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Case Report

HSV-1/HSV-2 Infection is Post- Bone Marrow Transplant Population, Case Review and Discussion of Testing

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Abstract

A male patient in his 70s with a past medical history of coronary artery disease, type 2 Diabetes mellitus, and myelofibrosis status post allogenic PBSCT and stage 1 /grade 2 graft versus host disease (GVHD) who reported new onset esophageal burning, trouble swallowing and dull right upper abdominal pain for 2 months. The patient reported decreased oral intake and a 40-pound weight loss over the past month.

Upon admission her was evaluated to rule out graft versus host disease (GVHD). He had undergone esophagogastroduodenoscopy with dilatation approximately 4 weeks before admission with unremarkable pathology findings and no improvement of symptoms. He denied any fevers, chest pain, shortness of breath, abdominal pain, diarrhea, urinary symptoms, increase in joint pain, or new paresthesia.

Keywords: HSV-1/HSV-2; Discussion of Testing

Medications

He had taken famotidine, omeprazole and over the counter antacids for his symptoms.

Physical examination

The patient appeared alert and oriented. He was afebrile with a temperature of 97.9°F (36.6°C), with normal blood pressure of 116/63 mm Hg, pulse 64 beats per minute, and respirations 18 breaths per minute, with an oxygen saturation of 98% while breathing ambient air. He had diffused non-painful maculopapular rash on the back and two previously noted healed ulcers, one on each foot. The physical examination was otherwise normal.

Studies

The white blood cell count was 11,100 cells/μL, with 82% neutrophils, 13% lymphocytes, and 4% monocytes. Serum alkaline phosphatase (ALP) was 187 U/L, alanine aminotransferase (ALT) was 119 U/L and aspartate aminotransferase (AST) 93 U/L. Bilirubin level was normal. Molecular tests for viral agents included. Epstein-Barr virus (EBV) PCR (< 500 copies, Dynamic range: 250 - 250,000,000 copies/mL), Cytomegalovirus (CMV) PCR (no Cytomegalovirus viral DNA detected, Dynamic range:137 - 9,100,000 IU/mL), Human herpesvirus 6 (HHV6) PCR (Negative), and Adenovirus PCR (negative). His HSV- 1/HSV- 2 IgM antibodies were negative at the time of his pre-transplant evaluation.

His C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Rheumatoid factor (RF), and antinuclear antibody (ANA) were within normal limits. Other routine laboratory tests were normal. A chest and abdominal radiographs were normal.

What is the cause of the patient difficulty of swallowing?

- GVHD.
- Esophageal candidiasis.
- Pancreatitis.
- Viral esophagitis.
- Autoimmune disorder.

Diagnostic procedure(s) and result(s)

Endoscopic examination showed esophageal erythema with patches of fibrinous material (Figure 1). Biopsies from these areas showed an ulcerated mucosa in inflammatory background with multiple multinucleated cells and cells with intranuclear inclusions (Figure 2) characteristic of herpes simplex virus (HSV) infection. Immunohistochemical stain for HSV- 1 was positive (Figure 3). HSV 1/2 virus was isolated from esophageal tissue viral culture, confirming the diagnosis.

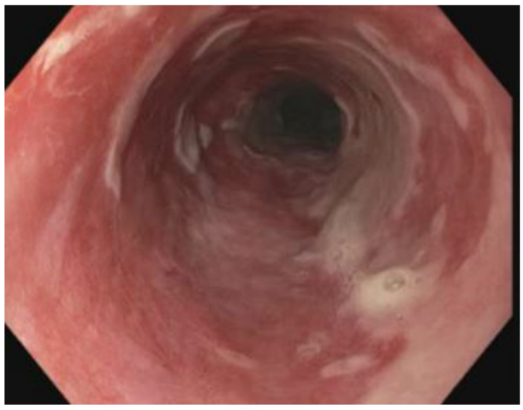

Figure 1

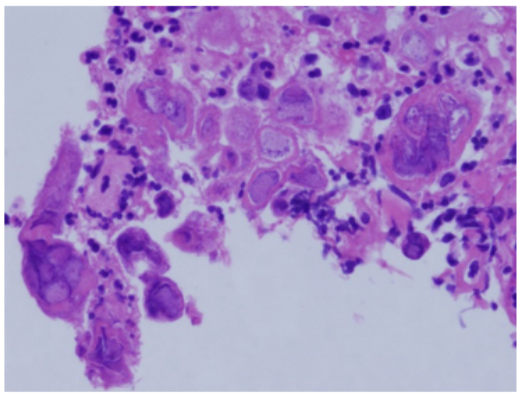

Figure 2

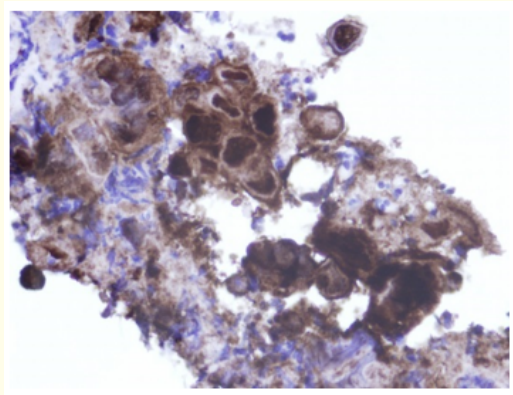

Figure 3

Treatment and follow-up

Intravenous acyclovir was begun at a dose of 10 milligrams per kilogram (mg/kg) QD. The patient was then transitioned to oral acyclovir suspension upon improvement of dysphagia to complete total 14 -day course.

Discussion

Herpes esophagitis (HE) is one of the leading causes of esophagitis (second to *Candida* sp.) in immunocompromised patients, although cases of herpes esophagitis have also been rarely documented in immune competent hosts [9]. HE is observed in up to 10 - 15% of bone marrow transplant patients [1,10]. HE occurs with more frequency in patients who are HSV seropositive prior to the transplant, supporting that HSV infection post-transplant is due to a viral reactivation of a latent infection in this population [2]. Prophylactic therapy is recommended for HSV-1/HSV- 2 IgG positive patients early in the course of transplant with longer duration recommended in patients with prior history of viral reactivation. Only HSV-1/HSV- 2 IgM antibodies were ordered in our patient as part of his pre-transplant workup which highlights a potential avoidable pitfall.

The most common observed symptoms were dysphagia and odynophagia in a series of 77 immunosuppressed patients [3]. The endoscopic findings can vary from multiple superficial ulcers with vesicles formation to erythematous non-ulcerated inflammatory changes, less commonly [4]. The lesions are typically found in the

lower third of the esophagus in immunocompromised patients [4]. The diagnosis is routinely based on endoscopic findings and histopathologic examination with brush cytology and biopsies. The observed changes on hematoxylin and eosin sections include ballooning degeneration, ground-glass nuclei, multinucleated giant cells and Cowdry type A inclusions (eosinophilic nuclear inclusions) [5] with typical histopathologic changes found at the edge of the ulcerated lesions. In addition, non-specific inflammatory changes with mixtures if neutrophils, macrophages and necrotic debris is typically present at the ulcer bed. Immunohistochemistry (IHC) is the most common method to detect the HSV viral particles and nucleic acid in the infected paraffin-embedded tissue [6]. IHC for CMV and special stains for fungal organisms should still be performed to rule out the possibility of a mixed infection [7]. Viral cultures and HSV qualitative PCR can be used in case of suspicion of HE remains following a negative biopsy or patients who fail to respond to acyclovir.

Conclusion

Recommended treatment is IV acyclovir (5 - 10 mg/kg three or 4 times a day for 7 to 14 days) for patients who can not tolerate oral therapy with possible transition to oral therapy upon improvement of symptoms [1]. Cases with suspected resistance to acyclovir can be managed with foscarnet which is associated with higher profile of negative side effects [8,11].

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Volume 3 Issue 12 December 2019