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REVIEW

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Herpetic Meningoencephalitis by Vertical Transmission: A Case Report and Systematic Review

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Abstract: Objective: To report a case of vertical herpetic meningoencephalitis. Results: The involvement of the central nervous system (CNS) in infection by HSV (herpes simplex virus), HSV-1 or HSV-2, causes an acute inflammatory process in the brain parenchyma, leading to herpetic encephalitis. It is a feared form of the disease due to its severity and its high rate of morbidity and mortality. Its rapid fatal progression can be prevented from early suspicion and treatment, which is essential when taking into account their neurological sequelae since survivors have motor sequelae, behavioral disorders, or epilepsy. The present work reports the case of a newborn male with spontaneous vaginal delivery who, at 19 days of age, started to experience fever, irritability, difficulty in eating, spasms, tremors of the upper limbs, deviation of the eyes, and seizures of difficult to control, together with CFE and serological changes, in addition to imaging tests compatible with herpetic meningoencephalitis, progressing with a very serious evolution despite the institution of specific treatment for CNS herpetic infection, evolving with important neurological sequelae. Conclusion: The sequels resulting from herpetic encephalitis not properly diagnosed, or even late, leads from severe neurological damage to death. Therefore, it is extremely important to start empirical treatment with antiviral drugs to reduce the sequelae mentioned above.

Keywords: Herpes, Vertical transmission, Meningoencephalitis, Newborn, Neonatology

1. Introduction

During pregnancy, pregnant women can be exposed to a variety of infectious agents, including viruses, bacteria, protozoa, or fungi [1]. These infectious agents, when they affect the fetus, can cause important perinatal morbidity and mortality. The fetus can be affected during intrauterine life, or the baby can be infected during delivery or in the first weeks of life [1,2].

The most frequent congenital infections are toxoplasmosis, syphilis, acquired immunodeficiency virus, rubella, cytomegalovirus (CMV), and herpes simplex virus (HSV). The agents most involved in congenital infections are viruses, with HSV being the largest pathogenic group for men [3]. In the case of HSV infection, the vast majority of vertical transmission occurs in the intrapartum period [4].

Neonatal HSV infections are uncommon. In contrast, infections by genital herpes in adults are very common [5,6]. Therefore, it is not uncommon to manage babies who may be exposed to HVS during delivery, making it essential to prevent the potentially devastating consequences of neonatal virus disease [7-9]. During pregnancy, the most common form of HSV is through recurrent infections [10]. According to American statistical data, approximately 10% of women who do not have HSV-2 have a sexual partner who carries this virus. Thus, these pregnant women are at risk of contracting a primary HSV-2 infection during pregnancy and thus transmitting the virus to the fetus [11].

Transmission of HSV-2 generally occurs through sexual intercourse. This virus can cause neurological syndromes such as meningitis, especially recurrent, encephalitis, particularly in neonates, and lumbosacral radiculitis [10].

The involvement of the central nervous system (CNS) in infection by HSV, HSV-1, or HSV-2, causes an acute inflammatory process in the brain parenchyma,

leading to herpetic encephalitis [12,13]. The diagnostic method considered to be the gold standard is brain tissue biopsy, however, in practice, the diagnosis is made by clinical correlation with complementary tests such as fever, headache, decreased level of consciousness, cerebrospinal fluid examination (CFE), electroencephalogram (EEG) and brain nuclear magnetic resonance (NMR). Neurological deficits can still occur, such as focal deficits or seizures, amnesia, ataxia, or emotional lability [10,12,13].

Herpetic encephalitis is a disease feared due to its severity and its high rate of morbidity and mortality. Its rapid fatal progression can be prevented from early suspicion and treatment [13,14], which becomes essential when taking into account their neurological sequelae since survivors have motor sequelae, behavioral disorders, or epilepsy [15].

In this context, therefore, the present study presents the case of an infant male patient, diagnosed with herpes simplex virus infection of vertical transmission that evolved to severe herpetic meningoencephalitis.

2. Methods

The present study is a case report whose bibliographic research used the descriptors (MeSH Terms) *herpes simplex, herpetic encephalitis, congenital infections.* The research was carried out through the study of digital articles and virtual books attached to the PubMed, Embase, Ovid, Cochrane Library, Web Of Science, ScienceDirect Journals, Scopus, academic Google, in database platforms such as Scientific Electronic Library Online (SCIELO), PubMed, and in scientific repositories, following the rules of systematic review - PRISMA (Transparent reporting of systematic reviews and meta-analyzes-HTTPS://www.prisma-statement.org/). Used as the main data sources, the most relevant works were selected for the theme for synthesis and presentation of information, excluding references that diverged from the purposes covered here.

2.1 Case Report

The present study was elaborated according to the rules of **CARE case report** (https://www.care-statement.org/) [16]. The study data were obtained through the analysis and collection of information contained in the patient's medical record at the Norte Pioneiro Regional Hospital, located in Santo Antônio da Platina-PR.

2.2 Patient Information and Clinical Findings

PHFO, a newborn male, was born at 39 weeks on 02/19/2020 via spontaneous vaginal delivery, with no crying at birth, hypotonic, and with APGAR 7 and 9. Assistance was performed in the delivery room, with good response. and the NB was kept together until discharge after 48 hours. His mother did not report any complications during pregnancy, other than the treatment of an *E. coli* urinary tract infection (UTI) at the beginning of the gestational period.

On 08/03/2020, with 19 days of life, the patient started a fever of 38 ºC at home, and for this reason, his mother sought the Emergency Room, where she was instructed to use Paracetamol for 6/6 hours. The following day, in addition to the fever, he presented irritability, difficulty in eating, spasms, tremors of the upper limbs, deviation of the eyes, and convulsions. The same day he was admitted to the Regional Hospital of Norte Pioneiro, in Santo Antônio da Platina-PR, being requested a place in the Intensive Care Unit (ICU). On physical examination at the time of admission, the patient presented with pustular lesions in the neck region, and it was reported that the newborn was using Neomycin for 8/8 hours and Cephalexin for 6/6 hours for 6 days.

After admission to the ICU, the newborn evolved into a state of epileptic malaise, with seizures that are difficult to control. It was necessary to use Phenobarbital up to 40 mg/kg intravenously and use Phenytoin. Even so, he presented convulsive crises, requiring the administration of Phenobarbital 14 mg/kg 24 hours after the last dose of Phenobarbital. He evolved with significant sedation, without the need to intubate, but with the use of oxygen in the incubator. He used Phenobarbital 2.5 mg/kg for 48 hours through the gastric route and had Hidantal suspended.

2.3 Timeline

From birth (02/19/2020) to the present.

2.4 Diagnostic Assessment

Initially, the diagnostic hypothesis of bacterial meningitis was made, CSF collection was performed and treatment with Vancomycin and Cefepime was started. The result of the CFE analysis showed a slightly cloudy, light yellow CFE containing 307 red blood cells/mL, 49 leukocytes/mL, 12% neutrophils, 1% eosinophils, 84% lymphocytes and 4% monocytes; glucose was 27 mg/dL, chlorides 118 mEq/L (within the normal range) and proteins 62 mg/dL.

Polymorphonuclear leukocytes were 13% and monomorphonuclear 87%.

Even with the antibacterial treatment instituted for meningitis, the patient continued to present seizures, needing to be maintained with Phenobarbital 5 mg/kg/day. Ophthalmology evaluation was requested and, due to the permanence of seizures, cranial CT was also requested.

The ophthalmological evaluation found a retina of usual color, and optic nerve apparently without edema, a macular alteration in both eyes, and a slight vitreous opacity in the left eye. The reassessment after one week showed areas of macular hyperpigmentation in both eyes, a slight pallor of bilateral papillae, a left eye with pigment in the lens, and a hyperpigmented lesion in the peripheral retina.

In cranial CT, an area of hypodensity was found, compromising the brain parenchyma in the topography of the anterior portions of the base nuclei and the thalamus bilaterally, which may correspond to ischemic hypoxic damage. Signs of subarachnoid and supratentorial hemorrhage have also been demonstrated, as well as hemorrhagic areas of the occipital and ventricular horns.

The radiologist responsible for the newborn CT scan of the newborn observed signs that could suggest encephalitis as responsible for the condition, and from this suspicion, the diagnostic hypothesis of meningoencephalitis was raised, and serologies for herpes simplex, cytomegalovirus, toxoplasmosis, syphilis, and rubella.

The serologies, all performed by the chemiluminescence method, were negative, except cytomegalovirus IgG - 81.70 AU/mL (reagent reference: ≥ 6.0 AU/mL), herpes 1 and 2 IgM> 3.5 (reagent reference: ≥1.1), and herpes 1 and 2 IgG 10.0 (reagent reference: ≥1.1). The positive result of serologies for herpes 1 and 2, added to the clinical picture of the newborn, closed the diagnosis of the case of herpetic meningoencephalitis. The CFE PCR diagnostic method was not performed due to the unavailability of the examination at the medical treatment center.

2.5 Therapeutic Intervention and Follow-up

The recommended treatment with intravenous Acyclovir was initiated for 21 days, with improvement in seizures and general conditions. However, the patient did not evolve with the full improvement of the neurological condition, remaining with sequelae of herpetic meningoencephalitis. With the evolution, the NB obtained remission of seizures with the use of Phenobarbital, but still had difficulty in feeding due to weak suction, which was still gradually improving. In continuity, he needed to perform a gastrostomy because he did not recover the suction and swallowing capacity.

Because of the sequelae, the patient was referred to the specialties of Physiotherapy, Neuropediatrics, Pediatric Cardiology, Speech Therapy, and Ophthalmology to receive adequate long-term follow-up.

2.6 Informed Consent

Those responsible for the patient signed the consent form.

2.7 Patient Perspective

Those responsible for the patient in the present study have the perspective that the interaction of a multidisciplinary medical team will favor the resolution of illnesses and the progression to a stable condition of the patient.

3. Discussion

Despite being rare, and with a prevalence of approximately 1%, congenital herpes simplex infection leads to high newborn morbidity and mortality [1,17]. Babies born to mothers with recent episodes of genital HSV infection are at a much higher risk of developing neonatal herpes [2,15].

The manifestations resulting from the infection can be cutaneomucosal, neurological, or disseminated [3]. In 50% of cases, the disseminated form occurs, with a mortality rate of 30%. The involvement of the nervous system can occur in isolation or disseminated forms, with the probability of neurological abnormalities or sequelae in more than 70% of the affected children [18-20].

Herpetic encephalitis consists of an acute process of the brain parenchyma, having a hemorrhagic necrotizing character, especially in the temporal-medial and frontal-basal regions. Encephalitis can progress quickly and end up having a fatal outcome in a matter of one to two weeks without treatment [4,13,20].

The newborn can have both HSV-1 and HSV-2 infections. HSV-2 is the most commonly found

serotype is found in older reports, however, currently, literature reports that HSV-1 has played a more important role in neonates [13,21,22]. This infection is rare, and data from 2014 report its appearance in approximately 1 in 2000 to 5000 births. Of the possible transmission routes, intrauterine is the worst one because it generates teratogenic effects, such as skin lesions or scars, CNS disorders, and chorioretinitis [24,25]. As the mother was not tested for HSV serology or asked about any signs or symptoms, it was not possible to say with certainty whether intrauterine, perinatal, or postpartum transmission occurred.

A nonspecific prodrome occurs in the initial infection, usually characterized by headache, fever, general malaise, vomiting, and behavioral deviations. Later on, focal neurological deficits appear, such as focal or generalized seizures, with olfactory or gustatory hallucinations and visual field disorders of the upper quadrant. Lethargy, irritability, poor diet, temperature instability, and bulging fontanelle can still be observed. Still, in 2/3 of the cases, skin lesions can occur, which alerts the diagnosis, since, in children with CNS disease, 60-70% have skin lesions at some point in the course of the disease [18,25].

Even with proper treatment, there can be severe neurological sequelae, including cortical hemorrhage, microcephaly, megacystic encephalomalacia with laminar necrosis, cortical atrophy and gliosis, subdural egromas, infratentorial hemorrhages or effusions, developmental delay, epilepsy, quadriplegia, and blindness [13,24]. One of the changes presented by the patient in question was the ophthalmology that maintains specialized monitoring, in addition to important neurological sequelae.

CFE analysis should be requested in newborns who have fever, irritability, and seizures, and the negative result for HSV infection does not exclude the result initially. CFE analysis has great value and usually presents with pleocytosis (10 to 200 cells/mm3) with a predominance of mononuclear cells, normal or elevated glucose, and increased or slightly increased proteins [27,28]. The result of the CFE analysis of the patient of the case obtained pleocytosis of 49 cells/mL with a predominance of monomorphonuclear cells (87%), decreased glucose (27 mg/mL), and increased proteins (62 mg/dL).

Among the tests that can be used to detect the virus, we can mention viral cultures of the oropharynx, nasopharynx, mucous swabs, rectal smear, leukogram, CFE PCR (viral DNA), skin lesions, mucous membranes, and blood; staining of immunofluorescent antibodies to skin lesions; enzyme immunoassays for HSV antigens in skin lesions [15]. In the case described, it was not possible to perform the diagnostic method by PCR, and instead, serology for HSV was performed, which showed reactants in more than one opportunity, closing the diagnosis.

The specific serological examination can be used for retrospective diagnosis. It helps to assess whether mothers with no previous history of HSV infection have a primary infection in late pregnancy and have transferred little or no antibody to the fetus. Due to the inherent immaturity of the immune response to systemic viral infections in this age group, IgM production is delayed or does not occur in infected newborns [28]. The patient in question had a positive serological result for IgM infection, which helped to close the diagnosis of the case. This serological result may remain positive until one year of age.

It is very important to consider that the use of PCR for HSV in the assessment of newborns will increase the length of hospital stay, the costs, and the risk of nosocomial infection. Even so, the CFE analysis of the cerebrospinal fluid is considered the gold standard and can be complemented by imaging tests such as CT, NMR, and EEG. Eventually, a brain biopsy may be ordered when clinical deterioration occurs despite treatment with acyclovir [27,29,30].

The diagnosis of the case in question, as well as in the literature, was based on the union of the clinic with the complementary exams. Thus, the combination of several factors pointed to the diagnosis of herpetic meningoencephalitides, such as the fact that the NB has a fever of 38 ºC, convulsions, tremors of the upper limbs, irritability, and deviation of the eyes added to the IgM and IgG serologies positive for HSV.

For non-localized diseases, the currently recommended regimen is intravenous acyclovir (60 mg/kg/day divided into 3 doses, ie 20 mg/kg every 8 hours), for 14 days, and for disseminated and CNS disease the duration is 21 days. The shorter treatment time is related to the risk of reactivation and damage to the central nervous system. The early use of acyclovir reduces the percentage of CNS involvement and increases the number of non-localized diseases. High-dose antiviral can improve morbidity and restore normal development of the nervous system in 83% of survivors, but for children with diseases of the central nervous system, only 31% of survivors are so successful [12,18,24,26].

It is recommended to start antiviral therapy within the first 4 days to avoid death and short-term complications and should be administered slowly to avoid nephrotoxicity. Therefore, due to the higher success rate of early administration, it is recommended to start the empirical treatment after the diagnosis is suspected until it is confirmed [15].

The treatment with acyclovir could not be started early in the case described due to the fact that the NB returned to the service only after 19 days of life, with symptoms of CNS involvement for some days. Even with the recommended treatment introduced, the patient ended up evolving with sequelae of herpetic meningoencephalitis.

There is controversy about the patient who needs empirical therapy. There are recommendations, by some authors, in cases of specific signs of HSV and symptoms, such as seizures, vesicles, signs of sepsis, or pleocytosis in the analysis of CFE. Others consider empirical therapy only in neonates with symptoms started before 21 days of age [30].

4. Conclusion

The sequelae resulting from herpetic encephalitis not properly diagnosed, or even late, leads from severe neurological damage to death. Therefore, it is of utmost importance to start the empirical treatment with the antiviral to reduce the sequels mentioned above. Although rare, HSV infection is extremely serious and, therefore, it becomes valid to adopt preventive measures during prenatal, delivery, and immediate postpartum. In addition, it is up to the doctor to investigate the past history of HSV in the pregnant woman and her sexual partner. The use of acyclovir is permitted in pregnant women over 36 weeks of gestational age with primary infection or risk of recurrence. And the mode of delivery of choice in the presence of the active disease is cesarean. With hospital discharge, the puerperal woman should be advised about the importance of monitoring the child by a neurologist, in order to observe their neuropsychomotor development.

References

[1] S.G. Pinninti, D.W. Kimberlin, Neonatal herpes simplex virus infections, Pediatric Clinics of North America, 60(2) (2013) 351-365. DOI | PubMed

[2] S.H. James, D.W. Kimberlin, Neonatal herpes simplex virus infection: epidemiology and treatment, Clinics in Perinatology, 42(1) (2015) 47-59 DOI | PubMed

[3] F. Baquero-Artigao, Actualizacion en infecciones herpeticas congenitas y neonatales: infeccion por citomegalovirus y herpes simple [Update on congenital and neonatal herpes infections: infection due to cytomegalovirus and herpes simplex], Revue Neurologique, 64(s03) (2017) S29-S33. PubMed

[4] M.M. Shipley, D.W. Renner, U. Pandey, B. Ford, D.C. Bloom, C. Grose, M.L. Szpara, Personalized viral genomic investigation of herpes simplex virus 1 perinatal viremic transmission with dual fatality, *Cold Spring Harbor Molecular Case Studies*, 5(6) a004382. DOI | PubMed

[5] O. Picone, Herpès génital et grossesse : épidémiologie, manifestations de la maladie, prévention et dépistage. Recommandations pour la pratique clinique du Collège national des gynécologues obstétriciens français (CNGOF) [Genital herpes and pregnancy: Epidemiology, clinical manifestations, prevention and screening. Guidelines for clinical practice from the French College of Gynecologists and Obstetrician (CNGOF)], Gynécologie Obstétrique Fertilité & Sénologie, 45(12) (2017) 642-654. DOI PubMed

[6] R. Lee, M. Nair, Diagnosis and treatment of herpes simplex 1 virus infection in pregnancy, Obstetric Medicine, 10(2) (2017) 58-60. DOI | PubMed

[7] A.J. Nahmias, W.E. Josey, Z.M. Naib, M.G. Freeman, R.J. Fernandez, J.H. Wheeler, Perinatal risk associated with maternal genital herpes simplex virus infection, American Journal of Obstetrics and Gynecology, 110(6) (1971) 825–837. DOI | PubMed

[8] Z.A. Brown, A. Wald, R.A. Morrow, S. Selke, J. Zeh, L. Corey, Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant, JAMA, 289(2) (2003) 203–209. DOI | PubMed

[9] D.W. Kimberlin, J. Baley, Committee on Infectious Diseases, and Committee on Fetus and Newborn, Guidance on Management of Asymptomatic Neonates Born to Women with Active Genital Herpes Lesions, Pediatrics, 131(2) (2013) e635-46. DOI | PubMed

[10] Y. Wang, K.P. Smith, Safety of alternative antiviral agentes for neonatal herpes simplex vírus encephalitis and disseminated infection, Journal of Pediatric Pharmacology and Therapeutics, 19(2) (2014) 72-82. DOI | PubMed

[11] J.A. Kulhanjian, V. Soroush, D.S. Au, R.N. Bronzan, L.L. Yasukawa, L.E. Weylman, A.M. Arvin, C.G. Prober, Identification of women at

unsuspected risk of primary infection with herpes simplex virus type 2 during pregnancy, New England Journal of Medicine, 326(14) (1992) 916-20. DOI | PubMed

[12] C. Andrade, L. Mocho, A. Carragoso, Um caso de encefalite herpética sem fibre, Ver de saud Amato Lusitano, 35(2014) 15-18.

[13] Romanelli RMC, Loutfi, K. S., Filho JMC. Herpes simplex neonatal recorrente: relato de caso. Rev Med MG. 2010. Vol 20: 422-6.

[14] J.A. Nogueira, J. Simões, N. Pontinha, A. Pinto, A. Freitas-Fonseca, H. Lecour, Diagnóstico etiológico da meningite vírica. Estudo de 142 casos [Etiologic diagnosis of viral meningitis. Study of 142 cases], Acta medica portuguesa, 12(12) (1999) 341-4. PubMed

[15] C.L. Moreno, M.G. Uribe, D.M. Prada, Encefalitis herpética: Um caso em la unidad de cuidado intensivo pediátrica del Hospital Occidente de Kennedy, Bogotá, Acta Neurológica Colombiana, 20(2) (2004) 85-89.

[16] D.S. Riley, M.S. Barber, G.S. Kienle, J.K. Aronson, T. von Schoen-Angerer, P. Tugwell, H. Kiene, M. Helfand, D.G. Altman, H. Sox, P.G. Werthmann, D. Moher, R.A. Rison, L. Shamseer, C.A. Koch, G.H. Sun, P. Hanaway, N.L. Sudak, M. Kaszkin-Bettag, J.E. Carpenter, J.J. Gagnier, CARE guidelines for case reports: explanation and elaboration document. Journal of Clinical Epidemiology, 89 (2017) 218-235 DOI | PubMed

[17] D.W. Kimberlin, C.Y. Lin, R.F. Jacobs, D.A. Powell, L.M. Frenkel, W.C. Gruber, M. Rathore, J.S. Bradley, P.S. Diaz, M. Kumar, A.M. Arvin, K. Gutierrez, M. Shelton, L.B. Weiner, J.W. Sleasman, T.M. de Sierra, S.J. Soong, J. Kiell, F.D. Lakeman, R.J. Whitley, Natural history of neonatal herpes simplex virus infections in the acyclovir era, Pediatrics, 108(2) (2001) 223-9. DOI | PubMed

[18] D.W. Kimberlin, R.J. Whitley, W.Wan, D.A. Powell, G. Storch, A. Ahmed, A. Palmer, P.J. Sánchez, R.F. Jacobs, J.S. Bradley, J.L. Robinson, M. Shelton, P.H. Dennehy, C. Leach, M. Rathore, N. Abughali, P. Wright, L.M. Frenkel, R.C. Brady, R.V. Dyke, L.B. Weiner, J. Guzman-Cottrill, C.A. McCarthy, J. Griffin, P. Jester, M. Parker, F.D. Lakeman, H. Kuo, C.H. Lee, G.A. Cloud, for the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group, Oral acyclovir suppression and neurodevelopment after neonatal herpes. New England Journal of Medicine, 365(14) (2011)1284-92. DOI

[19] R.J. Whitley, Herpes simplex virus infections. In: J.S. Remington, J.O. Klein, eds. Infectious Diseases of the Fetus and Newborn Infants. 3rd ed. Philadelphia, PA: WB Saunders Co; (1990) 282–305.

[20] I. Lamego, C. Brinckmann, A. Ciancio, R. Minotto, A. Hilbig, J.M. Ulbrich-Kulczynski, M.H. Fontana, L.M. Barbosa-Coutinho, Encefalite neo-natal pelo vírus do Herpes simplex, Arquivos de Neuro-Psiquiatria, 51 (1993) 377-381. DOI

[21] S.G.Pinninti, D.W. Kimberlin, Preventing herpes simplex virus in the newborn, Clinics in Perinatology, 41(4) (2014) 945-955. DOI | PubMed

[22] M. Bache, G. Andrei, L. Bindl, L. Bofferding, J. Bottu, C. Géron, C. Neuhäuser, S. Gillemot, P. Fiten, G. Opdenakker, R. Snoeck, Antiviral Drug-Resistance Typing Reveals Compartmentalization and Dynamics of Acyclovir-Resistant Herpes Simplex Virus Type-2 (HSV-2) in a Case of Neonatal Herpes, Journal of the Pediatric Infectious Diseases Society, 3(2) (2014) e24-7. DOI | PubMed

[23] G.L. Westhoff, S.E. Little, A.B. Caughey, Herpes simplex virus and pregnancy: a review of the management of antenatal and peripartum herpes infections, Obstetrical & Gynecological Survey, 66(10) (2011) 629-38. DOI | PubMed

[24] O.M. Takayanagui, Boletim de resumos e atualidades em neurologia, 3(5) (2007).

[25] U.D. Allen, J.L. Robinson, Prevention and management of neonatal herpes simplex vírus infections, Paediatrics & Child Health, 19(4) (2014) 201-12. DOI | PubMed

[26] A.C. Lopes, L.J.de Souza, P.C.L. Paravidine, G.A.C. Lima, M.A.E. Gomes, P.D. Araújo, Encefalite herpética em paciente do sexo feminino de 48 anos previamente hígida, Revista da Sociedade Brasileira de Clínica Médica, 6(2) (2008) 79-82.

[27] P.J. Woestenberg, J.H.T. Tjhie, H.E.de Melker, F.R.M. van der Klis, J.E.A.M. van Bergen, M.A.B. van der Sande, B.H.B. van Benthem, Herpes simplex vírus type 1 and 2 in the Netherlands: seroprevalence, risk factors and changes during a 12-year period, BMC Infectious Diseases, 16 (2016) 364. DOI | PubMed

[28] A.S. Miller, J.S. Bennett, Challenges in the care of Young infants with suspected neonatal herpes simplex virus, Hospital Pediatrics, 5(2015) 106-108. DOI

[29] L.C. Rodrigues, Encefalite herpética em lactente: relato de caso, Revista Medica de Minas Gerais, 17(2007) 149-152.

[30] C.C.D. Garrido, C.B. Meirelles, Encefalite herpética: relato de um recém-nascido com crises convulsivas de difícil controle. Herpetic encephalitis: Report of a newborn with convulsive crises of difficult control, Revista Rede de Cuidados em Saúde, (2017) 1-16.

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Data collection, analysis and preparation of initial draft (JTTP, ACTA, GM, MGPG, APOM, GMGH, RRDA & AJM); Designing the study, data collection, nalysis, preparation and finalizing the manuscript (IJZF).

Data sharing statement
No additional data are available

Ethics Approval
Not Applicable

Informed consent
A signed consent form were obtained from the patients

Conflict of interest
The authors declare no conflict of interest.