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Case Report

Varicella zoster encephalitis mimicking stroke

Abstract

Physicians need to consider a broad differential diagnosis when evaluating a patient presenting with a suspected stroke. The rates of overdiagnosis of stroke in studies of consecutive patients vary from 19% to 31%. The two most common stroke mimics are hypoglycemia and seizure, but several etiologies have been reported. We reported the case of a 41-year-old patient presenting to the emergency department with aphasia and right-side hemiparesis, initially suspected to have stroke and finally diagnosed of varicella-zoster encephalitis.

A 41-year-old, right-handed male patient was seen at home due to sudden language alteration and right-side weakness. The patient had been well until 1 hour earlier, when right-arm weakness, clumsiness, and slurred speech developed. His wife immediately called the Emergency services. When the emergency medical team arrived, the patient was conscious, had dysarthria and right-arm weakness, the code-stroke was activated, he was transported by ambulance to the emergency department (ED) of this hospital, arriving at 10:30 AM, 1 hour after symptoms began.

On examination, he appeared uncomfortable. The temperature was 36.4 °C, the blood pressure 145/95 mm Hg, and the pulse 93 beats per minute. The neck was supple. The patient exhibited poor comprehension, naming, and paraphasia. Transcortical sensory aphasia was diagnosed and confirmed by the consultant stroke neurologist. The pupils were equal and reactive to light, the facial expression was symmetrical, decreased muscle tone in the right arm, with strength 4 +/5; and normal muscle tone in the right leg, with strength 5/5. Strength on the left side was normal. Reflexes were brisker on the right side arm than on the left. No hemianopsia, anosognosia or neglect were present. He had hypertension and was allergic to penicillin; he had a smoking history of 35 pack-years. Medications included omeprazole, enalapril, and hydrochlorothiazide. Deficits were assessed by careful neurologic examination and the use of the National Institutes of Health Stroke Scale to quantify the severity of the neurologic deficit, scoring 4 points (no speech production 3 points, drift of the right arm 1 point). Computed tomography (CT) of the head showed no evidence of acute infarct, hemorrhage, or mass effect, chest radiograph normal. After the patient returned from imaging at 10 AM, the neurologist reexamined the patient, his speech was fluent with occasional circumlocution and semantic paraphasic errors, the remainder of the examination was normal, the emergency doctor and neurologist's first diagnostic consideration was acute ischemic stroke; however, according to the exclusion criteria mild neurological impairment [The National Institutes of Health Stroke Scale (NIHSS) <5] and rapidly improving neurological signs were considered and intravenous thrombolytic therapy was not initiated. The patient was admitted to the Hospital; a lumbar puncture was performed. Angio-magnetic resonance

imaging (MRI) showed asymmetry of venous sinuses (Fig). The results of cerebrospinal fluid (CSF) analysis on admission were: glucose 40 mg/dL, protein 258 mg/dL, colorless, clear, red-cell count 200/mm³, white-cell count 313 per mm³, differential count lymphocytes 99%, Gram stain; no bacteria, culture no growth, nucleic acid testing for herpes simplex virus (types 1 and 2) DNA negative. His hemogram showed a total leukocyte count of 11,400/μL (with differential of 31% polymorphonuclear leukocytes, 42% lymphocytes, 7% monocytes). His platelet count, bleeding and coagulation profile were within normal limits. The results of the human immunodeficiency virus (HIV) tests were negative by both enzyme-linked immunosorbent assay and rapid HIV test for HIV-1 and HIV-2 antibodies. He was empirically treated with intravenous acyclovir 500 mg every 8 hours and antibiotics (intravenous ceftriaxone 2 g every 12 hours) for the possible diagnosis of acute infective encephalitis or meningoenzephalitis most likely viral in origin, two days later varicella zoster virus (VZV) DNA was detected in the CSF by polymerase chain reaction (PCR).

There were no symptoms or findings suggesting pneumonia, skin involvement, or hepatitis. His serum VZV-specific IgM levels were not elevated, the IgG levels were found to be elevated. His history of VZV vaccination and VZV infection were unknown. Recent contact with VZV patients was unlikely. Screening tests for influenza A and B antigens were negative. Measurements of serum electrolytes, total protein, and globulin and tests of liver and renal function were normal. An electrocardiogram was normal. An ultrasonogram of the abdomen was normal. By the third day of



Fig. Angio-MRI showing asymmetry of venous sinuses.

hospitalization, the patient reported feeling markedly better. On the sixth day of hospitalization, the repeated lumbar puncture revealed undetected VZV DNA, the patient continued to improve and was discharged home on a course of oral acyclovir. He was finally diagnosed as a case of herpes zoster virus encephalitis.

The first challenge in the ED is a patient with minor, isolated and rapidly improving neurological signs. Minor and isolated symptoms are those that are not presently potentially disabling. Although most patients with potentially disabling symptoms will have NIHSS scores ≥ 4 , certain patients, such as those with gait disturbance, isolated aphasia, or isolated hemianopia, may have potentially disabling symptoms although their NIHSS score is just 2. Several studies have now reported that approximately one third of patients who are not treated with intravenous rtPA because of mild or rapidly improving stroke symptoms on hospital arrival have a poor final stroke outcome [1–5]. A persistent large-artery occlusion on imaging, despite minor symptoms or clinical improvement, may identify patients at increased risk of subsequent deterioration [6]; the practice of withholding intravenous fibrinolytic therapy because of mild or rapidly improving symptoms has been questioned.

Patients without a cerebrovascular etiology for their symptoms are considered to have a stroke mimic, and several small studies report that as many as one third of patients evaluated acutely by a stroke team, and up to 15% of patients treated with intravenous tissue plasminogen activator (t-PA), have such stroke mimics; potential etiologies include subdural hematoma, migraine, seizures, tumors, infections, multiple sclerosis, delirium, peripheral nerve injuries, and conversion disorders [7,8]. Patients presenting with symptoms similar to stroke are a true emergency. The emergency medicine physician must determine whether the acute neurologic deficits represent a transient event or a potential stroke. The first area of difficulty begins with the type of ED and the availability of resources that the emergency physician has at his/her disposal. Academic EDs that are designated as stroke centers have a stroke team that is activated by the emergency physician. A stroke neurologist is immediately available to assess the patient and a radiologist to interpret the CT. The stroke neurologist decides on further imaging (CT angiogram or MRI), thrombolysis, or interventional therapy. This case resembles a patient with minor neurological symptoms and the importance in the ED to differentiate between stroke and a mimic; recent studies suggest that factors associated with the greatest odds of having a stroke mimic were lack of a history of hypertension, atrial fibrillation, or hyperlipidemia; however, the diagnoses is still a challenge to emergency physicians.

Varicella zoster virus (VZV) is a virus of the Alphaherpesvirinae subfamily, responsible for human infections with various clinical presentations. Primary infection occurs most frequently during childhood and presents as varicella; it is followed by long-lasting viral latency in the spinal and cranial ganglia [9,10]. Although Varicella zoster virus (VZV) is a leading cause of acute viral encephalitis little is known about its clinical, biological and imaging features, in a recent study in France [11] a prospective cohort of 20 HIV-negative patients presenting with acute VZV encephalitis caused by primary infection or reactivation were studied. The median age of the 17 adults was 76 (19–86) years; the three other patients were children (0.5–5 years). Three patients were immunocompromised. Nine adult patients presented with a rash. Eighteen patients presented with fever and an acute encephalitic syndrome: diffuse brain dysfunction, focal neurological signs, seizures and cranial nerve palsies. Three patients presented with either ventricular or subdural hemorrhage, one with myelitis, and one with asymptomatic stenosis of the middle cerebral artery. The imaging was either normal or revealed non-specific abnormalities such as cortical atrophy but no evidence of stroke.

The isolation or detection of VZV from a CSF specimen is yet rare and difficult in cases of VZV infection of the central nervous system (CNS), owing to the poor yield of VZV in the CSF [9–16]. In addition,

virus presence closely depends on the timing of the CSF collection during the clinical course of CNS viral infection [10,14–16]. The choice of timing to collect CSF is very difficult because VZV infection in the CNS has various clinical courses: acute, subacute or chronic [10]. In CSF specimens previously collected at the acute phase within the first 7 to 10 days after the onset of rash, the rate of VZV DNA detection by conventional single PCR assay was reported to be 61% to 76% [14–16], and that of anti-VZV IgG antibody elevation by antibodies by enzyme immunoassay was 0% to 43% [14–16]. In contrast, at the subacute phase more than 1 week after onset, the rate for single PCR assay was 25% to 47% [14–16], but that of anti-VZV IgG antibody elevation was 83% to 100% [7–9]. Moreover, at the chronic phase more than 20 days after onset, the former was 0% and the latter was 100% [14–16]. Thus, the rate of a PCR-positive result for VZV DNA in the CSF tends to decline rapidly within 7 to 10 days after the onset of rash, whereas the rate of anti-VZV IgG antibody elevation tends to increase and then be maintained during the clinical course [14–16].

Empiric treatment for HSV-1 infection with acyclovir (10 mg/kg IV Q8h) should always be initiated as soon as possible if the patient has encephalitis without apparent explanation [17]. Early therapy is vital because it is associated with a significant decrease in mortality and morbidity. Acyclovir is given intravenously (10 mg/kg every 8 hours) for seven days in patients who are immunocompromised or in immunocompetent patients who have serious complications, such as varicella pneumonia or encephalitis.

Physicians in the ED see several neurologic diseases that can be confused with acute ischemic stroke (AIS). Time constraints and diagnostic technology limitations may challenge their ability to establish the correct diagnosis. With increasing usage of thrombolysis in the treatment of acute ischemic strokes within 4.5-hour window, it is becoming more important to recognize stroke mimics. Though the incidence of stroke mimics being thrombolysed is less than 3%, it is essential to diagnose them so as to avoid wrong thrombolytic treatment which carries potential complications of bleeding. Aseptic meningoencephalitis should be included in the differential diagnosis in patients presenting as stroke. The diagnosis of varicella zoster virus encephalitis should be considered in any case of central nervous system in all cases of lymphocytic aseptic, not only in the elderly or immunocompromised.

The absence of any rash as in the reported case should not be considered as evidence excluding the diagnosis of VZV encephalitis. Despite the low level of evidence, acyclovir treatment should be prescribed to these patients, because of its antiviral effectiveness against VZV.

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