

Successful treatment of herpes simplex–associated erythema multiforme with a combination of acyclovir and prednisone



CrossMark

Arny E. Muryah^{1,2}, Irna Sufiawati^{1*}

Abstract

Objective: Erythema Multiforme (EM) is an acute mucocutaneous hypersensitivity reaction triggered by certain infections and medications. EM is induced by the virus infection termed Herpes-associated erythema multiforme (HAEM). The use of corticosteroids for treating HAEM has been a long-debated issue. The aim of this case report is to present a patient with HAEM who was successfully treated with acyclovir combined with prednisone.

Methods: A 31 year old female presented with a complaint of pain and diffuse ulcers in mouth. The patient reported recurrent episode of ulcers of the mouth during the last two years. On extra-oral examination, we found that the lips were crusted and bleeding. Intraoral examination revealed multiple diffuse ulcerations on mucosa. No lesions were seen in other parts of the body. Laboratory investigation revealed normal, complete

blood count and positive HSV-1 serology. The patient was diagnosed as HAEM. The patient was treated with acyclovir (1000 mg/day) and prednisone (10 mg/day), topical mixture corticosteroid, chlorhexidine gluconate 0.2% and multivitamin during 7 days.

Results: All lesions healed without any further clinical sequelae within 7 days. The clinical success of corticosteroids as effective anti-inflammatory agents is largely attributed to their ability to reduce the expression of pro-inflammatory genes, to help maintain vascular integrity, and to decrease the expression of leukocyte adhesion molecules.

Conclusions: The addition of prednisone to acyclovir for HAEM resulted in a significant reduction of clinical signs and symptoms during the first week. The combination of acyclovir and corticosteroids may play an important role in the standard care for HAEM.

Keywords: Acyclovir, Erythema, Herpes simplex virus, Prednisone

Cite this Article: Muryah AE, Sufiawati I. 2017. Successful treatment of herpes simplex–associated erythema multiforme with a combination of acyclovir and prednisone. *Journal of Dentomaxillofacial Science* 2(3): 191-193. DOI: [10.15562/jdmfs.v2i3.656](https://doi.org/10.15562/jdmfs.v2i3.656)

¹Department of Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia
²Department of Oral Medicine, RSUD I Lagaligo, East Luwu, Indonesia

*Corresponding to: Arny E. Muryah, Department of Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia
irna.sufiawati@fkgunpad.ac.id

Received: 21 May 2017
Revised: 30 August 2017
Accepted: 31 October 2017
Available online: 1 December 2017

Introduction

Erythema multiforme (EM) is an acute mucocutaneous hypersensitivity reaction triggered by certain infections and medications.¹ This condition is a rare, acute mucocutaneous condition with the appearance of cytotoxic T-lymphocytes in the epithelium that induce apoptosis in keratinocytes, which in turn leads to satellite cell necrosis.²⁻⁴ EM usually occurs in adults 20-40 years of age although it can affect people of all ages.^{1,5-7} A recent multidisciplinary study reported that 70% of EM patients had oral involvement.⁸⁻¹² EM may also present as oral mucosal ulceration with no skin lesion.^{1,10} The same condition happened in this case. EM has been induced by a virus infection termed Herpes-associated erythema multiforme (HAEM).

Furthermore, the use of corticosteroids for treating HAEM has been a long-debated issue because the phase of cellular damage is over by the time the symptoms appear and the subsequent clinical course of the disease represents the repair phase.¹² The aim of this case report is to present a patient with HAEM who was successfully treated with acyclovir combined with prednisone.

Case Report

A 31-year-old female visited the Department of Oral Medicine Hasan Sadikin Hospital Bandung, with the chief complaint of pain and diffuse ulcers in mouth along with hemorrhagic crusts on her lips for about a week up until the time of her visit to the hospital. The patient reported that initially there were blisters on the lips which were then ruptured and became ulcers and erosions. She reported recurrent episode of the ulcers of the mouth, which she said she had experienced for about 2-3 months once in the last 2 years. She reported that ulcers healed without any medication but that when she felt tired or malaise the ulcers showed up again.

All her vital signs were within normal limits. Lymph nodes were non-palpable. On inspection, we saw the lips was droughty cracked, with splits and crusted blood [figure 1A](#). No lesions were seen in other parts of her body. Intraoral examination revealed multiple diffuse ulcerations on the lateral borders and ventral surface of the tongue, bilateral buccal mucosa, and labial mucosa [figure 1B-D](#). Laboratory investigation revealed normal complete blood count and a positive (59.9) IgG HSV-1 serology.

The patient was given oral treatment by non-pharmacology therapy administration, she was told to consume soft diets devoid of acidic and spicy foods along with emphasis on adequate fluid intake. She was instructed to brush her teeth using a soft, fluffy toothbrush especially before bedtime. The pharmacology therapy for the patient was provided to the patient, which included a 7-day course of acyclovir 200 mg 5 times/day (1000 mg/day), prednisone 5 mg 2 times/day (10 mg/day), and topical mixture corticosteroid (contains dexamethasone, Avil, lanoline and Vaseline) for the lips. Chlorhexidine gluconate 0.2% mouth wash as antiseptic oral and multivitamin minerals were also given considering the fact she admitted to loss of appetite because of the pain in her mouth. In her control appointment, 7 days after her first visit, she did not report any complaint



Figure 1 A. Multiple crusted and fragile on the lips, B. Ulcer in right buccal mucosa, C and D. Multiple ulcers on left and right lateral of the tongue

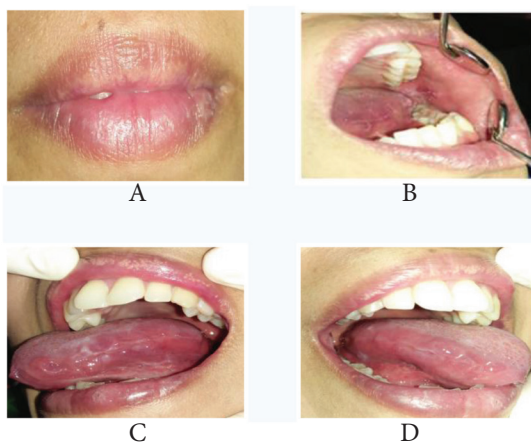


Figure 2 A. The lips healed; no blood crust, B, C, and D. Multiple ulcers on right buccal mucosa at the left and right lateral side of the tongue was also resolved

and all lesions healed without any further clinical sequelae as can be seen in [figure 2A-D](#).

Discussion

The diagnosis of HAEM was chosen based on the history and the disease characteristics ascertained during clinical examination at the first visit of the patient.^{1,13} We found hemorrhagic crusting of the lips and ulceration mainly of the non-keratinized mucosa, which is characteristic of oral lesion of HAEM.^{2,7,14} Laboratory examinations of serology were conducted to identify HSV and detect specific IgM and or IgG antibodies to confirm involvement of HSV infection.⁷ The pathogenesis of HAEM is consistent with a delayed-type hypersensitivity reaction. The disease begins with the transport of viral DNA fragments to distant skin sites by peripheral blood mononuclear cells. HSV genes within DNA fragments are expressed on keratinocytes, leading to the recruitment of HSV-specific CD4+ TH1-cells (helper T-cells involved in cell-mediated immunity). The CD4+ cells respond to viral antigens with production of interferon- γ , initiating an inflammatory cascade.^{2,6,9,15}

HAEM is often effectively managed with acyclovir 200 mg 5 times daily for 5 days minimum.^{3,6,16-18} In this case, acyclovir was given to the patient to reduce the viral load. Acyclovir is converted by viral thymidine kinase to acyclovir monophosphate, which is then converted by host-cell kinases to acyclovir triphosphate. Then it competitively inhibits and inactivates HSV-specified DNA polymerases, preventing further viral DNA synthesis without affecting the normal cellular processes.¹⁹ Oral administration of acyclovir (400 mg twice daily) has shown to be effective for preventing recurrence of HAEM, with valacyclovir (500 mg twice daily) and famciclovir (250 mg twice daily) used as alternate medications.^{1,14,20}

However, use of corticosteroids as anti-inflammatory medicines is taken into consideration only to manage and curtail the severity of the disease. They are not the end cure itself. Topical steroid also provides symptom relief.^{1,15} An adhesive pasta (orabase) form of clobetasol propionate is the most potent topical corticosteroid, or any other topical steroid agent needs to be applied to the affected areas 2-3 times per day.¹ Systemic steroids have been suggested as adjuvant therapy based on their anti-inflammatory effects. They suppress cytokine and chemokine response as well as T-cell function and decrease adhesion of inflammatory molecules to blood vessel endothelium.

There have been published suggestions from other practitioners in the field that steroid facilitated

faster treatment to prevent the recurrence of oral EM and decrease the duration and severity of major symptoms of EM. High-potency topical corticosteroid and a short course of systemic prednisone have been reported to be very effective in controlling the lesions of oral EM.

Several case reports provide evidence for the success of the treatment option of using a combination of antiviral medications and corticosteroids.^{8,10} The addition of prednisone to acyclovir for early HAEM resulted in a significant reduction of clinical signs and symptoms during the first week of treatment. Systemic corticosteroid is thus recommended as an efficient line of treatment of HAEM.¹⁰ Mechanistically, the clinical success of corticosteroids as effective anti-inflammatory agents is largely attributed to their ability to reduce the expression of pro-inflammatory genes.

Steroids inhibit the function of antigen-presenting cells and macrophages while also influencing the inflammatory response by reducing synthesis of prostaglandins, leukotrienes, and platelet-activating factors, which result from the activation of phospholipase.¹ Corticosteroids also help with maintaining vascular integrity, promoting synthesis of lipocortins, and decreasing the expression of leukocyte adhesion molecules, resulting in a beneficial, but also depressed inflammatory, reaction when treating EM. Early therapy with systemic prednisone (0.5–1.0 mg/kg/day) has been shown to be very effective.

Conclusion

The addition of prednisone to acyclovir for HAEM resulted in a significant reduction of clinical signs and symptoms during the first week of treatment. It is the clinician's choice to decide whether or not to use systemic corticosteroid therapy; research literature shows support for either decision; nevertheless, the decision is always based what yields the best benefits for patients given their specific conditions. The combination of acyclovir and corticosteroids gives an excellent healing response; hence, they may play an important role in the standard care for HAEM.

Conflict of Interest

The authors report no conflict of interest.

References

1. Samim F, Auluck A, Zed C, et al. Erythema multiforme. A review of epidemiology, pathogenesis, clinical features, and treatment. *Dent Clin North Am* 2013;57: 583-596.
2. Aadya, Singh HP, Kaur P, et al. Research and Reviews: Journal of Dental Sciences management of erythema multiforme secondary to herpes simplex by systemic corticosteroid. *Res Rev J Dent Sci* 2013;1: 45-49.
3. Jitender SSG. Recurrent erythema multiforme: a dental case report. *Glob Res J Public Heal Epidemiol* 2015;2: 71-74.
4. Parvinderjit S, Kohli JK. Erythema multiforme-oral variant: case report and review of literature. *Indian J Otolaryngol Head Neck Surg* 2011;63: 10-13.
5. John K, John MW, Carolyn KDH. Misdiagnosis of erythema multiforme: aliterature review and case report. *Pediatr Dent* 2012;34: 337-343.
6. Osterne RLV, Matos BRGD, Pacheco IA, et al. Management of erythema multiforme associated with recurrent herpes infection: a case report. *J Can Dent Assoc* 2009;75: 597-601.
7. Kishore M, Panat SR, Aggarwal A, et al. Herpes associated erythema multiforme-a diagnostic dilemma. *Int J Sci Study* 2013;1: 82-86.
8. Joseph K, Avi L, Joshua S, et al. Herpes simplex-associated erythema multiforme (HAEM): a clinical therapeutic dilemma. *Pediatr Dent* 1999;21: 359-362.
9. Bajaj P, Sabharwal R, Pk RM, et al. Erythema multiforme: classification and immunopathogenesis. *J Adv Med Dent Sci* 2013;1: 40-47.
10. Alfar MY, Alrousan M, Almajali Z, et al. The use of corticosteroids in management of herpes associated erythema multiforme. *J Pak Med Assoc* 2015;65: 1351-1353.
11. Davis K, Smith C, Halpern L, et al. Erythema multiforme associated with herpes simplex virus: a case report and literature review. *J Dent Oral Disord* 2016;2: 2-5.
12. Bulat V, Lugovica, Liborija MS. Prominent features and variations in clinical presentation of erythema multiforme. *Acta Clin Croat* 2007;46: 55-62.
13. Maharani Laillyza Apriasari RPR. Immunopathological aspects of oral erythema multiforme. *Dent J* 2009;42: 159-163.
14. Oliveira LRZ. Erythema multiforme minor: a revision. *Am J Infect Dis* 2008;4: 224-231.
15. Michele R. Lamoreux, Marna R. Sternbach WTH erythema multiforme. *Am Fam Physician* 2006;74: 1883-1888.
16. Kapse A. Herpes-associated erythema multiforme minor. *J Pediatric Infect Dis* 2012;4: 37-38.
17. Kamala KA, Ashok L, Annigeri RG. Herpes associated erythema multiforme. *Contemp Clin Dent* 2011;2: 372-375.
18. Krithika SS. Acute Oral Ulceration in young lady-erythema multiforme. *World J Pharm Sci* 2016;5: 542-547.
19. Zonable RR. Antiviral drugs for viruses other than human immunodeficiency virus. *Mayo Clin J* 2011;86: 1009-1026.
20. Jacinto OMSAS. Erythema multiforme associated with herpes labialis Jacinto. *CMAJ* 2013;185: 20.



This work is licensed under a Creative Commons Attribution