Clinical Reasoning: A 25-year-old man with headaches and collapse

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SECTION 1

A 25-year-old Caucasian man with a history of headaches presented to the emergency room for witnessed collapse. The emergency room physician who initially evaluated the patient reported that the physical examination had normal results.

The patient was currently incarcerated for violent assault and battery without any prior offenses. While walking, he had felt his legs become weaker before collapsing to the ground. Loss of consciousness occurred for approximately 1 minute. He denied any preceding symptoms such as chest pain, palpitations, or vision changes, and there was no head trauma. There was no incontinence, tongue biting, or witnessed abnormal movements. Within a few minutes, the patient became reoriented without confusion or lethargy afterward. He was able to stand and walk after the collapse.

The patient had a chronic history of headaches typically lasting a few hours, occurring once or twice per month, holocephalic in nature and responsive to simple analgesics. This time, however, the headache had persisted for several days. The headaches had never woken him up from sleep. In the 24 hours prior to presentation, he had been unable to eat or drink due to vomiting. Recently he also had 3 episodes of frank hemoptysis and in the last 2 months he had an unintentional weight loss of 30 lbs.

There was no history of hematochezia or hematuria. There was no history of smoking, IV drug use, or alcohol abuse. He denied HIV risk factors or history of travel. Family history was remarkable for pancreatic cancer in the paternal uncle and his father had a pacemaker (unknown reason).

Questions for consideration:

1. Given this information, what is the differential at this time?

2. What are the red flags in this history?

Syncope is characterized by a transient loss of consciousness and postural tone followed by spontaneous recovery and is usually caused by cerebral hypoxemia. It may result from cardiac or neurologic causes; however, the primary mechanism of syncope is typically a response to cerebral hypoperfusion.

Neurally induced syncope or vasovagal syncope may result from a cardioinhibitory response, a vasodepressor response, or a combination of the two.¹ A cardioinhibitory response results from an increase in parasympathetic tone, which may cause bradycardia. A vasodepressor response results from a decrease in sympathetic tone and leads to hypotension. Causes can include processes that increase intra-abdominal pressure, situational stressors, or dehydration. Underlying cardiac causes may include rhythm disturbances or structural issues and noncardiac causes like seizures and strokes may be a result of underlying intracranial mass or vessel disease. Additional etiologies include drugs, orthostasis, a pulmonary embolus, or it may be psychogenic in origin.

The patient's lack of relief with simple analgesia and the prolonged duration of the headaches were suggestive of a change in his headache pattern. The unintentional weight loss and hemoptysis were also concerning; in an older person, metastatic carcinoma would be a primary concern. However, given this history in a 25-year-old prisoner, an infectious etiology such as tuberculosis needed to be considered. Chronic alcohol use was also a possibility.

The pacemaker in the father may also suggest a familial cardiac abnormality, placing the patient at higher risk for a spontaneous arrhythmia and simple cardiogenic syncope.

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SECTION 2

On examination, the patient was alert and oriented to place, person, and time and in no acute distress. He was well-appearing and well-nourished. His blood pressure was 145/75 mm Hg, with a heart rate of 88 beats per minute. There was no orthostasis. Oxygen saturations were 96% on room air and the respiratory rate was 18 breaths per minute.

Mental state examination was unremarkable and he followed 3-step commands with ease. Extraocular eye movements were intact. Visual acuity and visual fields were unremarkable and the pupils reacted briskly. The optic discs were blurred. There was no facial asymmetry or sensory abnormalities and the tongue protruded midline. Speech was normal rate and rhythm; there was no dysphagia or dysphonia. Tone was normal and strength in the extremities was full. Reflexes were 2+ in the upper extremities, 4+ at the patellae, and 3+ at the ankles. There was patellar clonus bilaterally. Toes were mute. Finger to nose testing was normal. His legs were shackled.

His examination was negative for bruits, gallops, or rubs. Heart sounds were normal and the chest sounds clear to auscultation and resonant to percussion.

Question for consideration:

1. How does the examination help revise the differential?

In evaluating for an underlying etiology of syncope, it is necessary to take into consideration these additional signs and symptoms.

Given the relatively low saturations of 96% on room air in a 25-year-old patient, plus the history of weight loss and hemoptysis, infectious and neoplastic causes remained in the differential. No cardiac abnormalities were detected and there was no tachycardia to

suggest a pulmonary embolism. The quick resolution of the syncope and the well appearance of the patient and intact mentation suggest that meningoencephalitis or seizures were less likely.

Blurring of the optic discs can indicate swelling of the discs. Disc swelling commonly results from inflammation or increased pressure, though central serous retinopathy or drusen can mimic disc blurring.² Given the syncope and lower extremity hyperreflexia, more extensive nervous system involvement needed to be considered.

Reflexes are typically brisk in young adults; however, this pathologic degree of hyperreflexia and clonus implied more diffuse CNS involvement. Considering the patient's age, a demyelinating process such as neuromyelitis optica or multiple sclerosis had to be considered. However, the lack of pain on eye movement, photosensitivity, or loss of acuity made optic neuritis less likely. Increased intracranial pressure can result in hyperreflexia and papilledema.^{3,4}

The differential for raised intracranial pressure is very broad and includes the following:

- Space-occupying lesions (tumor, hematoma, granuloma, abscess)
- Hypoxic-ischemic injuries (resulting from hypertensive encephalopathy, liver failure, heart failure)
- Vascular insults (sinus thrombosis, infarction with edema, superior mediastinal and jugular vein obstruction)
- CSF interruption (pseudotumor cerebri, Arnold-Chiari, choroid plexus tumors, infection)
- Idiopathic/cryptogenic

Question for consideration:

1. What further workup at this time should be done?

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SECTION 3

Laboratory testing revealed a leukocytosis of 14.4 k/ μ L (70% neutrophils) with a normal hemoglobin and platelet count. Electrolytes were within normal ranges except a glucose level of 53 mg/dL. Coagulation was normal. Liver function tests were slightly elevated with alanine aminotransferase 53 (range 5–31), aspartate aminotransferase 43 (range 5–40), and alkaline phosphatase 126 (range 25–100). Urine toxicology was negative.

EKG showed normal sinus rhythm without tachycardia or S1Q3T3 abnormality.

Chest x-ray revealed numerous bilateral large masses measuring up to approximately 5 cm. There was no pneumothorax or pleural effusion and the cardiome-diastinal silhouette was unremarkable. There were no osseous or soft tissue abnormalities reported.

A noncontrast CT of the head was also obtained (figure).

Questions for consideration:

1. What is abnormal on the imaging?
2. What is the differential of this lesion?

The CT shows an obstructing mass in the center of the third ventricle with diffuse cerebral edema.

Based on the finding of pulmonary nodules, considerations included a granulomatous process such as tuberculosis or sarcoid, or a metastatic process. Mid-line tumors such as colloid cysts, neurocytomas, and embryonal tumors should be considered, though they are uncommon and tend to occur at a younger age. Pulmonary nodules make a primary brain tumor less likely. In young people, brain metastases may result from lung, breast, testicular cancer, teratoma, melanoma, or lymphoma. Lung cancer is unlikely from his presentation and his age. Breast cancer is more common in female patients. Melanoma would have

a primary lesion on the skin and lymphoma is more common in immunocompromised individuals.⁵

On further examination, the patient was found to have a testicular mass, and biopsy was consistent with choriocarcinoma.

After this finding, a lumbar puncture was obtained. CSF revealed 4 white blood cells, 0 red blood cells, and normal protein and glucose levels. Additional testing included herpes simplex virus PCR, West Nile virus PCR, and a paraneoplastic panel including anti Ma2 and Ma1 (MaTa), Yo, Ri, Hu, NMDA, and voltage-gated potassium channel antibodies—all negative. A routine EEG was normal. B12, rapid plasma reagin, thyroid-stimulating hormone, and thyroglobulin antibodies were also checked and were unremarkable.

DISCUSSION Testicular cancer is a source of metastases to the brain and choriocarcinomas is a subset that more predominantly metastasizes to the brain.⁶ Choriocarcinomas are rare and may originate from fetal trophoblasts or germ cells in the testes or ovaries. They account for about 1% of all testicular carcinomas. It is more common to see this subset of tumors in young men, with a peak incidence between 20 and 30 years of age. Among all testicular tumors, choriocarcinoma has the worst prognosis because of early hematogenous and lymphatic spread. There is a tendency for early involvement of the lungs. Spread from choriocarcinoma is generally more widespread and tends to involve the cerebellum (not seen in this patient). Cisplatin-based therapy is the treatment of choice.⁷ Poor prognostic factors include trophoblastic elements in the testicular tumor and high HCG levels. Despite improvements in chemotherapeutic therapy, the 5-year survival for these patients remains low at 48%.⁸

AUTHOR CONTRIBUTIONS

Concept and design: Dr. Westwood. Acquisition of data: Dr. Syed. Analysis and interpretation of data: Drs. Syed and Westwood. Drafting of the manuscript: Dr. Syed. Critical revision of the manuscript for important intellectual content: Dr. Westwood. Supervision: Dr. Westwood.

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Figure Axial section of noncontrast head CT obtained in the emergency room

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