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CLINICAL VIGNETTE

Thinking Beyond the Migraine

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A 28-year-old female presents to Primary Care with a new-onset of right sided headache for 2 days. The headache started rather suddenly and remains at a constant pressure 8-9/10 in severity. It was initially generalized, but soon localized around the right temporal area. The day prior to presentation, she had significant nausea and one episode of emesis which transiently improved her symptoms. Her symptoms also improved with Ibuprofen and she felt that it was possibly sinus-related as she has some congestion and seasonal allergies. Oxymetazoline spray also helped slightly. However, despite these measures the headache persisted without significant improvement. It worsened with straining coughing and sneezing, and awakened her from sleep on the second morning. She does not have a history of migraine and has not had previous headaches like this. She specifically denied photophobia, phonophobia, vision changes, eye pain, fevers, chills, unexpected weight loss, night sweats, numbness, tingling, dizziness, ataxia, tinnitus, hearing loss, new medications, or recent trauma. The patient's past medical history is significant only for obesity with a BMI 35. Her only chronic medication is ethinylestradiol/etonogestrel ring for contraception for the past 2.5 years. She has no history of surgery or drug allergies. Her family history includes hypothyroidism in her mother and diabetes in her father. COVID-19 vaccinations were up to date with 2-dose Pfizer series completed 3-4 months prior to presentation.

On exam, the patient's vitals were normal with BP 129/85, HR 80, Temp 97.2F, and spO2 99%. She was alert and oriented, with CN2-12 intact. Pupils were round and reactive to light. Tympanic membranes were normal as were nasal mucosa and palpation of frontal sinuses.

Cerebellar testing was normal, including: finger to nose, rhomberg, pronator drift, along with normal gait and heel to toe walking. Strength and sensation in extremities were normal.

Leading items on the differential included a process that could raise intracranial pressure such as pseudotumor cerebri or tumor. Common etiologies like a migraine or sinus infection, and less likely though serious conditions such as intracranial hemorrhage or temporal arteritis were also considered. Labs were drawn and the patient was sent non-contrast CT head given new onset of severe headache that worsens with straining. Lumbar puncture would be considered if CT was normal.

Lab results revealed a normal CBC, bHCG, CMP, ESR, homocysteine, and mildly elevated CRP 1.1 (normal <0.8 mg/dl), and significantly elevated hsCRP 11.3 (normal <1 mg/ml). The radiologist noted asymmetric high attenuation within the right transverse sinus extending into the torcular, the straight sinus and vein of Galen raising concern for sinus thrombosis. An immediate follow up CT brain venogram with contrast was recommended which confirmed a nonocclusive thrombus in the right transverse sinus extending into the torcular and lower straight sinus.

The patient was sent to the emergency department for admission to initiate treatment and monitoring. She was started on a heparin drip which transitioned to apixaban and she was admitted to ICU. Levetiracetam was also started for seizure prophylaxis. Hypercoagulable panel was unrevealing and the ethinylestradiol/etonogestrel ring was discontinued.

After 4 days, symptoms began improving and the patient was cleared for discharge. On follow up one week later, the patient's symptoms had resolved and she was back to baseline.

Discussion

This case highlights the importance of screening for danger signs in the evaluation of a headache. This patient's one-sided headache with nausea may have been easily misdiagnosed as a migraine. Having a firm grasp of red-flag symptoms can help guide potential life-saving therapy. "Red-flag" symptoms that should prompt further evaluation including a CT or MRI can be enumerated by mnemonic SNNOOP10 which includes¹: Systemic symptoms (such as fever), history of Neoplasm, Neurological deficit, abrupt Onset, Onset after 50 years old, Pattern change, Positional, Precipitated by sneezing, coughing, exercise, Papilledema, Progressive, Painful eye, Pregnancy, Post-traumatic, Pathology of immune system (ie HIV), and Painkiller overuse or new drug at onset of headache.

I recall "red flags" based on 5 etiologies: 1) infection (fevers/chills, night sweats, weight loss), 2) malignancy and/or increased ICP (positional changes, worse with straining/relieved with vomiting, papilledema, pattern change, pregnancy), 3) hemorrhage/stroke (trauma, sudden onset, progressive severity, neurological deficit) and 4) inflammatory or 5) ocular (onset after 50, vision changes, eye pain). This patient had high suspicion for increased ICP based on 3 red flags using the criteria: 1) positional, 2) precipitated by sneezing 3) and pro-

gresssive. While not a strict red flag, the one-sided nature should include a consideration of intracranial neoplasm, cervical arterial dissection, giant cell arteritis, and cerebral venous sinus thrombosis.²

Cerebral venous thrombosis is relatively rare, with an annual incidence of about <1.5 per 100,000³ and a median age of 39 years. Females are affected by a 3:1 ratio,⁴ possibly related to prothrombotic effects of estrogen associated with pregnancy and oral contraceptives. Pathogenesis involves a disruption of cerebral venous drainage and subsequent congestion, edema and increased intracranial pressure. In more than 85% of cases, identified risk factors include either genetic or acquired prothrombotic conditions. These include oral contraceptives, pregnancy, malignancy, infection, head injury, and mechanical precipitants.⁵ Several cases have been reported with COVID-19 infections, and cases have been reported following AstraZeneca and Janssen vaccine within 5-30 days after vaccination.⁶⁻⁸

Signs and symptoms of CVT include isolated intracranial hypertension syndrome (headache with or without vomiting, papilledema, and visual problems), focal syndrome (focal deficits, seizures, or both) and encephalopathy (multifocal signs, mental status changes, stupor, or coma).⁹ The headache can mimic that of migraine with aura which is why worsening with valsalva maneuver can be a particularly important history component, as is thorough evaluation for papilledema. Head CT has been normal in up to 30% of cases¹⁰ and CT or MRI with venography may be needed to make the diagnosis. LP may be performed if imaging is non-revealing with concern for pseudotumor cerebri or meningitis.

Initial treatment involves starting anticoagulation with heparin with transition to a DOAC or warfarin for 3-6 months in cases with an inciting event, and 6-12 months otherwise. Lifelong anticoagulation is reserved for recurrent cases. Seizure prophylaxis is indicated for those with seizures on presentation and with supratentorial pathology including edema, infarction, or hemorrhage. Universal prophylaxis for focal lesions may not be needed.^{5,11} The role for endovascular procedures is conflicting. Prognosis is generally good when treated early with 80% of cases making a full recovery. However, 5% of acute cases result in death, generally due to brain herniation.^{12,13}

This case highlights the importance of keeping a broad differential when evaluating headaches and having a firm grasp of potential red flag signs in order to catch a rare and potentially life threatening but easily treatable condition such as cerebral venous thrombosis.

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