

Letter to the Editor

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Usefulness of FilmArray Meningitis/Encephalitis panel in the management of an uncommon case of Herpes Simplex Virus type 2 meningitis

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Sir,

Meningitis and encephalitis are serious diseases with high morbi-mortality, especially in bacterial meningitis. Rapid identification of causative pathogens and prompt instauration of an appropriate antimicrobial therapy are crucial to reduce the morbi-mortality, length hospital stay and healthcare costs associated with these syndromes [1, 2]. Differential diagnostic between bacterial and aseptic meningitis is difficult; the former is a medical emergency that requires prompt recognition and treatment, while the latter is a relatively common and often-benign infection mainly caused by viruses [3, 4]. Consequently, cerebrospinal fluid (CSF) indices and microbiological studies are required to identify the etiologic agent [1, 2]. The classic diagnostic is based on a CSF Gram stain with culture and specific viruses PCR, which can delay the diagnostic [2]. Recently, U.S.A Food and Drug Administration (FDA) has approved the FilmArray Meningitis/Encephalitis (ME) panel (bioMérieux, Marcy l'Etoile, France) to detect central nervous system (CNS) infections. The FilmArray ME panel is a multiplex PCR that can identify the most frequent causative agents of CNS infections in an one-step assay, which decreases the diagnostic time [1, 2].

Herein, an uncommon case of aseptic meningitis due to herpes simplex virus type 2 (HSV-2) is presented as well as the usefulness of the FilmArray ME panel in prompt diagnostic, the optimization of antimicrobial therapy and the implementation of infection prevention measures.

A 25-year old man was admitted in our department with a 2-day history of general discomfort, fever, photophobia, nausea and acute headache. One week before admission, he was treated with oral amoxicillin/clavulanic acid for five days, up until 72 hours before hospital admission.

The admission physical exam showed increased body temperature (37.6°C), tachycardia and mild neck stiffness. CSF drawn on admission contained 852 cells/μL (100% lymphocytes), elevated protein (143 mg/dL), normal adenosine deaminase level (5.1 U/L) and normal glucose level (55 mg/dL in CSF and 120 mg/dL in serum). The Gram's stain was negative. Intravenous antimicrobial therapy with acyclovir and ceftriaxone, 750 mg/8h and 2g/12h respectively, were immediately administered and the patient was placed under contact isolation.

The CSF analysis was conducted in the microbiology laboratory as follows: Firstly, CSF was analysed for enteroviruses (EV) detection by targeted testing platform Xpert EV PCR (Cepheid, Sunnyvale, CA, USA), yielding negative results. At this point, a CSF aliquot was sent to a reference center (Hospital Universitario Donostia) in which FilmArray ME assay was performed. A few hours after the patient's admission, the FilmArray ME assay showed a positive result to HSV-2 being negative to bacterial targets. The patient's measures of contact isolation and ceftriaxone administration were disrupted after learning these results. Retrospectively, the patient admitted unprotected oral sex with his couple, but he did not remember any initial cutaneous or mucosal lesion. Screening for sexually transmitted infections and urogenital HSV detection of the patient was accomplished (table 1). The patient was discharged without symptoms after 14 days of intravenous acyclovir therapy.

EV is the most frequent agent of viral meningitis, followed by varicella zoster virus and HSV-2 [5]. Nonetheless, the prevalence of HSV-2 meningitis in Spain, is very low (1.2%), with few cases reported in the literature [5–7]. Infection with HSV-2 is mucocutaneous and is acquired vertically as a neonate or as an adult principally through sexual activity [8]. Moreover, HSV-2 is a recognized cause of CNS infection, mainly meningitis and it is also related to benign recurrent meningitis [8]. CNS infection due to HSV-2, usually correspond to the reactivation of a latent virus in sensory ganglia, mostly in young females [8, 9]. As shown in previous reports, only 30% of the

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Table 1	Screening of sexually transmitted infections.		
Serologic findings	HBV, HCV and HIV	Negative	
	Syphilis	Negative	
	HSV-2 IgG	Positive	
	HSV-2 IgM	Negative	
	HSV-1 IgG and IgM	Negative	
PCR of HSV 1 and 2 in oral and urethral swabs	Negative		

HSV: Herpes simplex virus; HBV: Hepatitis B virus; Hepatitis C virus; HIV: Human immunodeficiency virus.

patients with HSV-2 meningitis had cutaneous or mucosal lesion at the moment of CNS infection [4, 9]. Although standardized management for HSV-2 meningitis does not exist and it is often-benign infection, long-term neurological sequelae had been reported in some cases, so prompt diagnostic and antiviral treatments are recommended [3].

The recent development of the FilmArray ME assay could help the etiologic diagnostic of meningitis, but unfortunately the high cost of this assay only allows its implementation in reference hospitals. A rational use of this expensive assay could optimize the management of selected patients with CNS infections. Recently Hanson et al., suggested that immunocompromised patients and those who had received antimicrobials before the diagnostic lumbar puncture could be potential beneficiaries of this technology [2]. Although this assay has some advantages with respect to classical techniques for viruses CNS infections detection, like in house PCR or cultures, positive results must be interpreted along with entire clinical picture of the patient (symptoms, laboratory findings, cranial imaging...) because other host-virus state, like latency or asymptomatic viral reactivation, can also be detected [10].

Herein, we present an algorithm to the management of aseptic meningitis in a patient with predominance of lymphocytes in CSF and also had antimicrobial therapy before the admission. The implementation of new platforms, such as Xpert EV and FilmArray ME, under the aforementioned algorithm allows, in a relative short time, the identification of causative pathogens of CNS infections to optimize the therapy, avoiding unnecessary antimicrobial use and removing the necessity of contact isolation. The rational use of this new technology can improve the management of CNS infections, and when this assay is developed both under diagnostic algorithms and in selected patients, the FilmArray ME could be cost/effective, although further studies are necessary to assess this fact.

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None to declare

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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