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Aqeel Khanani

Lake Erie College of Osteopathic Medicine, akhanani94303@med.lecom.edu

Kayvan Mirhadi

Rochester Regional Health, kayvan.mirhadi@rochesterregional.org

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An Unexpected Case of Herpes Simplex Virus Esophagitis Presenting Amidst Corticosteroid Therapy for an Acute COPD Exacerbation: A Case Report

Author ORCID ID:

Aqeel Khanani, ORCID# 0000-0003-4899-510X

Abstract

Herpes simplex virus (HSV) is prevalent worldwide, with a recent report by the World Health Organization estimating that 3.7 billion individuals under the age of 50 have been infected by the virus. After the initial infection, HSV-1 enters a latent phase with the potential for intermittent reactivation, often secondary to episodes of infection, stress, or immunosuppression. Per current literature review, esophageal involvement in the form of herpes simplex virus esophagitis (HSVE) is more commonly associated with immunocompromised patients, such as transplant recipients and HIV-positive individuals. The patient discussed in this report is a 79-year-old female with a past medical history of COPD managed with a daily prednisone dose of 10mg, as well as inhaled fluticasone-umeclidinium-vilanterol, inhaled ipratropium-albuterol, and oral montelukast. During her acute COPD exacerbation, she was initially treated outpatient with an increase in oral prednisone to 20mg daily. Once admitted, patient went on to receive an additional ten days of intravenous methylprednisolone treatment for this prolonged COPD exacerbation. She subsequently developed severe odynophagia refractory to nystatin oral suspension and fluconazole, as thrush was initially expected. As symptoms worsened an EGD and biopsy were ordered, and the patient was later diagnosed with Herpes simplex virus esophagitis. Ensuing HIV testing was negative. Patient responded rapidly to IV Acyclovir, with resolution of symptoms within 48 hours. This unique case highlights that HSVE can be a potential sequela of prolonged corticosteroid treatment for an acute COPD exacerbation.

Keywords

herpes, herpes simplex virus, herpes simplex virus esophagitis, COPD, corticosteroids, corticosteroid therapy, COPD exacerbation, HSV-1, HSVE, chronic obstructive pulmonary disease, prednisone, corticosteroid

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Conflict of Interest Statement

Authors do not have conflicts of interest to declare.

Cover Page Footnote

Thank you to Dr. Nadia Kousar for her consultation, Dr. Joel Shapiro for the pathology report and images, and Dr. Robert Helft for esophagogastroduodenoscopy images.

CASE REPORT

An Unexpected Case of Herpes Simplex Virus Esophagitis Presenting Amidst Corticosteroid Therapy for an Acute COPD Exacerbation: A Case Report[☆]

Aqeel Khanani ^{a,*}, Kayvan Mirhadi ^b

^a Lake Erie College of Osteopathic Medicine, United States

^b Rochester Regional Health, United States

Abstract

Herpes simplex virus (HSV) is prevalent worldwide, with a recent report by the World Health Organization estimating that 3.7 billion individuals under the age of 50 have been infected by the virus. After the initial infection, HSV-1 enters a latent phase with the potential for intermittent reactivation, often secondary to episodes of infection, stress, or immunosuppression. Per current literature review, esophageal involvement in the form of herpes simplex virus esophagitis (HSVE) is more commonly associated with immunocompromised patients, such as transplant recipients and HIV-positive individuals. The patient discussed in this report is a 79-year-old female with a past medical history of COPD managed with a daily prednisone dose of 10mg, as well as inhaled fluticasone-umeclidinium-vilanterol, inhaled ipratropium-albuterol, and oral montelukast. During her acute COPD exacerbation, she was initially treated outpatient with an increase in oral prednisone to 20mg daily. Once admitted, patient went on to receive an additional ten days of intravenous methylprednisolone treatment for this prolonged COPD exacerbation. She subsequently developed severe odynophagia refractory to nystatin oral suspension and fluconazole, as thrush was initially expected. As symptoms worsened an EGD and biopsy were ordered, and the patient was later diagnosed with Herpes simplex virus esophagitis. Ensuing HIV testing was negative. Patient responded rapidly to IV Acyclovir, with resolution of symptoms within 48 hours. This unique case highlights that HSVE can be a potential sequela of prolonged corticosteroid treatment.

Keywords: Herpes, Herpes simplex virus, Herpes simplex virus esophagitis, COPD, Corticosteroids, Corticosteroid therapy, COPD exacerbation, HSV-1, HSVE, Chronic obstructive pulmonary disease, Prednisone, Corticosteroid

1. Introduction

Herpes simplex virus (HSV) has spread extensively throughout the global population, with studies reporting that as much as 67% of the population has been infected by HSV-1.^{1,2} Whereas HSV-1 can be transmitted orally, HSV-2 is more frequently sexually transmitted, explaining the gap in prevalence between the two types.^{2,3} Following a primary oral infection, HSV-1 goes on to persist in a latent phase with the potential for intermittent reactivation

due to immunodeficiency, stress, or illness.⁴ HSV reactivation may even present with cutaneous or, less commonly, ocular manifestations. However, in cases of severe disease there may be evidence of neurological, respiratory, or even esophageal involvement.^{2,4} Herpes simplex virus esophagitis (HSVE) has classically been more commonly associated with immunocompromised patients, namely transplant recipients and HIV-positive individuals.⁵

Incidences of herpes zoster reactivation, in general, have been evaluated among rheumatoid arthritis patients on chronic corticosteroid therapy.

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* Corresponding author.
E-mail address: akhanani94303@med.lecom.edu (A. Khanani).

Large population-based studies found that treatment with systemic corticosteroids of 10 mg or more per day was associated with a statistically significant increase in the risk of herpes zoster reactivation.⁷ The following case discusses an instance of Herpes simplex virus esophagitis arising amidst systemic corticosteroid therapy for a prolonged exacerbation of COPD.

2. Case presentation

A 79-year-old female with a past medical history of chronic obstructive pulmonary disease (COPD) on 3-L of oxygen at home, non-small cell lung cancer (NSCLC) s/p stereotactic body radiation therapy, and a recent exacerbation of COPD treated with corticosteroids presented to the emergency department with worsening shortness of breath over the last week. Patient's COPD was being managed by her primary care provider (PCP) with a regimen of inhaled fluticasone-umeclidinium-vilanterol, inhaled ipratropium-albuterol, oral montelukast, and 10 mg of oral prednisone daily. Her at-home medications included losartan, omeprazole, levothyroxine, amlodipine, aspirin, and atorvastatin. Patient had seen her PCP four weeks earlier for similar symptoms and was found to produce a sputum culture positive for pan-sensitive *Klebsiella pneumoniae*. She was diagnosed with a COPD exacerbation and bronchiectasis and was then prescribed amoxicillin-clavulanate with an increased dose of prednisone – now 20 mg total daily. However, her symptoms continued to worsen, necessitating an increase in her home oxygen requirements from 2 to 3 L and, with further deterioration, hospital evaluation.

Review of systems was positive for a productive cough, hemoptysis, shortness of breath, chills, and malaise/fatigue. Physical examination in the emergency department revealed respiratory distress, wheezing, prolonged expiration, and isolated systolic hypertension (182/68 mmHg). Pulse and respiratory rate were within normal limits, while SpO₂ was at 94% on room air. Initial EKG and troponins revealed no ischemia or arrhythmias. Further testing revealed an elevated BNP (115 pg/mL), leukocytosis (15.9 K/uL) with a neutrophilic predominance (85%), and lymphopenia (400/mm³). Chest X-ray was ordered and significant for emphysema and left lower lobe alveolar disease and nodularity, as seen in Fig. 1. Patient was admitted for COPD exacerbation and suspected community-acquired pneumonia. Treatment with IV methylprednisolone 40 mg Q6H, IV ceftriaxone 1g, and PO doxycycline 100 mg BID was initiated. During



Fig. 1. Chest X-ray obtained upon patient presenting to Emergency Department showed mild cardiomegaly and emphysema and suspected scar tissue in the left lower lobe.

admission, shortness of breath continued to worsen, and the patient began to experience gradual dyspnea on exertion. Transthoracic echocardiogram was normal and a D-dimer test was also normal, significantly reducing the likelihood of pulmonary embolism. PCR testing for SARS-CoV-2, Influenza A, Influenza B, Adenovirus, Rhinovirus, and Parainfluenza virus were negative. Blood culture results returned negative. Arterial Blood Gasses (ABGs) drawn showed hypoxemia with a PO₂ of 66 mmHg. Patient's pH (7.41), PCO₂ (39 mmHg), and HCO₃ (25 mEq/l) were within normal limits.

On hospital day three, the patient began to show signs of respiratory distress with increasing accessory muscle usage and was therefore transferred to the intensive care unit. Here, Bilevel positive airway pressure (BiPAP) was initiated. Follow-up ABGs were within normal limits and the patient clinically was beginning to show some signs of improvement. However, although the patient was able to be transferred out of the ICU, her overall clinical picture had not shown notable improvement after eight days of Ceftriaxone and Doxycycline. A repeat sputum culture grew *Stenotrophomonas maltophilia* sensitive to Trimethoprim/Sulfamethoxazole (TMP/SMX), so the patient was started on a seven-day course. She reported some improvement in respiratory symptoms with TMP/SMX.

After ten days of intravenous methylprednisolone treatment, the patient began to complain of a sore throat/mouth and pain with swallowing. Patient was initially treated for oral thrush with a nystatin oral suspension, which did not lead to any symptom improvement. Fluconazole was also initiated but the odynophagia continued to worsen, and the patient

was now struggling to eat and speak. On hospital day fifteen, gastroenterology was consulted and the patient was referred for an esophagogastroduodenoscopy (EGD), during which hemorrhagic esophagitis and several posterior pharyngeal erosions were noted and biopsied, as illustrated in Fig. 2. Pathology report found H&E staining notable for acute inflammatory exudate, neutrophils, desquamated epithelial cells of the esophagus, and viral inclusion bodies suggestive of a herpes simplex virus infection, indicated by the arrow in Fig. 3. Another field view can be seen in Fig. 4, which displays the acute inflammatory exudate with viral inclusions that present as 3 nuclei with pale centers. Finally, in Fig. 5, biopsies showed positive antibody-antigen immunohistochemical staining for herpes simplex virus type 1.

Follow-up serology testing was positive for HSV-1 IgG. Notably, HIV antigen/antibody tests were negative. Following these results, the patient was started on IV Acyclovir. Patient reported significant improvement in symptoms after just two days of treatment with the antiviral. Patient was kept an additional day to monitor for tolerance with PO food and medication intake. On hospital day twenty-one, patient was discharged with an 11-day course of Valtrex 1g to treat the Herpes Simplex Virus Esophagitis for a total of fourteen days of antiviral treatment and with a 30-day supply of Prednisone 20 mg.

3. Discussion

This report sought to highlight herpes simplex virus esophagitis as a possible risk of prolonged corticosteroid treatment. Though present literature more commonly associates this manifestation of HSV reactivation with transplant or HIV/AIDS patients, this case shows that herpes simplex virus esophagitis should remain on the differential if that patient is on corticosteroid therapy. Moreover, large

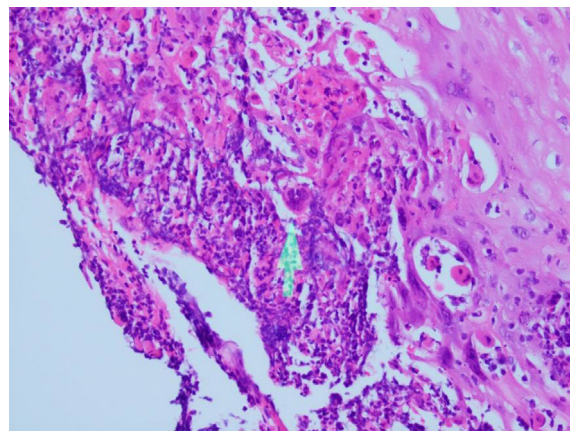


Fig. 3. H&E stain showing acute inflammatory exudate (neutrophils) and desquamated epithelial cells of the esophagus. Arrow is pointing to cell with viral inclusion bodies suggestive of herpes infection.

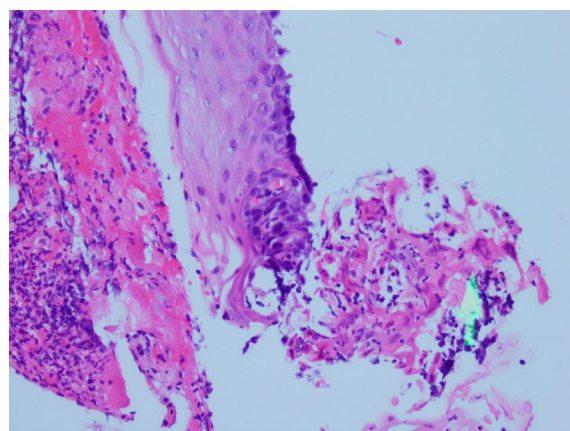


Fig. 4. The arrow points to acute inflammatory exudate on the right side with cell containing viral inclusions (3 nuclei with pale center).

population-based observational studies reviewing instances of HSV reactivation among rheumatoid arthritis patients on chronic prednisone therapy found statistically significant increases in risk of HSV reactivation in patients on at least 10 mg per

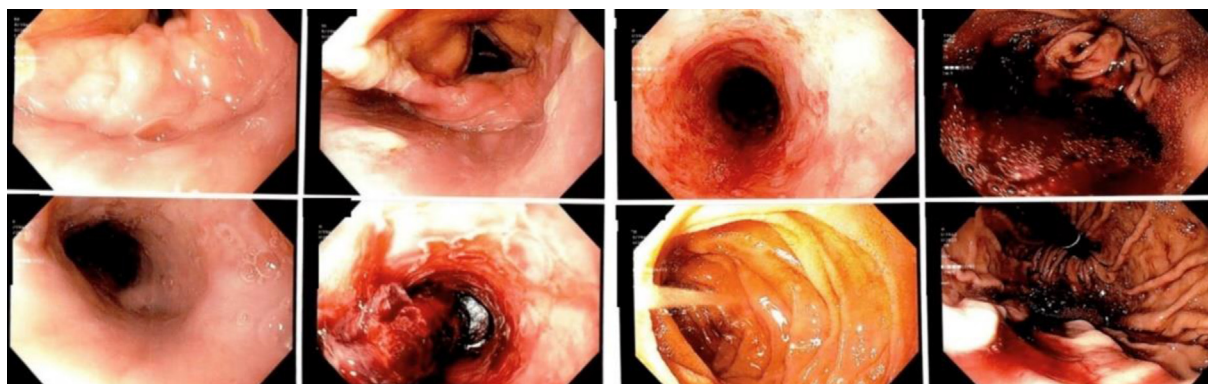


Fig. 2. Esophagogastroduodenoscopy showing posterior pharyngeal erosions and hemorrhagic esophagitis.

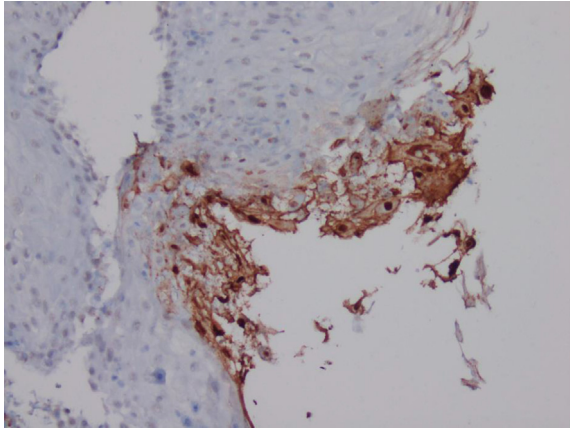


Fig. 5. Positive antibody-antigen immunohistochemical staining for HSV-1.

day. Therefore, it is important to recall that the patient discussed in this case received ten days of IV methylprednisolone 40 mg Q6H before finally showing symptoms of odynophagia; and this was in addition to the chronic 10 mg daily prednisone that this patient had been taking for at least two years, per chart review.

AAFP guidelines for management of COPD exacerbation note that high-dosage corticosteroid (over 30 mg daily) is beneficial in terms of shortening hospital stay and prolonging time between exacerbation among other benefits.⁸ Clinicians should therefore be aware of HSVE as a potential complication of corticosteroid therapy, especially given that such an overwhelming majority of the population has likely been exposed to HSV-1 and that COPD itself is quite prevalent and the third leading cause of death worldwide.^{1,6} Such risks of HSV reactivation should be conveyed to patients when prescribing corticosteroid courses greater than 10 mg daily. As a result, patients with COPD, rheumatoid arthritis, asthma, allergies, inflammatory bowel disease, and other autoimmune conditions would be at risk given their shared usage of corticosteroids for maintenance or abortive therapy.⁶

A limitation of the follow-up in this case is the absence of a repeat EGD or HSV serology either following the cessation of patient's symptoms or after the full 14-day course of antiviral treatment. This would allow the clinician to better evaluate when completed remission occurred, whether it occurred at all following 14 days, or if a longer course was necessary despite resolution of symptoms. Literature does state that immunocompetent hosts may respond quickly when treated with Acyclovir, though the recommended length of treatment ranges from 14 to 21 days depending on disease severity.⁵ Monitoring EGD findings and

HSV serology at various intervals of this disease course would add to current literature in terms of when to expect clinical improvements with this antiviral treatment in patients made susceptible to this disease due to prolonged corticosteroid use.

4. Conclusion

Herpes simplex virus esophagitis (HSVE) has commonly been associated with immunosuppressed patients, specifically HIV-positive or transplant patients. Nevertheless, prolonged corticosteroid treatments at doses of 10 mg or higher have shown to increase the risk of HSV reactivation. Physicians should therefore keep in mind that HSVE is a possible complication of long-term corticosteroid therapy for an acute COPD exacerbation.

Declaration of competing interest

The authors do not have conflicts of interest to declare.

Acknowledgements

Thank you to Dr. Nadia Kousar for her consultation, Dr. Joel Shapiro for the pathology report and images, and Dr. Robert Helft for esophagogastroduodenoscopy images.

References

1. World Health Organization. Herpes simplex virus. Available at: Accessed July 6, 2022 <https://www.who.int/news-room/fact-sheets/detail/herpes-simplex-virus>.
2. American Academy of Family Physicians. Herpes. In: *AAFP Conditions A-Z*. 2022.
3. Albrecht MA. Epidemiology, clinical manifestations, and diagnosis of genital herpes simplex virus infection. In: Hirsch MS, ed. *UpToDate*. UpToDate; 2022. Accessed July 3, 2022 <https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-genital-herpes-simplex-virus-infection#!>.
4. Johnston C, Wald A. Epidemiology, clinical manifestations, and diagnosis of herpes simplex virus type 1 infection. In: Mitty J, ed. *UpToDate*; 2022. Accessed July 3, 2022 <https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-herpes-simplex-virus-type-1-infection#!>.
5. Bonis PA, Kotton CN. Herpes simplex virus infection of the esophagus. In: Mitty J, ed. *UpToDate*; 2022. Accessed July 3, 2022 <https://www.uptodate.com/contents/herpes-simplex-virus-infection-of-the-esophagus#!>.
6. World Health Organization. Chronic obstructive pulmonary disease (COPD). Available at: Accessed May 20, 2022 [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)).
7. Youssef J, Novosad SA, Winthrop KL. Infection risk and safety of corticosteroid use. *Rheum Dis Clin N Am*. 2016;42(1):157–176.
8. Aaron SD, Vandemheen KL, Hebert P, et al. Outpatient oral prednisone after emergency treatment of chronic obstructive pulmonary disease. *N Engl J Med*. 2003;348(26):2618–2625. <https://doi.org/10.1056/NEJMoa023161>.