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Erythema Multiforme Associated With Herpes Simplex Virus: A Diagnostic Dilemma

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Abstract

Erythema Multiforme is an acute self-limiting condition with diverse mucocutaneous manifestations. It is considered to be a hypersensitivity reaction and clinically presents as macular, papular and urticarial lesions and sometimes as a classical target or iris lesions of skin and mucous membrane. It can be triggered by a number of factors among which Herpes simplex virus is the most common. When associated with the virus they are referred as Herpes associated Erythema Multiforme (HAEM). In 65-70% cases Recurrent EM is associated with HSV infection by history of HSV infection 1-3 weeks before onset of EM. They have an average of 6 episodes a year. Herein, we present a case of a patient with herpes associated erythema multiforme whose diagnosis was established clinically based on the history and signs and symptoms as erythema multiforme minor associated with herpes simplex infection and was successfully treated with acyclovir combined with prednisone.

Keywords: Herpes associated Erythema Multiforme, Erythema Multiforme, HAEM.

Introduction

Erythema Multiforme is an acute mucocutaneous hypersensitivity reaction which appears as symmetrical papules, later developing into "target" or "iris" lesions with an erythematous periphery and a central zone of necrosis.(1) It usually affects young adults and the peak age at presentation is 20-40years.(2)Herpes simplex virus has been has been identified in up to 70% of erythema multiforme cases. In these cases, recurrent episodes are related to HSV infection which is a predominant preceding event in individuals that experience recurrent episodes of erythema multiforme and they are labelled as having herpes-associated erythema multiforme. Herpes-associated erythema multiforme can be found several days or weeks following an episode of HSV. The diagnosis of HAEM is clinical and is easier when the patient develops target lesions with a preceding or coexisting HSV infection. The finding of typical skin or oral lesions or both in a patient with suspected HAEM supports the clinical diagnosis.(3)Management is directed towards treating symptoms and removing the cause and therefore

to treat the suspected infection or to discontinue the causative agents like medication use or to determine and eliminate the underlying systemic diseases.[1]

Case Report

A female patient aged 32 years reported with a chief complaint of pain in her lower lip region since 3days.On eliciting the history patient gave history of fever three days back followed by pain along with an itching sensation and slight burning sensation on eating food and also gave history of redness on her palate which gradually progressed to the present size. The patient also had visited different consultants for the same. Past medical history revealed similar attack one year back. Patient gave history of taking Ornidazole 500mg whenever she has dysentery and Paracetamol 650mg for fever. On clinical examination there was erosion noted on the lips and left commissure of upper and lower vermilion border along with encrustation with interspersed yellow discharge. The lymph nodes were not palpable. On intraoral examination diffuse erythema was noted on the right labial vestibule w.r.t 13 extending anteroposteriorly from the distal aspect of maxillary right lateral incisors to first premolar and superoinferiorly from upper labial vestibule to 0.3 cm above the vermilion border and it was tender on palpation. Also with respect to the palate there was a diffuse plaque noted involving the entire hard palate with surrounding erythema at the junction of the hard and the soft palate. On palpation it was non scrapable and tender.

Based on the clinical examination and the history of the patient a provisional diagnosis of Herpes Simplex Virus induced erythema multiforme was rendered. The differential diagnosis of Allergic Stomatitis was given. On investigation patient was advised for a complete blood count and the report appeared to be normal. Depending on the history, clinical examination and laboratory investigations, we arrived at the diagnosis of herpes associated erythema multiforme (HAEM). The patient was treated with a 7-day course of Tablet Wysolone 10 mg two times per day and was asked to dissolve in 10ml water and swish for 3-5 min and expectorate. Patient was also advised Tablet Zovirax 400mg four times daily for two weeks. Patient was asked to use Coolora mouthwash 3-4 times per day for one week and was recalled for follow up. Patient was advised to take soft diet and avoid junk food. Within a week, the oral lesions healed completely with transitory hyperpigmentation. The patient was followed up at intervals of two months for the next 6 months and there was no relapse.

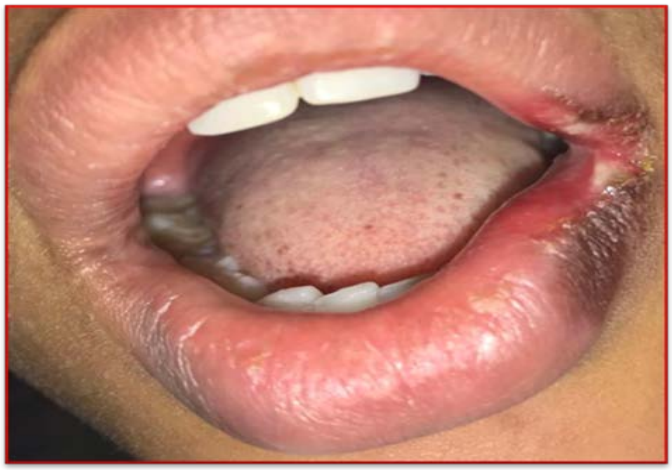

Figure 1: Erosion noted on left commissure of upper and lower vermilion border along with encrustation with interspersed yellow discharge.

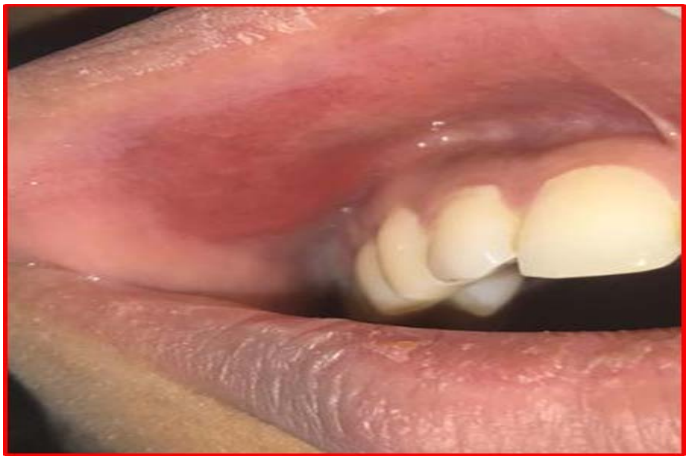

Figure 2: Diffuse erythema was noted on the right labial vestibule w.r.t 13 extending anteroposteriorly from the

distal aspect of maxillary right lateral incisors to first premolar and superoinferiorly from upper labial vestibule to 0.3 cm above the vermilion border.

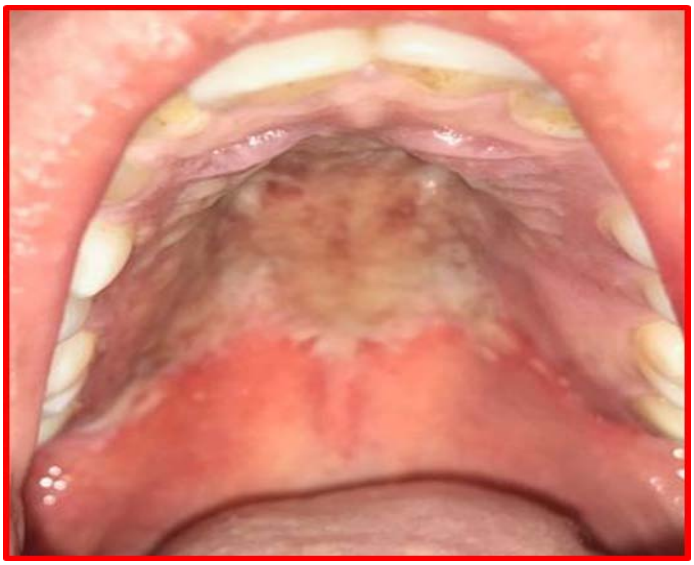

Figure 3: Diffuse plaque noted involving the entire hard palate with surrounding erythema in the junction between the hard and the soft palate.

After one week follow up- Healing of oral lesions after 1 week treatment with acyclovir combined with prednisone.

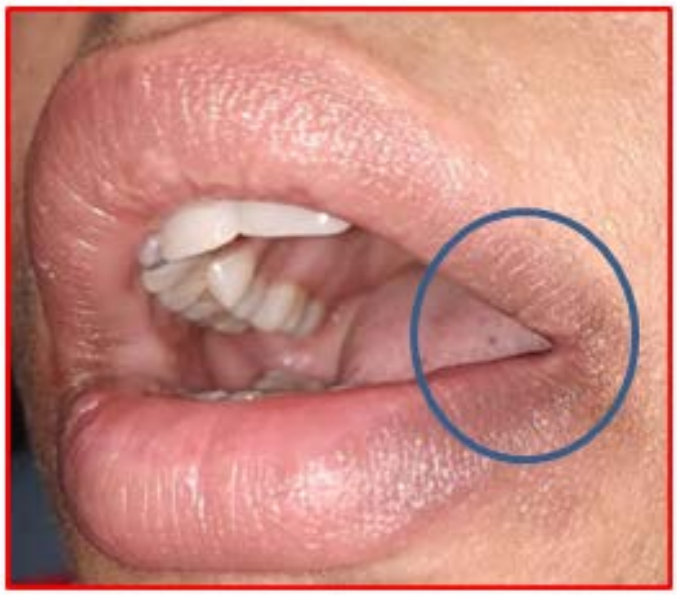

Figure 4: Completely healed lesion of lip with transitory hyperpigmentation.

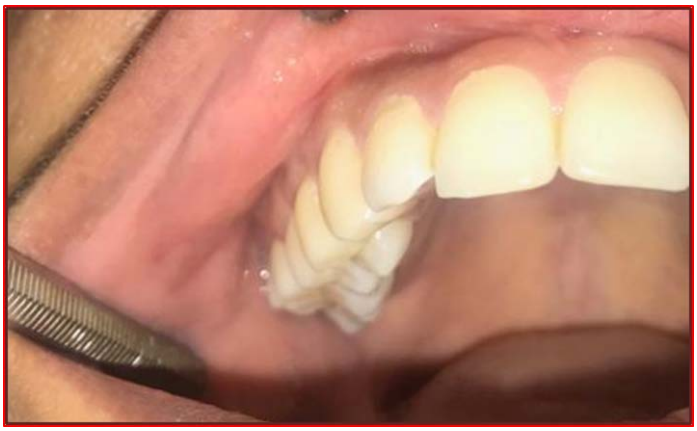

Figure 5: Completely healed vestibule region.

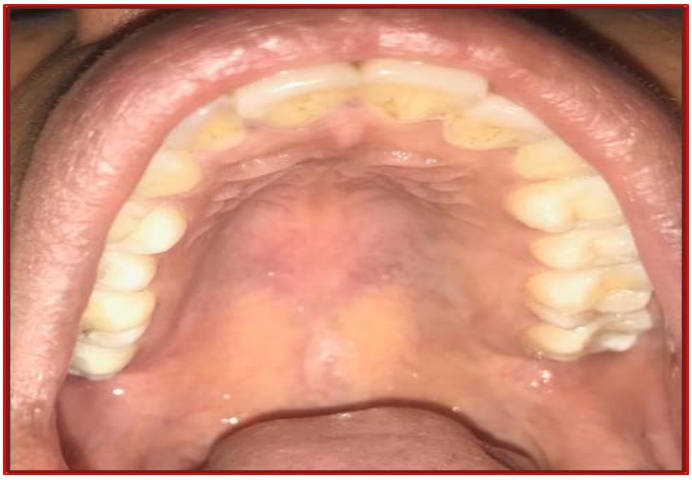

Figure 6: Completely healed hard and soft palate.

Discussion

EM is an acute, mucocutaneous condition of uncertain etiopathogenesis. Infection with HSV is the most common predisposing feature in the development of EM minor.[4]The pathogenesis of herpes associated erythema multiforme is consistent with a delayed hypersensitivity reaction. Both HSV 1 and HSV 2 trigger the erythema multiforme lesion. Recurrences are common in herpes associated erythema multiforme and they characterize the majority of the cases. Patient can experience 2-24 episodes per year with the mean duration of the disease being 10years.[5]The lesions of EM develops after 10 to 14 days of HSV infection and lip is the most common site of HSV infection that precedes EM lesions.[6]

The disease usually begins with the transport of HSV DNA fragments by circulating peripheral blood

mononuclear CD34+ cells(Langerhan cell) precursor to keratinocyte which leads to the recruitment of HSV-specific CD4+ TH1cells.The inflammatory cascade is initiated by interferon-γ (IFN-γ), which is released from the CD4+ cells in response to viral antigens, and immunomediated epidermal damage subsequently begins. Serology to identify HSV-1 and HSV-2 and to detect specific IgM and IgG antibodies may confirm a suspected history of HSV infection.[4] The characteristics of herpes-associated EM are typically those of EM minor with cutaneous or cutaneous and limited mucosal, which is usually oral involvement.[7]

HSV lesions can herald the appearance of target lesions by 2–17 days. In cases of primary HSV infection, there are frequently systemic signs and symptoms preceding the lesions, and the oral ulcers are typically much smaller. The EM minor lesions in HAEM can reach about 200 or more, evolve over 24–48 h, and are usually fixed and symmetrically distributed for about a week.[8]In a study conducted by Farthing P. et al, it was found that herpes-indused EM accounted for 20 %-50% of cases.[9]

The diagnosis of HAEM is clinical and is easier when the patient develops target lesions with a preceding or coexisting HSV infection.[4]HAEM is often effectively managed with acyclovir 200 mg 5 times daily for 5 days minimum. In this case, acyclovir was given to the patient to reduce the viral load.[10]In recurrent cases suppressive treatment using acyclovir (400 mg twice a day for 6 months) has also been effective in preventing recurrence. In addition, because EM is self-limited, symptomatic therapy with antiseptics, antihistamines, and analgesics is also recommended.[8]

The use of corticosteroids is taken into consideration only to manage and curtail the severity of the disease. They are not the end cure itself. 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. Early therapy with systemic prednisone (0.5–1.0 mg/ kg/ day) has been shown to be very effective. The addition of prednisone to acyclovir for early HAEM have shown a significant reduction of clinical signs and symptoms during the first week of treatment.[10]

Conclusion

The first and foremost step for management of herpes associated erythema multiforme is to reach an early diagnosis. Early clinical recognition of the disease is very essential for the prompt treatment. The combination of acyclovir and corticosteroids in the management of herpes associated erythema multiforme has shown excellent healing response therefore it may play an important role in the standard care for HAEM.

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