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A Case of HHV-6 Viral Meningitis

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Introduction:

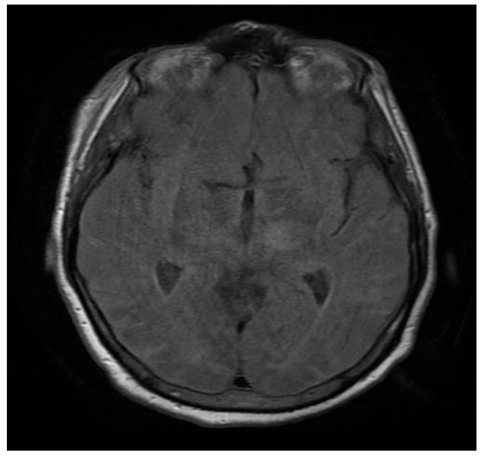
Meningitis is the inflammation of the meninges and associated with abnormal cell count in the cerebrospinal fluid (CSF). The lack of bacterial growth in cultures, most commonly referred to as aseptic meningitis, is frequently caused by viruses [2]. Viruses have become more common as the prevalence of bacterial meningitis has decreased secondary to vaccination use, with viral meningitis being the most common form among countries. Viral meningitis will present with fever, headache, photophobia, neck stiffness and nausea and vomiting. Younger children however may not show any signs of meningeal irritation . Viral meningitis is usually self limiting and with good prognosis however appropriate evaluation is critical.

Enteroviruses such as Coxsackie or Echovirus are the most common cause of viral meningitis across all age groups and parechoviruses are common among children . Herpesviruses leading to meningitis include herpes simplex virus (HSV) 1 and 2, varicella-zoster virus (VZV), cytomegalovirus, Epstein-Barr virus, and human herpesvirus 6. Additional causes include adenovirus, lymphocytic choriomeningitis virus (LCMV), influenza, parainfluenza, and mumps. Arboviruses that can cause viral meningitis include West Nile virus (WNV), Zika, chikungunya, dengue, LaCross, Saint Louis encephalitis, Powassan, and eastern equine encephalitis virus

Case Presentation:

The patient is a 70-year-old man with past medical history pleural effusion, pulmonary hypertension and aneurysm of thoracic aorta who is brought in by EMS today for evaluation of altered mental status. They report the patient has had altered mental status since this morning according to his family. He has also had shaking of his bilateral upper extremities. They say that yesterday he was in his usual state of health. They say that his baseline is AAO x3. Brought in by paramedics from home for reported change in mental status off baseline since last night and hypoxia. The patient was diagnosed with SIRS, nontraumatic rhabdomyolysis. Chest x-ray imaging revealed minimal peribronchial cuffing. Patient on re-evaluation was more alert and awake, no shaking. He was still disoriented however, re-oriented on history taking and able to communicate. His wife at bedside notes that the patient was not feeling well for the last 24 hours and had a fall out of bed while hitting his head. No focal deficits on examination. CT chest/abdomen/pelvis imaging revealed pulmonary arterial hypertension and a 4.3cm thoracic aortic aneurysm without rupture. No abdominal findings. CTH was without intracranial hemorrhage or mass effect. His ECG was sinus tachycardia. Additional family noted that the patient was tired and had a fever of 101 yesterday. Patient's wife tried to wake him up in the AM and noted that he was shaking with a temp of 103.She then called the ambulance and sent him to the hospital.

His examination revealed bilateral tremors, which was new. He was responsive to stimuli however fatigued. He arrived at the emergency department on a non-rebreather mask and titrated down to the nasal cannula. Labwork did not reveal leukocytosis. Creatinine kinase was >3000, creatinine was within normal limits. Labwork did not reveal lactic acidosis. Lactate normal. Tachycardia resolved with fluids. Broad spectrum antibiotics as part of sepsis protocol as the patient meets SIRS criteria without current source, swabs pending. After intravenous fluids and Ofirmev IV, the patient was able to communicate and be more alert. Computed tomography (CT) imaging of the head was negative, as was his CT chest/abdomen/pelvis imaging with IV contrast. He had an elevated troponin suspected secondary to Type II spill, no ECG changes. Wife stated that the patient;s sister was recently diagnosed with COVID-19. The patient had negative COVID/flu and respiratory PCR panel testing.



The patient's vital signs were as follows: heart rate 82 beats per minute, respiratory rate 22 breaths per minute, blood pressure 174/87 mmHg, temperature 99.3 degrees F and saturating 98% on room air. On evaluation the patient was alert and awake however disoriented and not participating in history. He was admitted with a diagnosis of altered mental status and concern for meningitis. His lumbar puncture was suggestive of pleocytosis, with elevated RBCs, protein and normal glucose. HHV-6 was detected in the cerebrospinal fluid. MRI imaging revealed abnormal signaling in bilateral thalami and the left temporal lobe. Per infectious disease recommendation, the results of CSF analysis and MRI with temporal lobe enhancement were suggestive of HSV meningitis. False negative results can occur in the setting of antiviral administration and HHV6 can also cause encephalitis however is less likely to cause clinically significant disease in an otherwise immunocompetent host. Lumbar puncture was repeated with persistence of dense encephalopathy and pleocytosis decreased however the patient was lymphocytic with HHV-6 detection. HHV-6 DNA via polymerase chain reaction (PCR) viral load was sent, and infectious disease recommended covering for both HSV and HHV-6. The patient was previously on foscarnet and continued ganciclovir which would cover both HSV and HHV-6 for a 21-day course. During the patient's hospital stay, the patient was treated for aspiration pneumonia and a swallow study was done per speech therapy. The patient completed his antiviral regimen and Keppra was added to his regimen. He was scheduled for discharge however a rapid response was called and the patient had removed his oxygen and ABG showed hypoxia. A CT angiogram of the chest was ordered to rule out pulmonary embolism however the patient collapsed and code blue was called with the patient expiring.

Discussion:

Viral meningitis most commonly affects young children and the incidence decreases with increasing age [1]. Among countries with high immunization rates, viral meningitis is more common than bacterial, with approximately 3 to 18% bacterial source among children. Since the immunization rates have increased for Haemophilus influenza type B, Streptococcus pneumoniae, and Neisseria meningitidis, they have significantly decreased the rates of cases of bacterial meningitis[5] Viral meningitis incidence ranges from 0.26 to 17 cases per 100000 people. In the US alone, there are up to 75000 cases of enteroviral meningitis annually[3] Viral meningitis is also most common among the summer and autumn months, and is present all year round among tropical and subtropical areas [4] Enteroviruses rank as the most common cause of viral meningitis in many places in the world, with up to 12 to 19 cases per 100000 population annually in some high-income countries[6]. Human immunodeficiency virus (HIV) meningitis can be present during seroconversion, occurring in 10 to 17% of symptomatic seroconversion illnesses, with a small number progressing to chronic meningitis[1,7] VZV can cause viral meningitis, more commonly with reactivation than in primary infection. Varicella meningitis can occur without cutaneous lesions[1] HSV 1 and 2 can cause viral meningitis. HSV-1 is more commonly associated with sporadic encephalitis, while HSV-2 can cause a benign recurrent viral meningitis; meningitis usually occurs in the absence of genital lesions or a history of prior genital herpes infection[4] HSV reaches the central nervous system via the cranial nerves[7].

Because of the lack of clinical findings to help distinguish between viral and bacterial meningitis and the risk of untreated bacterial meningitis, there has been much interest in identifying predictors of bacterial meningitis. Most viruses causing meningitis have no specific treatment other than supportive care. Fluid and electrolyte management and pain control are the mainstays of management of viral meningitis. Patients should undergo observation for neurological and neuroendocrine complications, including seizures, cerebral edema, and SIADH. Since there is difficulty in differentiating between viral and bacterial meningitis initially, empiric antibiotic coverage is indicated until the bacterial source can be ruled out [8]. Acyclovir is the antiviral of choice for HSV or VZV infections, though only shows benefit in encephalitis, rather than meningitis presentations.

Conclusions:

Human herpesvirus-6 (HHV-6) infection is a common infection in the pediatric population and is increasingly reported in immunosuppressed adult patients. It has been reported as the causative agent of disease in few case reports in immunocompetent adults. Other cases of HHV-6 meningitis reveal successful treatment with ganciclovir and no residual sequelae. Many cases of viral meningitis are idiopathic, but increased utilization of polymerase chain reaction testing has enabled physicians to better recognize rare causes of viral meningitis. This will likely continue to improve the rate of causative agent identification in seemingly idiopathic viral meningitis, including this case of human herpesvirus 6 (HHV-6) meningitis in an immunocompetent adult patient. By efficiently diagnosing HHV-6 meningitis, proper treatment protocols can be initiated earlier to reduce morbidity and mortality. Given the rarity of HHV-6 meningitis in immunocompetent adults, there are no established standard treatment guidelines; previous reported cases, as well as this case, suggest that either intravenous ganciclovir or intravenous foscarnet are the most reasonable first-line treatment options. Primary infection of HHV-6 or reactivation of latent infections of HHV-6 can infrequently lead to meningitis and there are very few cases of reported HHV-6, many of the cases with fatal results. Given the rarity of meningitis that is caused by HHV-6, it is appropriate to question how valid the test result is. A study of HHV-6 diagnostic assays for active infection found that PCR detection of the viral DNA was 92% sensitive in the identification of primary infection compared to viral isolation[18]. Furthermore, current guidelines for diagnosis of central nervous system involvement in HHV-6 infection call for positive viral identification in the cerebrospinal fluid and blood as well as IgM detection.

References:

Available upon request.