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Case Report

Unusual Coinfection of Central Nervous System

Arantxa Berzosa Sánchez*, Marta Illán Ramos, Esther Culebras, José Tomás Ramos Amador

Department of Pediatrics, Clínico San Carlos Hospital, Madrid, Spain

***Corresponding Author:** Arantxa Berzosa Sánchez, Department of Pediatrics, Clínico San Carlos Hospital, Madrid, Spain, E-mail: arantxa.berzosa@salud.madrid.org

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Abstract

Central nervous system infections may encompass a wide spectrum of manifestations from meningitis, if only meningeal inflammation is presented, to encephalitis, if the parenchyma is involved, although frequently both are affected leading to meningoencephalitis. Mainly caused by viruses, bacterial origin should always be ruled out because of its worse prognostic. An adolescent of 13-years-old is presented, who complained of fever, psychomotor agitation and altered level of consciousness of sudden onset. Once the diagnosis of meningoencephalitis was suspected samples from blood and cerebrospinal-fluid (CSF) were collected, and antibiotics were started. After 24 hours Neisseria meningitidis was isolated in blood culture and Human Herpesvirus 6 was detected by PCR in CSF, receiving treatment against both pathogens (cefotaxime and ganciclovir) with a prompt recovery. Even when bacterial and virus coinfection is not a common finding in CNS infections, it may occur, with high impact on clinical evolution of the patient. In order to stablish an accurate microbiological diagnosis, appropriate samples should be taken. It is also important to remark that treatment should be adjusted accordingly to microbiological results.

Keywords: Meningococcal Y meningitis; Human herpesvirus 6; Encephalitis

1. Introduction

Infection of the central nervous system (CNS) is a life-threatening condition. CNS infections consist in a group of infections that involves meninges (meningitis) or cerebral parenchyma (encephalitis) or both of them (meningoencephalitis). Depending on the CNS area

affected, clinical presentation would be different: encephalitis should be suspected if there are symptoms or signs of neurologic dysfunction (decreased level of consciousness, seizures, focal deficits, papilledema, behavioral changes); while in meningitis fever predominates as well as stiff neck, vomiting, severe headache or weakness. Viruses are responsible for the vast majority of these infections. The most common pathogens are enteroviruses, followed by herpesviruses (HSV, VZV, CMV, EBV and HHV-6) and arboviruses [1, 2]. Bacteria may also be involved in these infections and paediatricians must always rule out bacterial origin and start treatment promptly because their potential severity [3].

2. Case Presentation

We present a 13-year-old adolescent born in Spain. Past medical history was unremarkable and vaccination updated according to age and Spanish immunization program that includes free conjugate meningoccus C vaccine at infancy. No meningoccus B nor tetravalent meningococcus vaccines (A,C,W,Y) were given. He was a frequent traveller to Morocco (last visit 6 months ago). He consulted due to an episode of psychomotor agitation and altered level of consciousness of sudden onset, after a 4-day of a catarrhal episode with vomiting and fever. In the emergency room he was febrile (38.6º), tachycardic (140 bpm) and with abnormal neurological examination: Glasgow 10/15 (lethargy, poor ocular opening and response to only to painful stimulus) and meningeal signs positive. Some scattered petechial-ecchymotic lesions were observed in the right hemithorax. Lab test and blood culture were performed (14700/uL leukocytes: 93.9% neutrophils; Protein-c-reactive 25.6mg/dL, Procalcitonin 10.95 ng/dL), and cefotaxime and vancomycin were started. Patient was admitted into the intensive care unit (ICU).

CT scan was performed to rule out intracranial hypertension. Afterwards lumbar puncture was performed disclosing cloudy CSF, hyperproteinorrachia 374mg/dL, hypoglycorrhachia 61mg/dL (120mg/dL in blood sample) and pleocytosis 1015/l (88% PMN). Gram stain was negative. Once infectious meningoencephalitis was suspected, dexamethasone, acyclovir and ampicillin were added to the initial treatment. Medical study was completed with rapid influenza test and PCR for respiratory viruses (all were negative) and EEG (no epileptiform activity).

After 24 hours, the microbiology report revealed isolation of *Neisseria meningitidis* in blood culture. Cefotaxime and acyclovir were maintained but others antibiotics were stopped. 24 hours later, the detection of HHV-6 in CSF was also reported. Our patient still referred severe headache and presented neurological symptoms so acyclovir was modified to ganciclovir iv. Treatment was completed with cefotaxime 10 days and ganciclovir 8 days iv. Progressive improvement of the neurological involvement was observed. Serogroup Y of *meningococcus* was identified before the patient discharge. Our final diagnosis was meningococcal Y sepsis and meningitis associated with HHV-6 encephalitis. Followed up with fully recovery and without complications.

3. Discussion

CNS infections require immediate attention from physicians. The extent of the infection ranges from diffuse involvement of the meninges, parenchyma or the spinal cord to localized lesions. According to the symptoms present and medical history, physicians should guide their investigations [4]. In the approach to a patient with CNS infection, an attempt should be made to establish an etiological diagnosis of the infection. To identify a specific agent may be important not only for treatment, but also for prognosis, potential prophylaxis,

counselling of patients and family members and for public health interventions. Some clinical and epidemiological clues may be helpful in considering specific etiology as season of the year, prevalence of disease in the area, travel history, animal contact or immune status of the patient [5]. In our patient the history of frequent traveller was an important key point and finally *Neisseria meningitidis* Y was isolated (unusual serogroup in adolescents in Spain).

To achieve the etiological diagnosis, cultures and molecular biology test (i.e., antigen detection or nucleic acid amplification tests, such as PCR) in blood and CSF samples are needed. CSF cultures are generally of limited value in the assessment of the viral causes but are essential in the diagnosis of bacterial infections. The availability of nucleic acid amplification testing (PCR) in CSF samples has greatly increased the possibility of diagnose viral infections of the CNS. In our case, there were two keys for the diagnosis: blood culture (growth of *Neisseria meningitidis* Y) and PCR in CSF (detection of HHV-6).

Confirmation of HHV-6 as a causative pathogen is complicated by the persistence of HHV-6 DNA after primary infection and the possibility of integration of HHV-6 DNA into chromosomes (presented approximately in 1% of the population).Thus, its detection in CSF does not implicate definitive active infection, and quantitative PCR is recommended to support the diagnosis [6]. In our patient HHV-6 was detected by qualitative PCR (viral load measure was not available), but because he suffered severe headache and symptoms of encephalitis after 48 hours of antibiotics and also because HHV-6 PCR was “highly positive”, it was interpreted as active infection by HHV-6, and as a result antiviral treatment with ganciclovir was prescribed [7].

In patients with suspected severe infection, the initiation of antibiotic treatment should not be delayed, as well as the obtention of appropriate microbiological samples that allow the identification of the potential infectious agents involved. Although it has been seldom reported viral and bacterial coinfections in CNS infections may coexist, modifying clinical evolution. A high index of suspicion is important in order to provide appropriate both combined antiviral and antibiotic treatment, which should not be adjusted until the etiology of the infection is confirmed.

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