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PRIMARY INFECTION BY HSV-1 IN PEDIATRIC PATIENTS: A CASE REPORT

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ABSTRACT - Herpetic gingivostomatitis is the most frequent clinical manifestation of the primary episode of HSV-1 infection and is most commonly observed in children. Transmission occurs through direct contact with a host infected by the virus. The clinical symptoms consist of significant discomfort in the mouth, inability to feed, irritability, fever, adenopathy, redness, septic aspect and bad breath. The signs and symptoms can persist for 2 weeks. The diagnosis is made clinically, in the majority of cases, and can be confirmed via laboratory testing.
KEY-WORDS: Herpetic gingivostomatitis. Type 1 herpes simplex. Orofacial infections.

RESUMO- A gengivoestomatite herpética é a manifestação clínica mais freqüente do primeiro episódio de infecção por HSV-1 e é observada mais comumente em crianças. A transmissão ocorre a partir do contato direto com o hospedeiro infectado pelo vírus. O quadro clínico consiste em desconforto significativo na boca, incapacidade de alimentar-se, irritabilidade, febre, adenopatia, rubor, aspecto séptico e hálito fétido. Os sinais e sintomas podem persistir por 2 semanas. O diagnóstico é feito clinicamente, na sua maioria, e pode ser confirmado por testes laboratoriais.
PALAVRAS-CHAVE: Gengivoestomatite herpética. Herpes simples tipo 1, Infecções orofaciais.

1 INTRODUCTION

HSV-1 infections are extremely common. The majority of the main HSV-1 symptoms are asymptomatic or light enough to pass unnoticed. Mild cases can be confused with dental disease or other mal-defined conditions. When clinically evident, however, the most frequent initial manifestation of HSV-1 disease in children is primary herpetic gingivostomatitis. This occurs in 25-30% of affected children (BLEVINS et al., 2003). The clinical diagnosis of an HSV infection, particularly life threatening infections and genital herpes, should be confirmed via laboratory exams, preferably through isolation of the virus and/or detection of viral antigens or more frequently viral DNA by polymerase chain reaction. The histological findings or the imaging studies can support the diagnosis, but should not substitute the specific exams for the virus. The viral culture continues to be the gold standard for diagnosis (KLIEGMAN et al., 2009).

Due to the HSV diagnostic tests requiring some days to be concluded, treatment should not be delayed, but rather should be initiated immediately with the aim of ensuring maximal therapeutic benefit (KLIEGMAN et al., 2009).

2 METODOLOGY

With the aim of making the clinical manifestations, diagnosis and treatment of herpetic gingivostomatitis in children infected by HSV-1 known a case accompanied during hospitalization will be described in the following.

K.G.P.F., breast-feeding, male, 2 years of age, white, a native of Campos dos Goytacazes, RJ. The complaint at the first consultation, in March 2010 was a lesion in the

mouth. The mother reported the presence of lesions in the oropharynx and tongue and palate aphthous lesions for the previous 4 days. The patient was prescribed penicillin benzathine and nimesulide, but the lesions did not subside. The fever was high (40°C), only showing improvement with the use of dipyrone. There was an absence of vomiting, and diuresis and bowel movements were normal. With the persistence of the profile, the mother went to the emergency ward, where hospitalization was recommended.

In August 2008, the patient presented Gastroesophageal Reflux Disease, being prescribed prokinetic and ranitidine, which were stopped in 2009. In May 2009, pneumonia was treated through the outpatient clinic. In the following month, the patient manifested signs of varicella. No prior surgeries, blood transfusions or hospitalization were reported. Allergic to dipyrone, no other allergies to medication were reported.

The patient had undergone incomplete prenatal care, initiated in the third gestational trimester, with 3 check-ups, and the realization of exams, the results of which were normal. Birth was normal, without gestational or neonatal complications. Weight at birth was 2.450g and height was 45cm. Vaccination was late, with the vaccination record not being seen. The maternal uncle presented cardiopathy, which was being monitored. There was no history of diabetes mellitus, systemic arterial hypertension or respiratory pathologies in the family. The patient walked and talked at 9 months. There were no records to provide further information. There was exclusive breastfeeding for five days. The use of whole milk was initiated starting from then, when the patient began to present episodes of regurgitation. Nestogen was introduced followed by the use of Patamil. Subsequently, goat's milk was provided, but good acceptance was not observed, being substituted then for whole milk. At 1 year and 8 months, the use of industrially produced juice was introduced. There were no restrictions for other types of food. Currently the patient does not include milk in their diet.

Physical exam: awake, regular general state, eupneic, acyanotic, anicteric, hydrated, hypocritical +/4+, peripheral capillary perfusion in 2 seconds, nape of the neck clear, axillary temperature of 37.4°C. Weight 11.8 Kg. In the Oropharynx presence of diffuse aphthous lesions on the tongue and gums, with difficulty to visualize the posterior pharyngeal region (Figures 1 and 2). Heart auscultation: regular cardiac rhythm in 2 times, normophonetic sound, increased heart rate, without record of value. Pulmonary auscultation: bilaterally audible vesicular murmur with diffuse wheezing, respiratory frequency with 42 incursions per minute. Abdomen: flaccid, without masses or distension, peristalsis present. Inferior limbs: without edemas. Breastfeeding, without managing to feed. Procedure: hygiene of the oropharynx with bicarbonated water; application of oral nystatin solution, four times a day; smooth liquid diet; venous and symptomatic hydration. After presentation of the allergic reaction with the presence of urticariform lesions, dipyrone was stopped and promethazine IM was used, followed by hydrocortisone 5 mg/Kg/dose 6/6h; dexchlorpheniramine solution. The following exams were carried out during monitoring: Chest X-ray in AP, without record of the result; complete blood count: VHS, Na^+, K^+. Results of the laboratory exams (02/03/10): Erythrocytes 3,710 million / mm3; Hemoglobin 9.6 g%; Hematocrit 29.3%; Leukocytes 12,400 / mm 3; Basophils 0%; Eosinophils 1%; Sticks 6%; Segmented 52%; Lymphocytes 35%; Monocytes 2%; Platelets 330,000 / mm3; VHS 20 / mm 1 hour; Na: 135 mEq / l; K: 4.8 mEq / l.

Evolution: 03/03/10: infant presented urticariform lesions on limbs and trunk, maintaining high fever. Oral cavity with apthous lesions accompanied by white covering at the corners of the mouth, lips, gums and palate, with difficulty to accept food; 04/03/10: child feverish (38°C), irritable, hypoactive, crying, not managing to feed. Continued to present urticariform lesions, however more evident on the face and trunk; 05/03/10: remained irritable, was feverish to the touch, with appearance of pustules on the left hand of the back. With improvement in oral acceptance of food, venous hydration was suspended and oral rehydration treatment was initiated; 06/03/10, without fever, with the presence of crusty lesions on the lips.

Diagnosis: Herpetic gingivostomatitis; 03/07/10: remained irritable, feverish, with the tongue presenting white lesions, lips with crusty lesions and purulent secretion; 08/03/10: profile persisted. Discharged. On 10/03/10, the patient returned for a clinical check-up. Presented as asymptomatic at the time, accepting food well. On examination, good general state, good color, hydrated, eupneic, afebrile. In the oropharynx some lesions were present on the tongue accompanied by pustules on the lower lip. Tonsils, gums and the internal part of the cheeks were without alterations. Procedure: general hygiene instructions; discharge from Infectology monitoring.

Figures 1- Infant with ulcerated lesion and with whitened covering on gums, tongue, lips and perioral region.

Source: author

Figures 2- Infant with ulcerated lesion and with whitened covering on gums, tongue, lips and perioral region.

Source: author

3 RESULTS AND DISCUSSION

Herpetic gingivostomatitis is most common between 2 and 5 years of age, and is rare in children younger than six months. By nine years of age, 10 to 15% of children have already presented an episode of the disease. The occurrence of more than 2 episodes in one year is

highly suggestive of the presence of immunodeficiency. The infection is generally caused by HSV-1, being acquired from family members or at school. As happens with other infectious diseases, the rates of infection by this virus are more elevated amongst children who frequent crèche. Proximity during activities increases the risk of exchanging oral secretions and viral organisms. Examples of potential transmission behaviors observed in young children include touching the mouth, sharing utensils, cups and spoons; sucking the thumb, and putting toys in the mouth (FOCACCIA, et al., 2009; ABRAMCZUK, et al., 2010; BLEVINS, et al., 2003).

According to the literature, it is an extremely painful disturbance with a sudden beginning, pain in the mouth, salivation, a refusal to eat or drink, irritability and fever of up to 40-40,6°C. The gums show marked edemas and vesicles can develop throughout the oral cavity, including gums, lips, tongue, palate, tonsils, and pharynx with the possibility of manifestations on the facial area. Generally, vesicles are only present some days prior to the formation of hardened superficial ulcers that can be covered by a greyish-yellow membrane. Sensitive submandibular, submaxillary and cervical lymphadenopathies are common. Respiration can have a fetid odor due to an excessive growth of anaerobic oral bacteria. Additionally, the child can present a reddish and septic aspect. In the present case, the patient met these criteria, presenting evident lesions on the face, oral cavity and aphtous lesions accompanied by a whitish covering in the corners of the mouth, lips gums, tongue and palate with the evolution of crusty lesions and purulent secretion on the lips. Additionally, the child was irritable, with fever (38 °C) and difficulty feeding (KLIEGMAN et al., 2009; FOCACCIA et al., 2009).

The average incubation period is six days, being able to vary from 2 to 12 days. If it goes untreated, the disease disappears in 7 to 14 days, though the lymphadenopathy can persist for some weeks (KLIEGMAN et al., 2009, FOCACCIA et al., 2009). In older children, oral infection by HSV can manifest as tonsillitis and not as gum disease. The vesicular phase has frequently already passed when the patient seeks medical attention and the signs and symptoms can be indistinguishable from streptococcal pharyngitis, with fever, feeling unwell, headache, sore throat and white plaques on the tonsils. The course of the disease is typically longer than for untreated streptococcal pharyngitis. The presence of typical intra-oral and extra-oral vesicular lesions is highly indicative of primary herpetic gingivostomatitis. This finding can help to characteristically differentiate this disease from others that evolve with the appearance of vesicles in the oral cavity in small children. Herpangina (Coxsackie/ECHO), for example, is characterized by the appearance of vesicles in the posterior portion of the oral cavity and palate, together with inflammation of the pharynx, however there are no extra-oral lesions associated. Stevens-Johnson syndrome (multiform erythema) presents oral lesions, however its extra-oral manifestations differ from those that occur in primary herpetic gingivostomatitis. Other differential diagnoses include **t**onsillopharyngitis from the Epstein- Barr virus and diphtheria (*Corynebacterium diphteriae*) (KLIEGMAN et al. 2009; BLEVINS et al., 2003; TONELLI et al., 2000).

In the majority of cases, herpetic gingivostomatitis is diagnosed based on the clinical profile. However, as well as the associated clinical profile, a complete blood count can reveal leukocytosis or neutropenia associated with the viral infection. In agreement with the literature, patient blood count in this report showed leukocytosis confirmed on the blade (BLEVINS et al., 2003).

In cases in which early diagnosis is necessary, laboratory tests are available. The preferred method for diagnostic confirmation is the isolation of the HSV-1 virus, utilizing cell culture techniques. Serology can also be carried out, mainly to verify the presence of antibodies for the virus. More recently, specific DNA tests for HSV-1 are available via nucleic acid probes (BLEVINS et al., 2003).

The antiviral treatment with oral acyclovir is recommended for the treatment of herpetic gingivostomatitis. This pharmaceutical interferes with the synthesis of DNA,

inhibiting viral replication. The oral dosage suggested for HSV-1 infections is 15mg/Kg, 5 times a day, for a period of 7 days. The oral formulation of the drug is available in suspension (200mg/5mL) for small children. The collateral effects of acyclovir can include dizziness, headaches, nausea, vomiting and diarrhea. The medication can be nephrotoxic at high doses of oral administration and it should be used with caution in children with renal insufficiency. Hypersensitvity to drugs represent a contraindication and the treatment is generally realized in a clinical manner. Children hospitalized with serious cases, can receive acyclovir intravenously, given that they are unable to tolerate the oral medication. The dose is 250mg/m² every eight hours. However, the majority of pediatric infectious disease specialists do not treat the disease with acyclovir, reserving its use for immunosuppressed patients, seeking therefore, to avoid the emergence of drug resistant strains (BLEVINS et al., 2003). Additionally, acetaminophen (10/15mg/Kg every 4 hours) or ibuprofen (10mg/Kg every 6 hours) can be given in the case of light or moderate pain. Lidocaine Viscous (2%) can be prescribed for topical application, providing a local anesthetic that lasts around 10-15 minutes, though there are specialists who do not agree with this conduct due to the possibility of a serious allergic reaction in the mucous. The fever can be controlled with antipyretics such as paracetamol or ibuprofen. Aspirin has not been used since it is a known viral infections (BLEVINS et al., 2003).

The patient underwent symptomatic treatment and evolved without complications. However, in a study realized in Karachi with 50 patients with Bell's palsy, 35 presented IgG and IgM positive for HSV, emphasizing the association of infection with the herpes simplex virus and this type of palsy. This evidence has already been confirmed by other authors for example Khine and collaborators. In this study, the authors underline that the antiviral treatment should be considered in the initial phase of Bell's palsy to achieve a rapid clinical recuperation (MUSANI et al., 2009; KHINE et al., 2008).

We cannot neglect to report on cases of acute retinal necrosis related to primary HSV-1 infection, in which the authors call attention to the time relation between the appearance of the immunological response and the development of retinal necrosis, in immunocompetent individuals (MORA et al., 2009).

4 CONCLUSION

Herpetic gingivostomatitis, the primary infection by type 1 herpes simplex virus, is a very common pathology in pediatric practice. Despite the significant discomfort that it provokes, in the great majority of cases, there is spontaneous resolution, with antivirals mainly being reserved for immunosuppressed patients.

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