

CLINICAL VIGNETTE

A Case of Benign Recurrent Lymphocytic Meningitis Attributed to HSV-2

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A 48-year-old male presented to the emergency department with a day of severe headache, neck pain, and photophobia. He reported over 20 episodes of meningitis over the last couple decades. He denied fever and had taken two doses of Acyclovir 800 mg that he had remaining from a prior genital herpes outbreak. He denied any travel, sick contacts, or recent illnesses. He had no herpes episodes in over 6 months. On arrival, he was afebrile and hemodynamically stable. He was obese and appeared uncomfortable but was alert and oriented. Exam was notable for a positive Kernig's test. The remainder of his neurological exam was normal, and his skin exam showed no lesions. His initial labs including CBC, chemistry 7, and rapid HIV were normal. An LP was performed. Opening pressure was unable to be obtained due to body habitus. WBC 257, 95% lymphocytes, RBC 0. CSF glucose 50 mg/dL and protein 124 mg/dL. A chart review showed that he had 4 prior LPs performed dating back to 1994 all with the same parameters. All his prior CSF viral cultures were negative. CSF, HSV, DNA, and PCR, which had been checked 3 times, were always negative. Past autoimmune workup, fungal, and TB testing had been negative as well. He was started on acyclovir 10mg/kg IV and was admitted to a medical service for pain control. Within 24 hours, he reported improvement and was discharged with acyclovir PO. On this admission, HSV-2 CSF DNA by PCR returned at 461 copies/ml. His final diagnosis Recurrent HSV-2 meningitis.

Benign Recurrent Lymphocytic Meningitis (BRLM) is a rare form of unpredictably recurrent self-limited brief episodes of aseptic meningitis. The entity was first described by French neurologist Pierre Mollaret in 1944.¹ Hence the historical use of the term Mollaret's meningitis to describe the syndrome. Originally diagnostic criteria was established by Bruyn et al.² in 1962 (table 1.).

BRLM presents with at least 3-10 episodes of aseptic meningitis with symptom free interval of time in between. Time to recurrence is patient-dependent and can take several years.³ These episodes may present with fever, severe headache, photophobia, paresthesia, myalgia, nausea, vomiting, and meningismus. In addition, up to one-half can develop transient neurological abnormalities including seizures, hallucinations, altered mental status, and hard neurologic findings. These are self-limited, will last 2-5 days, and have spontaneous recovery.³⁻⁵ Given the acute onset of the initial presentation, it is difficult to distinguish from other forms of life threatening meningitis.⁵ Persistence of symptoms should elicit additional neurological evaluation. It is usually seen in young adults with a female predominance.⁵⁻⁸

The available data have now demonstrated that the majority of cases are caused by HSV-2 and less frequently HSV-1. BRLM is estimated to occur in up to 20-30% of cases after primary HSV meningitis.⁹⁻¹⁰ Population prevalence is estimated at 1-2.2/100,000.¹⁰⁻¹¹ In up to 60% of cases, there are no active skin lesions, and many patients are unaware of prior genital infections.^{4,12,13} Even though there is suspicion that other viruses may lead to recurrent lymphocytic meningitis, the data are scant.⁶ The disease may also be caused by autoimmune disorders, intracranial epidermoid cysts, and medications.^{4,10,14}

Diagnosis is confirmed by CSF analysis. CSF shows a predominant lymphocytic predominance. The classic Mollaret cells, which are relatively arbitrarily large endothelial cells, may be seen within the first 24 hours.^{3,5,13} CSF usually will have normal glucose level and elevated protein level. The gold standard is CSF PCR for HSV DNA with sensitivity of 95% and specificity 100%.^{5,7} PCR is most sensitive when the sample is taken between day 2-5 after onset of symptoms.¹⁰ HSV DNA is not always found in recurrent episodes despite prior HSV DNA positive episodes, and this is speculated to be related to lower viral loads and sample timing collection of subsequent episodes.¹⁰ CSF cultures are usually negative.^{3,15} Notably, RBLM begins with lymphocytic predominance and Mollaret's begins with a polymorphonuclear pleocytosis followed by lymphocytic predominance.^{3,15} Even though most cases of RBLM generally fit the accepted diagnostic criteria of Mollaret's the term Mollaret's meningitis should be used for recurrent episodes of aseptic meningitis of unknown etiology.^{3,7,13}

As in other HSV infections antivirals have been the mainstay of treatment.³ Suppressive antiviral therapy has been studied for genital herpes and has been found to be effective in diminishing recurrence.¹⁶ The utility of chronic suppressive therapy has not been confirmed in recurrent aseptic meningitis. In a recent prospective, randomized, double-blinded, placebo-controlled, multicenter trial in Sweden enrolling over 100 patients with primary or recurrent HSV-2 meningitis found no effect of antiviral suppression therapy in terms of preventing recurrent meningitis. However, suppressive therapy did decrease the number of genital herpes outbreaks. There was also a statistically insignificant increased frequency of meningitis after cessation of the antiviral speculated to be a rebound phenomenon.⁸ This led the authors to assert that their data do not support the use of antivirals suppression following HSV-2 meningitis. Yet, they could not rule out tailored suppressive therapy in patients with recurrence and hence "appropriate use of antivirals is justified."⁸ Many experts recommend the use of suppressive therapy.³ As to other adjuvant therapies there are a

few case reports showing that indomethacin administration has resulted in faster recovery in patients.¹⁷ Otherwise steroids, colchicine, and antihistamines have not been found to be helpful.³

Table 1.

Mollaret's meningitis Diagnostic Criteria
Recurrent episodes of severe headache, meningismus and fever
CSF pleocytosis with large endothelial cells, neutrophils and lymphocytes
Attacks separated by symptom-free periods of weeks to months
No etiological agent identified
Spontaneous remission of symptoms and signs

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