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CASE REPORT

Primary Herpetic Gingivostomatitis: A Therapeutic Approach to Primary Health Care

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ABSTRACT

Background Primary herpetic gingivostomatitis (PHGS) is the most common manifestation of herpes simplex virus type 1 (HSV-1) infection with characteristics of oral and/or perioral vesicular ulcerative lesions, inflamed gingival margins, and characteristic prodromal symptoms. This disease is common in children. It is a self-limiting disease and no need for a laboratory test to confirm the diagnosis. Treatments include causative, symptomatic, and supportive therapies. The drug of choice for causative agent elimination used in this case was acyclovir. **Case Report.** This paper reported and discussed a case of PHGS diagnosed based on the patient's anamnesis and typical clinical picture. It was in the form of ulcerated lesions on the oral and perioral mucosa and generalized inflammation of the gingiva. The treatment result was the patient recovered with routine Acyclovir therapy, Benzidamine HCl mouthwash, antipyretic and supportive therapy i.e multivitamins, hydration, liquid diet of High Calories High Protein (HCHP), and adequate rest. The patient was then followed up closely each third day to record the disease's progress. Although antiviral acyclovir was only indicated for immunocompromised children, in this case, it helps the patient to prevent further exacerbation and shorten the duration of illness. **Conclusion** PHGS therapy includes causative, symptomatic, and supportive therapy. Administration of the antiviral drug acyclovir was still effective and if the patient arrives after the 72-hour phase acyclovir is still needed to prevent further spread of the virus.

Keywords: primary herpetic gingivostomatitis, therapeutic approach, acyclovir, aloe vera

INTRODUCTION

Primary herpetic gingivostomatitis *(*PHGS) is the most frequent manifestation of herpes simplex virus type 1 (HSV-1) infection with the characteristic presence of oral and/or perioral vesicular ulcerative lesions. PHGS usually occurs after first time exposure to HSV-1 in seronegative individuals or who have not produced enough antibodies in previous infections. Most infections are subclinical, occurring in children (>30%) aged 1-5 years, but can also occur in adulthood.[1-3]

The disease is transmitted through direct exposure to mucous membranes or abrasive lesions of the skin or mucous secretions of individuals with active or recurrent primary infections. The virus can also be transmitted through respiration droplets or exposure to mucocutaneous secretions from a person with an asymptomatic shedding virus in the absence of clinical symptoms and incubated for several days to several weeks. The patient has a high fever (up to 38.5 - 40^{o}C), irritability and anorexia. Clinically, severe gingivitis and vesicular lesions of the tongue, buccal mucosa and palate extend around the lips and face (especially the chin and neck), *fetor oris*, and may be accompanied by cervical adenopathy. Vesicles in the oral cavity that occur rapidly will rupture and become grayish-white ulcerations of 1-3 mm with erythematous base. The disease is a self-limiting disease that lasts between three days to three weeks. Patients may still be infectious a few days to several weeks after the clinical symptoms disappear.[2-5]

Classical signs such as the presence of oral or perioral vesicular ulcerative lesions, inflammatory gingival margins, and prodromal symptoms are the characteristics of PHGS so generally no laboratory examination is needed to diagnose this disease.[5-7] This paper reported a case of PHGS diagnosed based on the classical clinical sign and the treatment options.

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CASE REPORT

On August 21, 2020, a 6-year-old girl came to the Oral Medicine Clinic with major complaints of pain at the corners of the mouth and several ulcers on the tongue, labial and buccal mucosa. Patients had fever accompanied by the raised body temperature (39.5^{o}C) four days prior to visiting the clinic. The corners of the lips and the entire mouth were painful so that the patient had difficulty eating and drinking. The next day the parents took her to a general practitioner, and she was given antibiotics and concoction prescribed drugs. After being given treatment for two days, the patient's body temperature began to drop but the symptoms in mouth did not heal. There were some canker sores on her tongue and lips, discomfort in her gums and scabs on the corners of the lips. The patient was still having difficulty in opening her mouth. The patient never had canker sores before, medical history includes no abnormalities. On extraoral examination, an enlargement of the left sub mandibular lymph node gland was palpable, soft, and painful. The upper lip looked dry, chapped and sore. The corners of the mouth had yellowish crusts, painful and bleed easily which preventing her from opening the mouth.

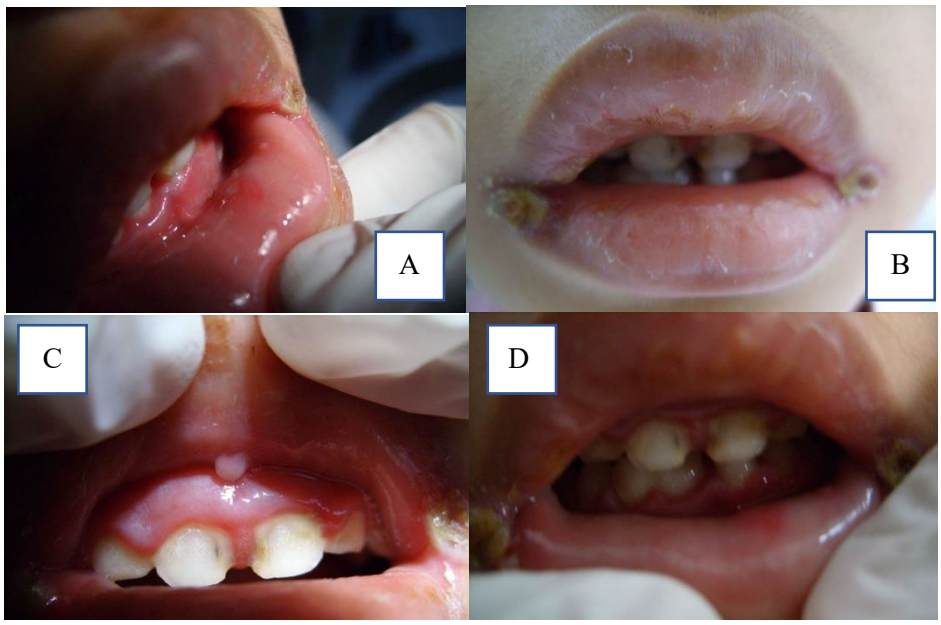

Figure 1. Extra- and intra-oral examination of the patient. (A) Multiple ulcers on the lower labial mucosa, (B) Yellowish crusts at the corners of the mouth that easily bleed, (C) Inflamed upper labial gingiva, (D) Multiple ulcers at the lower labial mucosa.

Intraoral examination showed two ulcers on labial mucosa with a diameter of 1 mm with a white-based, erythematous halo and no elevation on the edges. The patient also complained of aches and pains in her right and left buccal mucosa. However, due to the difficulty in opening her mouth, no lesions could be confirmed. The gingiva of the upper and lower jaw looked reddish, slightly edema, with aches and pains. There were two ulcers on the tip of the tongue with a diameter of about 1 mm, a white base with erythematous halo, pain and without elevation of the edges.

Based on the anamnesis and oral clinical signs, the patient was clinically diagnosed as PHGS with differential diagnosis of erythema multiforme, herpangina and acute necrotizing ulcerative gingivitis (ANUG). The treatment plans were antiviral agent, symptomatic therapy, and supportive therapy such as sufficient nutrition, well resting, and rehydration. The patient was given acyclovir 300 mg per day taken three times a day for seven days. The symptomatic drug consisted of benzydamine HCl gargle for use three times a day and paracetamol syrup were given if there was still any increase in body temperature, while aloe vera extract gel was applied on the lips and corners of the mouth. For supportive therapy, she was prescribed multivitamin syrup (per 5 ml: Vitamin A 1500 u, Vitamin B1 8.33 mg, Vitamin B2 4.16 mg, Vitamin B6 1.67 mg, Vitamin B12 8.33 µg, Vitamin C 83.33 mg, Vitamin D 100 u, Niacinamide 8.33 mg, Pantenol 3.33 mg) once a day. She was also advised to improve her nutrition with a liquid High-Calorie High Protein diet, get enough rest, and was encouraged to maintain oral hygiene by brushing her teeth.

The parents were also given an explanation that their child's condition was infectious, and it was advisable to isolate the patient not to come into direct contact with other people (especially other children). Furthermore, it was emphasized to the patient's parents to administer medicines according to the rules and come back for follow up in the next three days.

1st follow-up (August 24th, 2020)

At the first follow-up, which was held on the 3rd day, the patient felt more comfortable and was willing to eat a little bit and drink milk. The medications had been taken regularly.

The patient's body temperature had become normal. The corners of the mouth, tongue and lips were still in pain. This condition prevented the patient from opening her mouth. The ulcers on the right buccal mucosa were still present. There were no other complaints besides these findings. Extraoral examination showed that the lips were still dry and chapped. The corner of the left mouth looked like there was a bit bleeding due to breakfast she had that morning, and the corner of the right mouth was crustaceous.

Intraoral examination showed two ulcers on the tip of the tongue, with a white base, a diameter of 0.5 mm, and a slight pain. There was also an ulcer on the lower lip with a white base, 0.5 mm in diameter. The patient also complained of pain in the right buccal mucosa but could not be seen due to the limitation of opening the mouth. Edema and redness of the gingiva of the upper and lower jaws have decreased, and the patient was not complaining of any pain.

Acyclovir with the same dose was continued for the next three days and the topical application medicine for the lips and corners of her mouth was replaced with the administration of aloe vera extract gel. Any other drugs were continued on as prescribed.

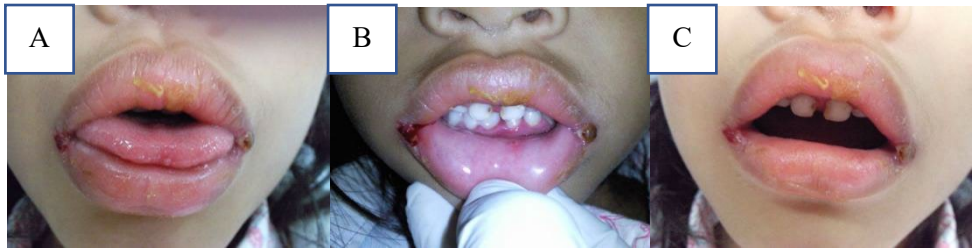

Figure 2. First follow-up examination. (A) Lips were still dry and chapped, although overall lesions have been reduced compared to before, (B) Ulcer on the tip of the tongue, with a white base, diameter 0.5 mm, (C) The corner of the left side of the mouth was a bit bleeding, on the right corner of the mouth was visible crustaceous, on the lower lip was still observable some ulcers with white base, diameter around 0.5 mm.

2nd follow-up (August 28th, 2020)

The second follow up was on the 7th day. The patient had felt very comfortable and she could already eat and drink comfortably. The canker sores had healed, the condition of the lips had improved with only a slight pain in the corners of the mouth, and she also reported that she took the medicine as advised.

The extraoral examination of the lips were still a little bit dry but had no sore anymore. There was still a small crust with a little pain on the corners of the mouth. There was no longer visible ulceration in intraoral examination. The gingiva and tongue appeared normal.

The patient was instructed to continue taking the Acyclovir per oral until the tablets finished off and the use of Aloe vera extract gel was resumed for the corners of the lips. The next follow up was planned on August 31, 2020.

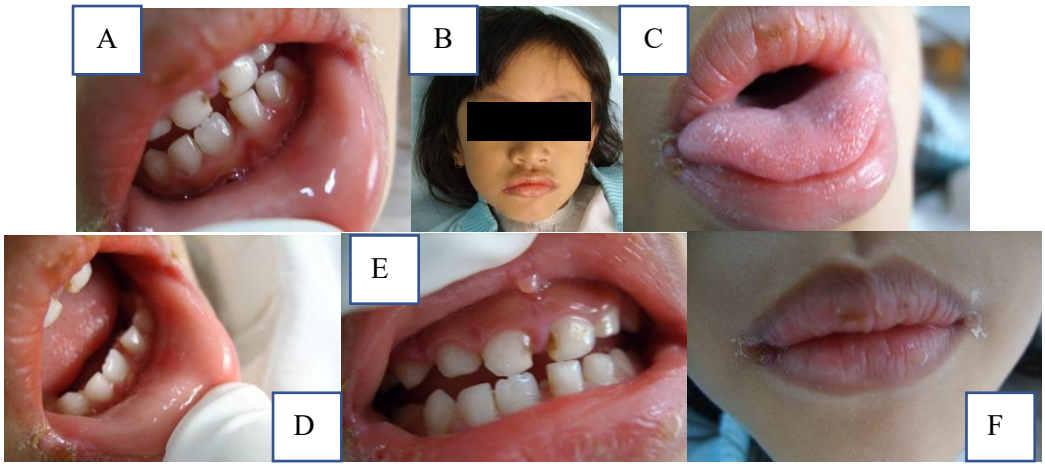

Figure 3. Second follow-up examination. (A, B) was still a little dry but was not hurtful anymore, the corners of the mouth still have a little crust with a slight pain, (C, D) On intra oral examination there was no longer visible ulceration, (D, E, F) The gingiva and tongue look normal, while lips showed only a bit crusty.

3rd follow-up (August 31st, 2020)

The third follow up was on the 10th day, the patient had felt very comfortable. She could eat and drink again well and do activities as usual. On extraoral examination, lips were still a bit dry but did not hurt and intraoral examination showed normal oral mucosa. Body temperature was normal and there were no complaints of any pain. The patient was declared cured and the drugs were discontinued.

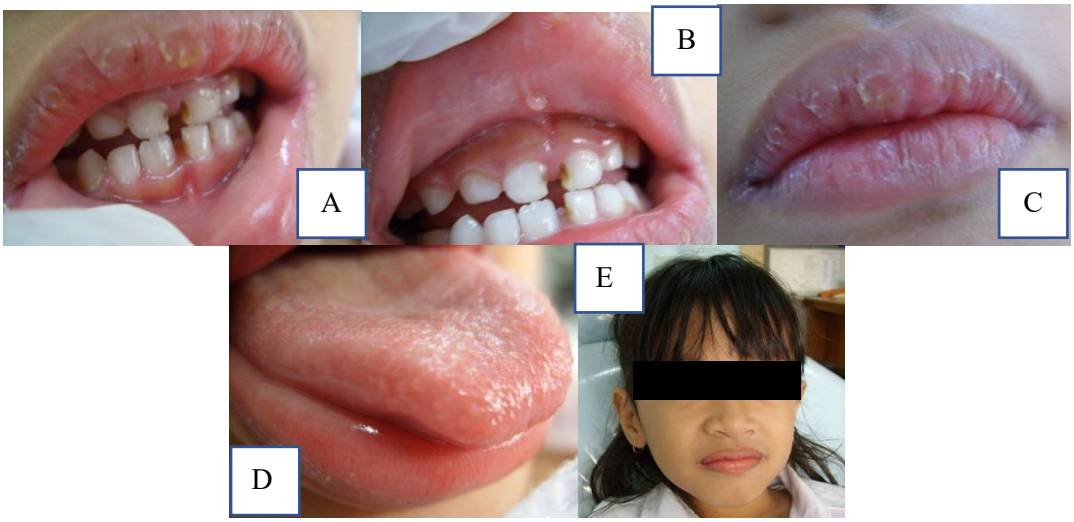

Figure 4. Third follow-up examination. (A, B) the patient felt very comfortable, the lips were still a bit dry but do not hurt, (C, D, E) Tongue, buccal mucosa, gingiva and lips looked normal.

DISCUSSION

Primary herpetic gingivostomatitis is a vesiculo-ulcerative disease caused mostly by *Herpes Simplex Virus* (HSV) type 1 infection although it can also be due to type 2 due to urogenital contact.[1,2] HSV infection is the most common viral disease in all races around the world. HSV belongs to the family Herpesviridae which does not have an animal vector but spreads between individuals. HSV is a double-stranded enveloped DNA virus and could be latent in host nerve cells.[9]

Most of PHGS diagnosis are obtained based on both anamnesis and characteristic clinical findings such as history of previous exposure to HSV, classical symptoms, the appearance and distribution of lesions, and a history of previous exposure to HSV.[2] In this case report, the diagnosis was established based on the classic symptoms such as the presence of prodromal symptoms, multiple round shape and shallow acute ulcerations, and generalized marginal gingivitis. These findings are consistent with previous reports.[5-7]

Laboratory examinations that can be done are cytology of vesicles (smear/Tzanck preparation), viral culture, direct fluorescent antibody (DFA), tissue biopsy, serology and detecting viral DNA with PCR.[10] Cytology examination was carried out by smearing the contents of the vesicles, namely by scraping the base of the lesion and then painting Giemsa, Wrigth's or Papanicolau's then viewed under a microscope to see a picture of multinucleated giant cells, syncytium and ballooning degeneration.[9] Diagnosis by this examination is only obtained in 50%-67% of vesicular lesions and cannot be distinguished in varicella zoster virus infection, chickenpox and shingles infection. DFA painting or antibody immunoperoxidase in vesicular smear preparations will be more sensitive (70%-88%), but this examination is difficult to do because it requires a vesicular stage and there is often a false negative.[10]

Isolation and neutralization of viruses in tissue culture is the most effective method for identification and has 100% specification and sensitivity. However, HSV isolation from lesions does not mean that the virus is the cause, there are patients with asymtomatic shedders of HSV found lesions in their oral cavity due to other causes.[9] Biopsy can help detect the type of degeneration that occurs as a result of HSV infection, but histologically it is indistinguishable between HSV1, HSV2 and varicella-zoster viruses.[8]

Serological examination in PHGS is conducted by examination of complement bonds or neutralization of antibodies (IgG and IgM) in the acute phase and healing phase. This method is rarely used because the results of the examination will be maximum after the infection occurs. HSV antibodies will begin to be seen after one week and increase steadily to peak after three weeks, while patients with acute complaints should be treated immediately.[9] Nucleic acid amplification examination, in this case polymerase chain reaction to detect HSV DNA antigens and virus types, was a very sensitive test and faster than viral cultures but very expensive and often gave false positive, so this method too was rarely used.[8]

Diagnosis of PHGS in this report was established with differential diagnosis of erythema multiforme, herpangina and ANUG. The presence of prodromal symptoms in PHGS can be the distinguishing thing from erythema multiforme. Signs that distinguish PHGS from herpangina are the absence of ulceration in the region of pharyngeal and palate and the presence of marginal gingivitis in PHGS.[9,10] This disease can also be distinguished from ANUG by the presence of nontypical ANUG clinical picture of a crater-like ulcer along the gingival margin due to gingival papillae necrosis which causing a characteristic necrosis odor.[11]

The antiviral therapy given in this case was Acyclovir with the recommended dose was 15 mg/kg body weight for 7-10 days with the calculation of the patient's body weight of 20 kg, so that in this patient it was given 300 mg per day.[2,10] At first visit Acyclovir was given for seven days, but the healing of lesions of the oral cavity of the patient was still not optimal so the dosage was continued for three more days.

Acyclovir was an acyclic guanosine derivative that has effective clinical activity against HSV. HSV encodes thymidine kinase phosphorylated by acyclovir into a monophosphate derivate. Cellular kinase was then converted by acyclovir monophosphate into acyclovir triphosphate which was in turn as a competitive inhibitor against viral DNA polymerase and prevents further display of viral DNA chains as well as DNA chain destroyers.[12] Therefore, even though the arrival of the patient in this report passed the first 72 hours of onset as indicated for the administration of acyclovir, this antiviral agent could be given. The goals of giving antiviral agent at this time were to prevent further spread of the virus, to reduce pain, to subside the fever and to minimize new oral lesions emergence in acute phase.

Benzidamine HCl, as a symptomatic therapy agent, was prescribed to relieve pain especially during eating dan drinking. Benzidamine was a nonsteroidal agent that has mild analgesic, anti-inflammatory and anesthetic effects. Benzidamine was used topically and stable on cell membranes, inhibits granulocyte degranulation, alters prostaglandin synthesis, and decreases tissue TNF.[13] Paracetamol syrup as antipyretic was given if there was still an increase in body temperature.[12]

In the first follow up visitation, lesions on the lips were still present because the patient still had not gotten the antibiotic ointment prescribed before. The Aloe vera extract gel was given to accelerate improvement of lips condition. Aloe vera was one of the well-known plants that was believed to have the ability to accelerate wound healing. The leaves contain more than 200 biologically active substances. It contains mannose polysaccharide molecules that work synergistically including Acemannan (biopolymer*)* which was efficacious in accelerating wound healing, antivirals effect and

immunostimulant properties. Extract of Aloe vera Gel helps maintain wound moisture, improves the migration of epithelial cells, accelerates collagen maturation and lowers inflammation.[2,4,15]

Supportive therapy was necessary for patients with viral infections, with consideration that patients might have a deterioration in their general condition. Related to the weak condition of patients, it is hoped that the administration of multivitamin can help improve the general health. Vitamin A is necessary for the differentiation and growth of epithelial tissue and improves the functioning of the immune system. B-complex vitamins play a role as a coenzyme in many biochemical reactions in the body which ultimately helps to facilitate the metabolism of the human body, increasing the stamina of the body in general. Vitamin C (ascorbic acid) has an important role as a cofactor in the hydroxylation of proline residues in collagen. Vitamin C is also useful for maintaining connective tissue and helping the synthesis of connective tissue during healing.[13] The administration of a liquid High Calories High Protein diet was expected to help replace the nutrients that the patient should get since she has difficulty eating so that it can add to the energy needed by the patient for the healing process. In addition, adequate rest was highly recommended for the healing process.

CONCLUSION

The conclusion of the case was that PHGS therapy includes causative, symptomatic and supportive therapy. The administration of acyclovir 72 hours after the lesion onset was still adequate to prevent further spread of the virus.

CONFLICT OF INTEREST

The authors declare that there were no conflicts of interest related to this case report.

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