CASE REPORT

The woman without a history

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SUMMARY

The differential diagnosis for altered mental status (AMS) is broad and aetiological pathologies can arise from nearly all organs and body systems. Further complicating the matter, the altered patient is poorly suited to provide a comprehensive and accurate historical account. Thus, the physician must rely on collateral information, laboratories and imaging, and their own clinical suspicion. We present the case of a 75-year-old woman, found prone in her home with AMS, who was unable to provide a history. As her hospital stay evolved, we were forced to consider the entire breadth of possible causes of AMS. Eventually, the patient was found to have cerebral venous thrombosis, the significant extent of which is rarely reported. During the course of caring for the patient, we were reminded of the importance of remaining unbiased and unanchored while attempting to identify the source of the patient's ailment.

BACKGROUND

Altered mental status (AMS) is one of the most common acute presentations to the emergency department.¹ AMS is a broad term encompassing both decreased level of arousal ('alertness') and change in content of consciousness. The differential diagnosis for AMS is expansive, encompassing benign as well as life-threatening causes including infection, fluid/electrolyte disturbances, medication toxicity, metabolic disorders and withdrawal from alcohol. Therefore, one must be thorough and systematic when diagnosing the cause of AMS. After the patient's airway, breathing and circulation have been stabilised, initial evaluation includes a full history (especially baseline cognitive status and medications), physical examination (especially neurological assessment), glucose, complete blood count, basic metabolic panel (including calcium, magnesium, phosphorus), liver function tests, kidney function studies, urinalysis and urine culture, urine toxicology screen, chest X-ray and ECG. We present a case of a rare cause of persistent, unexplained AMS. This case demonstrates the need to avoid diagnostic anchoring to the most common causes of this presentation.

CASE PRESENTATION

A 75-year-old Caucasian woman was found prone in her home around mid-day. She was witnessed to be in her usual state of health 5 h prior to presentation. Neighbours described her as having a normal mental status at baseline, caring for her own activities of daily living and caring for her pet dog. When found, she was conscious and moving her extremities spontaneously. However, according to emergency medical personnel, she was severely disoriented. It was noted

at the scene that two empty beer cans were lying on the floor beside the patient. She was unable to give an account of the events leading to her presentation. She was also unable to answer questions or provide history; therefore, medical, surgical, medication, allergy, family and social history were unknown.

On presentation, the patient's temperature was 100.5°F, heart rate was 113 bpm, blood pressure was 138/74 mm Hg, respiratory rate was 18 breaths/min and her blood oxygen saturation was 98% breathing room air. She was alert and oriented only to person, demonstrating significant agitation requiring chemical sedation. There were no focal neurological deficits and physical examination was otherwise within normal limits.

INVESTIGATIONS

Laboratory studies were notable for white cell count 17.2×10^9 cells/L, haemoglobin 189 g/L, creatine kinase 33.4 μ kat/L (2000 U/L), glucose 178 mg/dL, negative urine toxicology (including alcohol) and a urinalysis demonstrating large amounts of ketones, trace blood, two red blood cells (RBC) per high-power field and no bacteria or white blood cells. A lumbar puncture (which was traumatic) performed in the emergency department was significant for a xanthochromic supernatant, 15 680 RBC and 12 nucleated cells (97% neutrophils, 3% lymphocytes). Cerebrospinal fluid (CSF) samples were sent for herpes simplex PCR.

Chest X-ray was unremarkable and ECG demonstrated sinus tachycardia. Non-contrast head CT scan was read as being significant only for chronic microvascular disease. An initial CT angiogram was non-diagnostic due to patient motion, but was suggestive of superior sagittal sinus venous thrombosis. The patient was empirically started on broad-spectrum intravenous antibiotics and acyclovir, given the concern for bacterial or viral meningoencephalitis. Repeat CT venography demonstrated thrombus in the entirety of the superior sagittal sinus extending into the right transverse sinus, the right sigmoid sinus, and the right internal jugular vein (figure 1). MR venography/angiography of the brain was not obtained. Hypercoagulability work up, including pan-CT scanning for neoplasm, was notable only for the presence of lupus anticoagulant on dilute Russell's viper venom test and immunological detection of low-titre anti- β 2-glycoprotein-1 IgM antibodies.

DIFFERENTIAL DIAGNOSIS

Prior to diagnosis of cerebral venous thrombosis (CVT), consideration was given to the following conditions.

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Figure 1 Imaging studies. (A) Non-contrast axial CT image showing hyperdense torcula and right transverse sinus, suggestive of thrombosis; (B) sagittal reformatted intracranial CT angiogram showing enhancement of the deep vascular structures and non-opacified clot within the superior sagittal sinus and (C) intracranial CT venography showing triangular filling defect within the superior sagittal sinus ('empty delta sign').

Alcohol withdrawal

Given the patient's altered level of consciousness, persistent agitation, tachycardia and low-level fever, as well as the collateral history of empty beer cans at the scene, this was initially our leading diagnosis.

Medication overdose

As the history of the patient was unknown, we were unsure of her medical problems or the medications she may or may not have been taking.

Herpes encephalitis

This is a common cause of altered consciousness in elderly individuals.² Further, the patient exhibited fever and elevated white count on initial presentation, suggestive of infection. Confounding the matter, the lumbar puncture was traumatic and therefore the CSF RBC count was of questionable diagnostic utility. Our concern for this diagnosis is evidenced by the induction of acyclovir therapy while CSF herpes PCR results were pending.

Systemic infection

Given fever, tachycardia and high white cell count, consideration was also given to sepsis secondary to either urinary tract infection or pneumonia, as is common in elderly individuals. However, urinalysis and chest X-ray were not suggestive of this.

The list of conditions potentially causing altered consciousness is extensive and other possible aetiologies were entertained. The clinical presentation and initial investigative studies helped to rule out many of these diagnostic considerations and made others less likely. Venous sinus thrombosis is a relatively rare condition that was initially low on the differential. It was not until more likely explanations were ruled out and additional imaging was pursued that this diagnosis became the most likely.

TREATMENT

The patient was started on anticoagulation with enoxaparin as a bridge while warfarin treatment reached therapeutic levels. Owing to the extent of the thrombosis, she was not a candidate for endovascular clot removal.

OUTCOME AND FOLLOW-UP

Throughout her 3-week hospital stay, the patient exhibited waxing and waning mental status and did not return to her baseline cognitive state. She was discharged home with 24 h nursing services without any significant improvement in her mental status. She continues on chronic warfarin therapy and awaits repeat antiphospholipid panel testing.

DISCUSSION

In 1974, discussion of a clinical pathological conference entitled 'The Man Without a History', appeared in the *Journal of the American Medical Association*.³ In that case, a man with unknown medical history was found prone in his home, and was eventually diagnosed with systemic and cerebral thrombosis secondary to malignancy. Similarly, we have described the unique case of 'The Woman Without a History', who also suffered hypercoagulability and cerebral thrombosis, likely due to antiphospholipid syndrome.

CVT is rare, with a prevalence of about 5/1 million.⁴ This, coupled with the breadth of possible presenting symptoms, makes it a difficult diagnosis to make. It is most common in younger females, likely due to hormonal differences between sexes and the resulting thrombophilia. However, in general, unprovoked CVT should prompt investigation into causes of hypercoagulability, including prothrombotic conditions (protein C/S deficiency, antithrombin deficiency, factor V Leiden mutation, G20210A prothrombin gene mutation, antiphospholipid syndrome, nephrotic syndrome and hyperhomocysteinaemia), oral contraceptives, pregnancy, malignancy and infection.

Patients experiencing CVT may present in many ways, generally reduced to four distinct clinical syndromes: (1) isolated intracranial hypertension, (2) focal neurological deficit, (3) encephalopathy and (4) seizures.⁵ The clinical presentation usually depends on the location of the thrombosis. Headaches, though rarely occurring in isolation, are the most common symptoms of patients with CVT.⁶ The superior sagittal sinus and the transverse sinus are most commonly affected and generally present with less severe symptoms. Those patients with deep sinus thrombosis will more often present with altered level of consciousness and rapid deterioration. Diagnosis relies on neuroimaging (CT and/or MRI), instigated by high clinical suspicion.

Non-contrast head CT scan is the most frequently performed imaging study in patients with suspected CVT, though it has poor sensitivity with direct signs of venous thrombosis present in only 20% of patients.⁷ One direct sign on non-contrast head CT scan is hyperdensity in the area of a sinus vein or cortical veins, as demonstrated in this patient (figure 1A). However, CVT is more rapidly and reliably detected using contrast-enhanced imaging studies. In contrast-enhanced CT venography studies, the primary finding is non-opacification of the affected vessel (figure 1B). Otherwise, a triangular hypodense filling defect can be seen in the superior sagittal or transverse sinuses in images perpendicular to the affected vessels. This is called the 'empty delta sign' (figure 1C) and is seen in 25–75% of CVT cases.⁷ In suspected subacute or chronic CVT cases, or in cases in which prior imaging has failed to provide a definitive diagnosis, MRI may be employed. In general, MRI is more sensitive than CT, though this is rarely the initial study

recommended in patients with suspected CVT.⁸ Nonetheless, MR venography and enhanced MRI can show equivalent imaging findings to those seen on enhanced CT studies. Moreover, MRI of the brain may demonstrate focally precise venous or arterial occlusion that can provide an explanation for the AMS, for example, thalamic or temporal lobe infarct.

In the above patient, diagnostic consideration pivoted from alcoholism to CVT based on imaging findings. However, two points regarding this paradigm warrant discussion. First, chronic CVT is known to be an incidental finding in some elderly patients. Thus, the search for causes of AMS should not be prematurely ended in the presence of solely this finding. Second, alcoholism and CVT are neither mutually exclusive nor unrelated. Chronic alcohol intake causes reduced sodium and water absorption in the small intestine and resultant diarrhoea. Coupled with nausea, vomiting and poor *per oral* intake, dehydration and hyponatremia can result, which contributes to a hyperviscous state and predisposes to thrombosis. Therefore, diligence is required both in continuing to search for aetiological explanations of AMS and in attempting to confirm the presence or absence of alcoholism.

Treatment of CVT hinges on supportive care, anticoagulation and identification of inciting underlying pathology.

Learning points

- ▶ The patient with altered mental status can be a poor historian, so the clinician must maintain suspicion for even the rarest of causes.
- ▶ Cerebral venous thrombosis is an infrequent cause of altered mental status, but one that must not be overlooked.
- ▶ It is important to remain unbiased and unanchored in the face of questionable collateral information regarding the altered patient until sufficient diagnostic information is available to rule out other causes.

Identification of the aetiology will guide choice and duration of anticoagulation.⁸

In conclusion, it is important to remain unanchored during the initial clinical evaluation of a patient with AMS. Empty beer cans near the patient when she was found down, coupled with the clinical presentation, strongly suggested to the authors a diagnosis of alcohol withdrawal. However, a severe, potentially life-threatening condition was present, requiring specific work up and treatment approaches. To remain unbiased and critical is the primary clinical lesson of which the authors were reminded as a result of the encounter with this patient.

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