previous question. Often, patients are distracted by irrelevant stimuli.

The changes in cognition are most evident as recent memory impairment. Recent memory can be tested by asking the patient to remember several unrelated objects and to repeat them after a few minutes of distraction. Disorientation to time can be one of the first symptoms to appear in mild delirium. The patient might have difficulty naming objects (dysnomia) or writing (dysgraphia). Speech can be rambling, pressured, or incoherent, or the patient might unpredictably switch from subject to subject.

Delirious patients usually have a disturbed sleep-wake cycle, including daytime sleepiness or nighttime agitation. Their psychomotor activity can also be disturbed: they might be restless or hyperactive, they might be lethargic and sluggish bordering on stuporous, or they might swing from the one extreme to the other in the course of a day. The impairment in judgment can interfere with appropriate medical treatment.

The differential diagnosis of delirium should begin with the four general categories mentioned above. The causes of delirium as a consequence of general medical conditions include systemic infections, metabolic disorders (eg, hypoxia, hypercarbia, hypoglycemia), fluid or electrolyte imbalances, hepatic or renal disease, thiamine deficiency, postoperative states, hypertensive encephalopathy, postictal states, and sequelae of head trauma.[1]

Herpes Simplex Encephalitis

HSV type 1 (oral herpes) is the leading cause of sporadic encephalitis in North America with an incidence of 1 in 250,000 to 500,000 persons per year (2,000 cases per year in the United States)[2] and accounts for 10% to 20% of all encephalitic viral infections. There is a bimodal age distribution, with one third of all cases occurring in patients between 5 and 20 years old, and one half of cases in patients older than 50 years.[3] It should be remembered that herpes sepsis and encephalitis in the newborn are caused by HSV type 2 (genital herpes).

The pathogenesis of HSV encephalitis is variable. One third of cases result from a primary HSV 1 infection (usually in the young), whereas two thirds of all cases result from reactivation of a previously acquired oral infection (most older patients).[4] Young children with a primary infection and HSV encephalitis might initially complain of gingivostomatitis. Young adults can have pharyngitis or a mononucleosis-like syndrome.[3] Transmission of the virus is through respiratory contact and saliva.

Clinical symptoms include headache, lethargy, confusion, personality changes, behavioral changes, and focal neurologic (temporal lobe) symptoms. Physical examination frequently shows fever, lethargy, decreased level of consciousness (even coma), focal neurologic signs, seizures (in 40% to 60% of patients), and aphasia if the dominant temporal lobe is involved. Clinical signs in HSV encephalitis characteristically tend to fluctuate more than in other causes, and they can develop within several days.[5] Histologically, HSV 1 causes an acute inflammatory process in the brain with a predilection for edema and hemorrhage in the temporal lobes.

The patient's cerebrospinal fluid usually has a normal or slightly elevated protein level. Glucose levels are normal or slightly low, and there is generally an elevated white cell count with a lymphocytic predominance. Red blood cells are frequently found in the cerebrospinal fluid because of brain hemorrhage, often with an increase in pressure. The cerebrospinal fluid can be normal in 5% to 10% of patients at initial evaluation, however.[3] A CT scan can show hypodense areas and edema and a mass effect in the temporal and orbitofrontal lobes, but an MRI will show lesions earlier.

A firm diagnosis of HSV as the cause of encephalitis is made much easier today by finding DNA in the cerebrospinal fluid using polymerase chain reaction. Antibody titers to the virus in the serum and cerebrospinal fluid might not rise for 10 days into the illness, and thus are not useful for diagnosis or for guiding treatment. A finding of HSV antigen, DNA, or replication in brain tissue obtained by biopsy is very sensitive and can be helpful if polymerase chain reaction is not available or is negative despite a strong suspicion of the disease, or it can help detect other treatable causes of encephalitis. Even so, cerebrospinal fluid polymerase chain reaction has become the study of choice for confirming the diagnosis because it is less invasive and has an excellent sensitivity and specificity if performed at an experienced laboratory. Biopsy studies and a polymerase chain reaction will remain positive for several days even with appropriate treatment.

The most effective treatment is intravenous acyclovir. Mortality with treatment approaches less than 30% but is 70% or more if the infection is untreated.[6] Because mortality is directly related to

mental status at the time treatment is initiated, empiric treatment should be started as soon as HSV encephalitis is suspected. Permanent neurologic sequelae appear in approximately 60% of patients even after treatment and can vary from mild deficits to severe disability. Up to 10% of patients will relapse.[4] Long-term morbidity includes motor and sensory deficits, aphasia, dysnomia, and amnestic syndromes. Rehabilitation can be lengthy.

Language and Cultural Barriers

As a result of the recent influx of immigrants to this country from Asia, Africa, Eastern Europe, and South and Central America, health care providers often find themselves working with patients from diverse cultural backgrounds. Diagnosis of simple or common health problems will be possible with some incongruence in communication, but difficult and complex medical conditions (especially those with psychosocial dimensions) demand more precise communication.

Professional interpreters can help overcome some barriers. Legal precedents resulting from litigation and federal regulations (especially Title VI of the 1964 Civil Rights Act) are beginning to define the responsibility of health care providers in making appropriate interpretive services available.[7] Using the patient's friends or family members as interpreters is improper and can result in breach of confidentiality or reluctance on the part of the patient to reveal critical information. Lack of a trained interpreter can lead to improper diagnoses and treatment and can call into question the ability to obtain an informed consent.

Using an interpreter will not reduce all the cultural barriers. Real understanding in a cross-cultural setting requires negotiating nonlinguistic differences (such as gestures and body language), perceptions, and stereotypes. Health care providers need to understand that their own cultural values and biases influence the care they provide.[8]

In retrospect, language and cultural differences hindered the chance for an early diagnosis of this patient's HSV encephalitis. The initial confusion about his initial complaint could have been cleared up had his mother been given a chance to voice her concerns through a medical interpreter. It might also have helped to consider how her previous experiences of health care in a more authoritarian Eastern European system made it difficult for her to raise her concerns more forcefully. Had she been given a chance to describe her son's clear alteration from his normal mental status and had she been given a chance to communicate the waxing and waning nature of his problem that she had been observing at home, his physicians might have been able to begin a workup of delirium on his first day instead of the third. Perhaps his lengthy hospitalization and rehabilitation could have been shortened.

In conclusion, it is necessary to be vigilant when caring for a patient who has vague changes in mental status. The differential diagnosis of a developing delirium can be very broad, from the benign to the potentially fatal. HSV encephalitis is a rare but specific cause of delirium for which prompt diagnosis and treatment can prevent serious sequelae or death. If HSV encephalitis is suspected, treatment should be started before a definitive diagnosis is made (usually by cerebrospinal fluid polymerase chain reaction). The complexity of caring for patients from different cultural backgrounds (resulting from both linguistic and nonlinguistic differences) requires extra vigilance because of the additional level of uncertainty inherent in these encounters.

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