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Letter to the Editor

Mollaret meningitis

1. Introduction

Mollaret's meningitis is a rare complication of Herpes simplex virus, type-2 infection (HSV-2) [1]. The most common presentation is characterized by attacks of sudden onset aseptic (viral) meningitis followed by complete recovery and unpredictable recurrences [2]. In addition to symptoms typical of meningitis, patients may also have transient hallucinations, seizures, cranial nerve palsies, or altered level of consciousness. Acyclovir is an acrylic purine nucleoside analog that inhibits the herpesvirus DNA polymerase of herpes simplex virus types 1 and 2 (HSV-1, HSV-2). Prophylactic antiviral therapy is not universally effective in decreasing the incidence of recurrences [3].

2. Case report

A 44-year-old female from Pennsylvania with a history of viral meningitis 14 years prior presented with sudden onset of generalized headaches, posterior neck pain, photophobia and nausea. Physical examination revealed maximum temperature of 99.3°F, positive Brudzinski sign, negative Kernig sign, and no rash. Laboratory results showed mild neutrophilic, lymphopenic leukocytosis. Blood cultures were negative. Cranial Computed Tomography (CT) scan was unremarkable. Cerebral spinal fluid (CSF) analysis revealed lymphocytic pleocytosis with elevated protein at 231 mg/dL (ref. 15–45 mg/dL) and low glucose at 35 mg/dL (ref. 40–70 mg/dL). CSF Gram stain showed many leukocytes, few red blood cells and no microorganisms. Empirical antimicrobial therapy with vancomycin (15 mg/kg intravenous every 12-h), ceftriaxone (2 g intravenous every 12-h) and acyclovir (10 mg/kg intravenous every 8-h) was initiated.

On hospital day three, blood and CSF cultures remained negative for bacterial growth. Large granular plasma cells (e.g. Mollaret cells) were never detected. CSF molecular testing for Herpes Simplex Virus type 1 was negative with less than 100 copies/mL. Herpes Simplex Virus type 2 was reported at 8039 copies/mL. Clinical symptoms resolved, and she was discharged to complete a seven-day course of oral Valacyclovir 1 g every 8 h and fourteen-day course of oral Doxycycline 100 mg every 12 h due to suspected Lyme disease. Empirical treatment for Lyme disease was discontinued upon subsequent negative serology testing.

3. Discussion

French neurologist Pierre Mollaret in 1944 described three patients with recurrent benign endothelioleukocytic aseptic meningitis [1]. This syndrome has also been termed benign recurrent endothelial meningitis, benign recurrent endothelial-leukocytic meningitis, benign recurrent aseptic meningitis and recurrent benign lymphocytic meningitis (RBLM). Infection is mainly caused by Herpes simplex virus type 2 (HSV-2). Among 665 patients treated for Lymphocytic meningitis, Kallio-Laine and colleagues reported a prevalence of HSV-2 associated meningitis of 2.2/100,000 population [2]. RBLM is estimated to occur in 20–30% of cases following primary HSV-2 meningitis [1,3]. HSV-2 is a common sexually transmitted infection (STI) associated with oral and genital mucocutaneous lesions with an estimated seroprevalence of 10–25% [3]. The double-stranded deoxyribonucleic acid (DNA) virus is neurotropic and usually colonizes the sacral sensory ganglia during the latent period following primary infection. The majority of patients with HSV-2 infection has subclinical viral shedding and remain unaware of infection. Meningitis usually occurs without genital lesions or a prior genital herpes infection history. Among 21 patients suffering from RBLM, Kallio-Laine and researchers reported low serum immunoglobulin G subclass 1 (IgG1) levels were associated with an increased frequency of recurrent meningitis episodes [4]. Authors also reported a trend toward lower serum immunoglobulin G subclass 3 (IgG3) [4]. Immunoglobulin (Ig) G subclasses 1 (IgG1) and 3 (IgG3) mediate antibody-dependent cellular cytotoxicity known to be important for clearance of bacterial and viral infections [4]. Deficiencies of humoral immunity increase susceptibility to infections as well as modulate disease progression [4]. While our patient denied formal STI testing, her prior history of “viral meningitis” is likely HSV-2 associated. This patient was never tested for IgG1 subclass levels. While guidelines from the Infectious Disease Society of America (IDSA) regarding the management of HSV encephalitis recommend initiation of intravenous acyclovir at 10 mg/kg every 8 h, there are no current guidelines or controlled clinical trials to guide the optimal treatment of HSV meningitis among immunocompetent patients. Noska and colleagues evaluated the benefit of antiviral therapy in a retrospective observational study among forty-two immunocompromised patient episodes of HSV meningitis and reported fewer neurologic sequelae with a 7–10 day course of therapy [5]. A prospective, randomized, double-blind, placebo- controlled multicenter trial among 101 patients with HSV-2 meningitis demonstrated no benefit in preventing recurrences with suppressive therapy using twice daily valacyclovir [3]. Our patient was provided with no subsequent viral suppression therapy.

4. Conclusion

Our case report and the other published cases [2–5] suggest that the appearance of recurrent benign lymphocytic meningitis (RBLM) is most likely due to herpes simplex virus type 2 (HSV-2) infections. The underlying process could be due to low serum immunoglobulin G subclass 1 (IgG1) levels [4]. Therefore, recognition of RBLM should lead not only to suspect HSV-2 but also to additional investigations assessing the presence of low serum immunoglobulin levels.

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Conflicts of interest

We declare no competing or conflicts of interests.

Authorship

WW, KP and SB took care of the patient and drafted the report.

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