Journal of Clinical Virology 80 (2016) 20–23

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Case report

Focal epilepsy as a long term sequela of Parvovirus B19 encephalitis

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ARTICLE INFO

Article history:
Received 1 February 2016
Received in revised form 8 April 2016
Accepted 11 April 2016

Keywords:
Parvovirus B19
Encephalitis
Immunocompetent host
Polyclonal intravenous immunoglobulins

ABSTRACT

Human Parvovirus B19 (PVB19), the etiological agent of the fifth disease, is associated with a large spectrum of pathologies, among which is encephalitis. Since it has been detected from the central nervous system in children or in immunocompromised patients, its causative role in serious neurological manifestations is still unclear. Here we report the case of an 18-year-old healthy boy who developed encephalitis complicated by prolonged status epilepticus. The detection of PVB19 DNA in his serum and, subsequently, in his cerebrospinal fluid supports the hypothesis that this virus could potentially play a role in the pathogenesis of neurological complications. In addition, the detection of viral DNA and the presence of specific IgM and IgG antibodies in serum, together with clinical findings such as skin rash, support the presence of a disseminated viral infection. In the presence of neurological disorders, especially when there are no specific signs, but seizures and rash are present, it is important to search for PVB19 both in immunocompromised and immunocompetent patients. Moreover, the introduction of the PVB19 DNA test into diagnostic protocols of neuropathies, especially those undiagnosed, could clarify the etiological agent that otherwise could remain unrecognized.

1. Why this case is important

Encephalitis is a serious disease with high morbidity and mortality, and patient management can be difficult. The clinical presentations as well as the causative agents are heterogeneous; moreover, specific treatments for many etiologies are lacking. Parvovirus B19 (PVB19) is rarely considered in the diagnostic protocols usually adopted in the management of patients suffering from neurological diseases. The pathogenic role of this virus in such pathologies is unclear since the virus infects only cells presenting the P-antigen that is present in cell lines such as proerythroblasts, endothelial and microglial cells [1,2]. PVB19 is associated with a wide spectrum of diseases and the virus has a special tropism for erythroid progenitor cells causing hematological disorders such as transient aplastic crisis and pure red cell aplasia in immunocompromised subject [3]. Cardiac and neurological diseases have recently been postulated to have a link to this virus [4]. Moreover, PVB19 is being recognized as potentially playing a role in the pathogenesis of central nervous system disorders [5]. The purpose of this case report is to summarize PVB19 potential association with neurological manifestations, specifically parvovirus-associated encephalitis documented by molecular techniques. Herein we present the case of an 18-year-old healthy boy with status epilepticus possibly due to parvovirus B19 encephalitis who was successfully treated with IgM and IgA enriched polyclonal intravenous immunoglobulins. Nevertheless, despite adequate treatment, he suffered from focal epilepsy for a long period.

2. Case report

2.1. Case description

An 18-year-old healthy male presented a subacute frontal headache and shaking chills with high-grade fever (40 °C) resistant to paracetamol (day 1). Seven days before the onset of these symptoms he had had an erythematous rash involving all four limbs. Moreover, other symptoms, including tiredness with diffi-

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http://dx.doi.org/10.1016/j.jcv.2016.04.007
1386-6532/

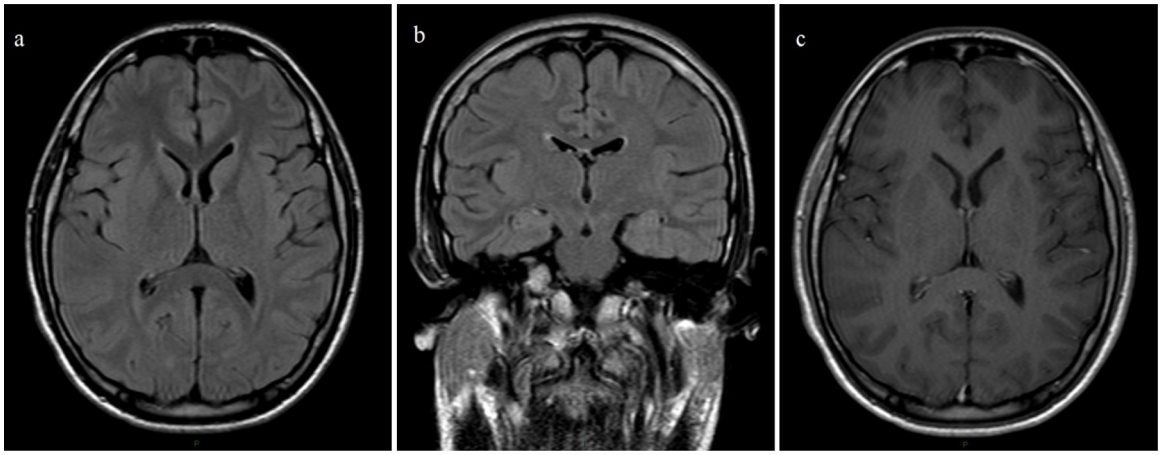

Fig. 1. Brain MRI of the patient during the acute phase of the encephalitis (day 6 of fever onset). FLAIR axial and coronal sequences (a and b) and contrast T1 weighted sequence (c) showing no abnormalities.

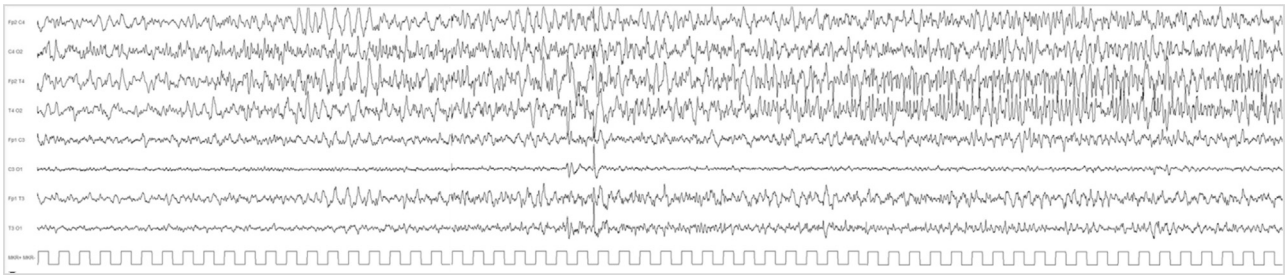

Fig. 2. EEG recorded during the acute phase of the encephalitis (day 9 of fever onset). Recording of a paroxysmal recruiting activity over the right fronto-temporal regions correlated to the clinical manifestation of the patient characterized by version of the head to the left and generalized stiffness of the body.

culty to carry out everyday activities, sleepiness and irritability, arose in the same period. For this symptomatology the patient went to the emergency department where routine blood analyses showed the presence of thrombocytopenia and leukopenia. He was then discharged, however, after five days he returned to the emergency department for the appearance of recurrent generalized tonic clonic seizures with body stiffening, drooling and confusion; the generalized seizures were preceded by auditory sensations, version of the head to the right and hyperextension of the right arm. Brain computed tomography (CT) scan and brain magnetic resonance imaging (MRI) (Fig. 1a, b and c) were normal. Twenty-four hours later, the patient was admitted to the Department of Emergency Medicine, where he was treated with levetiracetam (initial dose of 250 mg/day). Nine days after the onset of the fever (day 9), he was seen by a neurologist, CSF was collected, and an EEG was recorded. The EEG showed diffuse and persistent slow delta activity, prevalent over the right fronto-temporal region and the presence of subcontinuous recruiting sharp theta activity over the right fronto-temporal regions, consistent with a diagnosis of focal status epilepticus (Fig. 2). The lumbar puncture showed the presence of 8.2 leucocytes/mm^3 and 5.8 red blood cells/mm^3, protein concentration of 26 mg/dl (range 20–45 mg/dl), and glucose of 59 mg/dl. Fungal and bacterial CFS cultures were negative. Therefore he was transferred, one day later, to the neurology unit where empirical treatment with ceftriaxone and acyclovir was started and antiepileptic treatment with levetiracetam, phenobarbital and clonazepam were implemented. Despite two days of treatment, persistent seizure activity characterized by eye blinking and generalized tonic-clonic seizures were observed. Because of the worsening of the clinical and neurological conditions, on day 13, the patient was transferred to the intensive care unit (ICU) where, due to prolonged status epilepticus, sedation, intubation, and mechanical ventilation was necessary. On the same day a second lumbar puncture was carried out. Virological investigations, PVB19 results and data from hematological tests are shown respectively in Tables 1–3 .

Table 1
Virological investigations performed on the patient on day 9.

Test performed	Results	Assay
CSF		
HSV1 DNA	Negative	Realtime QPCR
HSV2 DNA	Negative	Realtime QPCR
VZV DNA	Negative	Realtime QPCR
EBV DNA	Negative	Realtime QPCR
CMV DNA	Negative	**Realtime QPCR**
HHV6 DNA	Negative	Realtime QPCR
HHV8 DNA	Negative	Realtime QPCR
Enterovirus RNA	Negative	Realtime QPCR
Serum		
HSV1 DNA	Negative	Realtime QPCR
HSV2 DNA	Negative	Realtime QPCR
VZV DNA	Negative	Realtime QPCR
EBV DNA	Negative	Realtime QPCR
CMV DNA	Negative	Realtime QPCR
HHV6 DNA	Negative	Realtime QPCR
HHV8 DNA	Negative	Realtime QPCR
Enterovirus RNA	Negative	Realtime QPCR

CSF, cerebrospinal fluid; PCR, polymerase chain reaction; HSV, herpesimplex virus; VZV, varicella zoster virus; EBV, Epsteina Barr virus; CMV, cytomegalovirus; HHV6, human herpesvirus type 6; HHV8, human herpesvirus type 8.

The detection of PVB19 DNA (Parvovirus B19 ELITe MGB® Kit, ELITech group, Milan, Italy) both in CSF and in serum, and serum IgG and IgM detection (Anti-Parvovirus B19 ELISA IgG and IgM, Euroimmun AG, Luebeck, Germany), led to a diagnosis of PVB19 encephalitis.