

A Rare Case of Herpetic Esophagitis in an Immunocompetent Patient with No Risk Factors

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Abstract

Introduction: Herpetic esophagitis (HE) is an esophageal infection caused by herpes simplex virus (HSV). It commonly occurs in immunosuppressive patients but rarely affects immunocompetent people. It presents with odynophagia, dysphagia and/or retrosternal pain. An upper gastrointestinal endoscopy with biopsy is essential to establish the diagnosis. **Case Description:** This is a rare case of a patient who presented to our endoscopic department complaining of epigastric pain, gradual worsening of odynophagia and mild dysphagia within one month with a medical history of hypercholesterinemia and hypertension. He had no history of immunosuppression, or any risk factor for HE such as malnutrition, excessive alcohol consumption or use of corticosteroids, not even gastroesophageal reflux disease. An upper gastrointestinal endoscopy was performed, revealing multiple erosions and ulcers at distal esophagus. Biopsies from the margins of the ulcers and PCR led to the diagnosis of herpetic esophagitis. Due to the severe symptoms, despite the immunocompetent status treatment of acyclovir was administrated leading to a gradual improvement of the symptoms. **Conclusion:** This case highlights that HE could exist in an immunocompetent patient despite the rarity of occurrence and therefore physicians should have a high level of suspicion to make the diagnosis.

Keywords

Herpetic, Esophagitis, Immunocompetent, Risk Factors

1. Introduction

Herpetic esophagitis (HE) is defined as an esophageal infection which occurs by

herpes simplex virus (HSV) and usually affects immunocompromised patients. The vast majority is caused by HSV-1, although very rare cases of HSV-2 infection have been reported [1]. HE is the second most frequent cause of infectious esophagitis, after *Candida albicans* [1] [2]. It may result either from primary infection with HSV and spread of the virus to the esophagus or from reactivation of a latent infection [3] [4]. Esophagus is the most commonly affected organ of the gastrointestinal tract in HSV infected patients, with an incidence of 1.8% [4]. It is worth noting that HE is more common in men compared to women, with a ratio of 3:1 [5].

There are few cases of HE in healthy patients with intact immune systems [2]-[4]. Additionally, risk factors have been identified including malnutrition, excessive alcohol consumption, use of corticosteroids and gastroesophageal reflux disease (GERD) [3] [4].

HE presents with odynophagia (34.8% - 42.6%) and/or dysphagia (30.4% - 42.6%) and gastrointestinal bleeding (13% - 31%) or other symptoms such as fever, nausea, vomiting and retrosternal/epigastric pain [3] [4]. Its diagnosis is based on endoscopy and histopathology examination [3]. Symptoms and complications (stenosis, perforation, bleeding) are more frequent in immunosuppressed patients [1]. In immunocompetent patients, HE often resolves spontaneously within one to two weeks and initiation of treatment further reduces the time course of the disease [3].

We reported a case of HE which is rare because the patient was not immunocompromised and additionally had no risk factors.

2. Case Description

A 69-years-old man, with a history of hypercholesterinemia and hypertension presented to our endoscopic department complaining of epigastric pain, gradual worsening of odynophagia and mild dysphagia within one month without visible oropharyngeal lesions and no previous history of herpes infection. He denied heartburn, anorexia or significant weight loss. He had no history of immunodeficiency syndrome, malnutrition, excessive alcohol consumption or use of corticosteroids. Clinical examination was unremarkable. Initial laboratory tests were normal, except for an elevation of inflammatory markers, such as CRP and ESR. The patient had no evidence of acquired immunodeficiency syndrome, hematologic malignancies, solid tumors, and no history of transplants or undergoing treatment with immunosuppressive drugs. To our knowledge there are few cases of HE in immunocompetent patients and fewer cases of HE in patients with no risk factor for HE not even esophageal reflux disease.

An upper gastrointestinal endoscopy was performed which showed multiple erosions and ulcers at the distal esophagus (**Figure 1**) and biopsies were obtained from the margins of the ulcers. The patient was referred for esophageal pH monitoring which was normal and gastroesophageal reflux disease (GERD) was excluded as possible diagnosis.

Pathology exam from esophageal biopsies revealed acute inflammatory cell infiltrate and marked mononuclear cell infiltrate adjacent to the infected squamous epithelium (**Figure 2**) and presence of eosinophilic intranuclear inclusions of virus (**Figure 3**) without evidence of malignancy or other causes of inflammation. Suspicion of viral infection was raised and the polymerase chain reaction was positive for herpes simplex virus type 1 (HSV-1).

Additionally, IgM and IgG antibodies to HSV-1 were detected. Laboratory studies, were unremarkable including serum tumor markers, such as CEA and Ca19-9. Further tests (serum protein electrophoresis, HIV serology and antinuclear antibodies) to exclude underlying disease were normal. Imaging studies, such as computer tomography and MRI of the neck and thorax did not show any evidence of malignancy.

The final diagnosis of HE was herpetic esophagitis and per os acyclovir was administrated (400 mg three times a day for 10 days) in combination with a proton pump inhibitor (PPI) once a day. The clinical improvement was remarkable, and the oral feeding was well tolerated after the first three days of therapy. PPI continued for the following 6 months once a day.

A repeat upper gastrointestinal endoscopy was performed for 6 months which showed improvement but no elimination of the lower esophageal ulcerations (**Figure 4**). The PPI continued for 6 more months. A follow-up endoscopy at one year revealed a complete response and there was no evidence of inflammation of the esophagus (**Figure 5**).

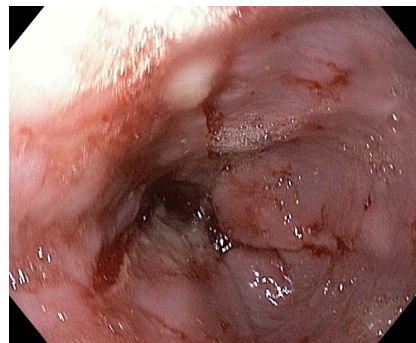


Figure 1. Multiple erosions and ulcers at distal esophagus.

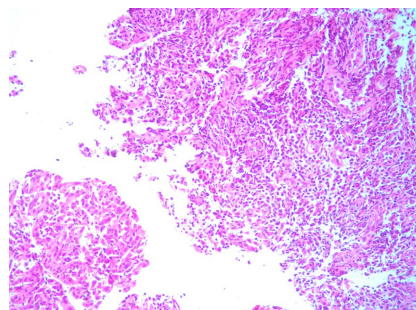


Figure 2. Acute inflammatory cell infiltration and marked mononuclear cell infiltration adjacent to the infected squamous epithelium.

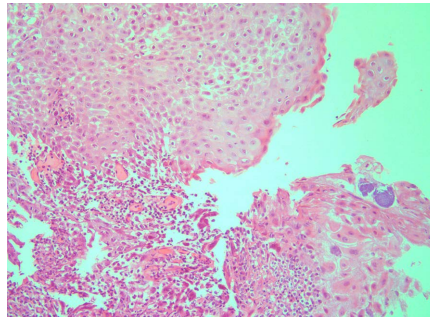


Figure 3. Presence of eosinophilic Intranuclear inclusions.

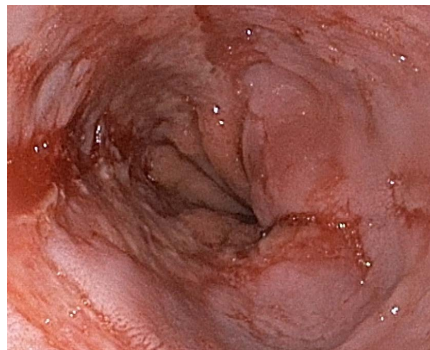


Figure 4. Slight improvement but persistent erosions and ulcers of virus suggestive of HSV infection.



Figure 5. Normal esophageal epithelium.

3. Discussion

Herpetic esophagitis mainly occurs in immunocompromised patients, such as those who suffer from acquired immunodeficiency syndrome, hematologic malignancies, solid tumors, transplant recipients and patients undergoing treatment with immunosuppressive medication but can rarely occur in immunocompetent patients [5]-[8]. Therefore, it is important to suspect this diagnosis especially when there are risk factors such as malnutrition, alcohol consumption or use of corticosteroids [9]. Because GERD is common, esophageal pH monitoring should be performed so esophageal reflux disease would be excluded because it is a risk factor for HE and these two diseases may co-exist [9].

It usually affects young males and is manifested by the acute onset of

odynophagia, dysphagia, retrosternal pain and fever [7]. The most common cause of HE is HSV-1, but HSV-2 may occasionally be incriminated. It may occur after reactivation of a latent infection, but more often is due to primary infection, by local spread of virus. It is proven that herpes virus may infect any traumatized tissue [3]. Several factors that disrupt the esophageal mucosa integrity, such as gastroesophageal reflux are involved in the pathogenesis of HE in the immunocompetent host [3] [4]. The infection may occur from contact of the virus with the traumatized mucosa [10]-[13].

HE usually affects the lower half of the esophagus, and the endoscopy reveals the presence of multiple, small ulcers that may be superficial or may have a “volcano-like” appearance [14]. Biopsies from the margins of the ulcers and PCR detection of HSV DNA in esophageal tissue are the gold standard for the diagnosis [3] [4]. PCR is a technique with a very high sensitivity and specificity in the diagnosis of herpetic infection [15]. Serology tests are of limited value, because of the high prevalence of antibodies to HSV in the healthy adult population, but they are helpful in diagnosing primary infections [1].

Usually, in immunocompetent patients, HE resolves spontaneously after one or two weeks and symptoms improve faster with acyclovir administration (400 mg tid for 7 - 10 days) [15].

The paradox in our case was that despite the fact that patient's symptoms improved with combined therapy of acyclovir and PPI, the endoscopic picture was only partially improved at 6 months from treatment initiation. Long-term PPI therapy for another 6 months led to full esophageal healing for 1 year. This fact raises the question of whether there was an element of GERD contributing to prolonged esophageal pH monitoring. Unfortunately, we have no clear explanation for this paradox. Another question is whether HE affects lower esophageal sphincter function that predisposes to GERD.

4. Conclusion

HE in immunocompetent patients with no risk factor is rare. High levels of suspicion and endoscopy with esophageal biopsies are necessary for accurate diagnosis. Our case indicates that in practice excluding other diseases that may co-exist with HE may be challenging.

Learning Points

- Herpetic esophagitis can cause serious symptoms and requires an increased level of suspicion for diagnosis.
- Upper endoscopy with biopsies and pathology examination is necessary for accurate diagnosis.
- It is common in immunosuppressive patients and rare in immunocompetent patients.

Underlying or co-existent diseases may obscure the diagnosis of HE and cause dilemmas in clinical practice.

Contributors

All the authors contributed to the diagnosis and management of the clinical case. The article was written by AK, with an important contribution of IT.

Patient Consent for Publication

Obtained.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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