

CASE REPORTS

# Upper GI Bleeding with Hemorrhagic Shock Caused by Infectious Esophagitis

Daniela Tabacelia<sup>1</sup>, Madalina Ilie<sup>1</sup>, Gabriel Constantinescu<sup>1</sup>, Radu Tincu<sup>2</sup>, Bogdan Popa<sup>3</sup>, Raluca Stanciulescu<sup>4</sup>, Valentin Enache<sup>5</sup>, Dragos Ene<sup>6</sup>

## Abstract

Massive gastrointestinal bleeding is rarely caused by infectious etiologies especially with esophageal localization. Even if Cytomegalovirus Infection (CMV) is not often encountered in the clinical practice, it has to be taken into account when the cause of GI hemorrhage is not obvious. We report a case of a 53 years old, male patient, with diabetes who is admitted in the hospital for cellulitis of the left calf and who developed massive hematemesis with no obvious source at the upper GI endoscopy. The patient was treated conservatively with PPI and transfusions of blood but he repeated the hemorrhage after 5 days with severe hypotension and a drop of hemoglobin to 6g/dl. The second endoscopy revealed massive clots in the esophagus with erythema and deep ulcers underneath while the stomach and duodenum were normal. Multiple biopsies were taken from esophageal ulcers and normal mucosa. We suspected viral esophagitis with CMV and we started treatment with Valganciclovir for 21 days with favorable clinical course. The infection was then confirmed by the pathology department and the immunohistochemical studies. The control endoscopy after one month showed healed esophageal ulcers with minimal residual lesions.

**Keywords:** Cytomegalovirus infection, GI hemorrhage, Valganciclovir

## Rezumat

Hemoragia digestivă superioară este rar cauzată de etiologii infecțioase, mai ales cu localizare esofagiană. Chiar dacă infecția cu Citomegalovirus nu este foarte frecvent întâlnită în practica clinică, trebuie luată în considerare când cauza hemoragiei digestive nu este evidentă. Raportăm cazul unui pacient de sex masculin în vârstă de 53 de ani, cu diabet zaharat care se internează pentru celulita gambei stângi și care prezintă pe parcursul internării un episod de hemoragie digestivă superioară fără sursă decelabilă endoscopic. Pacientul este tratat conservator cu inhibitor de pompă de protoni și transfuzii de MER dar după 5 zile dezvoltă un nou episod de hematemază masivă cu hipotensiune și scăderea hemoglobinei la 6 g/dl. Endoscopia evidențiază multiple cheaguri în esofag, ulcere adânci și eritem fără leziuni gastrice sau duodenale. Se prelevează biopsii multiple esofagiene. Suspectăm esofagita virală cu CMV și inițiem tratament empiric cu Valganciclovir timp de 21 zile. Infecția este ulterior confirmată de departamentul de anatomie patologică și studiile imunohistochimice. Endoscopia de control după o lună arată ulcere esofagiene vindecate cu minime leziuni reziduale.

**Cuvinte cheie:** Infecția cu Citomegalovirus, Hemoragie gastrointestinală, Valganciclovir

<sup>1</sup> Department of Gastroenterology, Emergency Clinical Hospital, Bucharest, Romania

<sup>2</sup> Department of ICU and Toxicology, Emergency Clinical Hospital, Bucharest, Romania

<sup>3</sup> Department of Radiology, Emergency Clinical Hospital, Bucharest, Romania

<sup>4</sup> Department of Gastroenterology, Sanador Hospital, Bucharest, Romania

<sup>5</sup> Department of Pathology, Emergency Clinical Hospital, Bucharest, Romania

<sup>6</sup> Department of General Surgery, Clinical Emergency Hospital, Bucharest, Romania

### Corresponding author:

**Madalina Ilie**

Emergency Clinical Hospital, 8<sup>th</sup> Floreasca Avenue, 1<sup>st</sup> District, Bucharest, Romania.

E-mail: drmadalina@gmail.com

## BACKGROUND

CMV infection in healthy hosts is generally asymptomatic, producing a latent infection with antibodies persisting for months or even years after the recovery. In the population at risk, CMV infection is one of the most frequent opportunistic infection<sup>1,2</sup>. The most frequent GI manifestation of CMV infection is colitis followed by esophagitis although it can affect all organs<sup>1,3</sup>. CMV esophagitis has been reported in immunocompromised hosts by conditions like organ transplantation, bone marrow transplantation, in patients with HIV infection and AIDS or other debilitating diseases<sup>2,4</sup>.

The most common symptoms in CMV esophagitis are severe pain (odynophagia) and /or dysphagia. Fever is seen in only 20% of patients and a higher percent exhibit nausea and vomiting. Symptoms are indistinguishable from other forms of esophagitis (Candida or HSV esophagitis)<sup>1,5,6</sup>. The histological feature is represented by mucosal ulcerations; the endoscopic appearance is variable, with multiple or solitary large “punched-out” ulcers located in the middle or distal esophagus<sup>2,7</sup>. Rare complications include strictures, fistulae to the tracheobronchial tree and gastrointestinal bleeding (5% of patients)<sup>8</sup>. Serological testing is not always helpful, especially in immunosuppressed patients who fail to develop antibodies making the mucosal biopsies the best diagnostic method<sup>9</sup>.

The treatment requires intravenous administration of antiviral therapy with ganciclovir, foscarnet or cidofovir, Valganciclovir for a variable period of time based on clinical and endoscopic response<sup>1,10</sup>. For the immunocompetent host a course treatment of 2 to 4 weeks is usually recommended. In transplant recipients, treatment should be maintained for 1 to 2 months in contradistinction to patients that receive the HA-ART treatment and only need closely surveillance after a complete response to the antiviral therapy has been recorded<sup>11</sup>.

## CASE REPORT

We present the case of a therapeutically neglected 53 years old, male patient, with diabetes, who is admitted in the hospital for cellulitis of the left calf. Arteriography of the left femoral artery and amputation of the three toes were performed. After 10 days of hospitalization, the patient developed massive hematemesis but the upper GI endoscopy revealed a large number of clots in the esophagus with no obvious source of bleeding. The control endoscopy showed erosions and erythema in the lower third of the esophagus with no

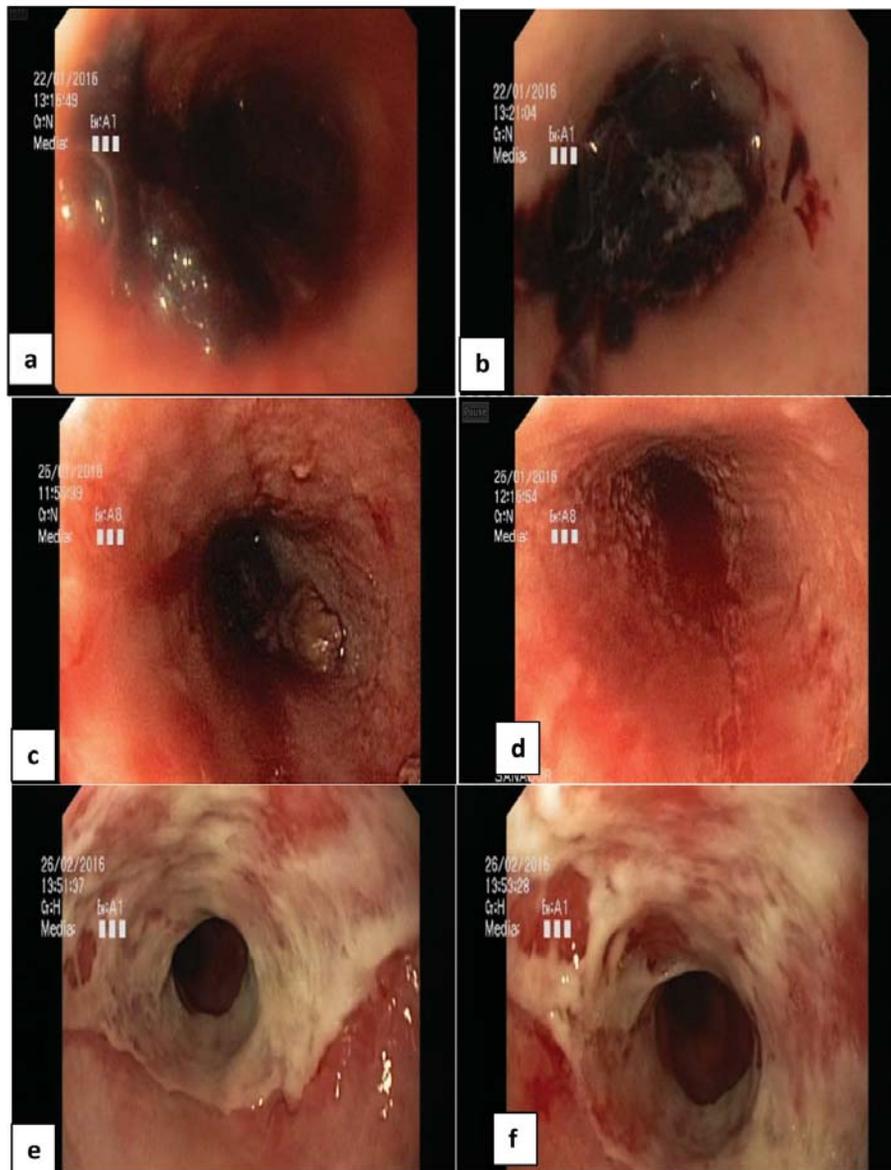
blood. The patient is treated conservatively with PPI and transfusions of blood. He is apparently well but after 5 days a new episode of massive hematemesis was encountered with altered conscious state, severe hypotension (90/50 mmHg) and a drop of hemoglobin from 8g/dl to 6g/dl. The endoscopy was performed in the ICU department with the patient intubated and it revealed massive clots in the distal esophagus that were removed with the snare. Underneath the clots severe esophagitis lesions with erythema and deep ulcers throughout the esophagus were noticed while the stomach and duodenum were normal raising the suspicion of viral esophagitis. Multiple biopsies were taken from esophageal ulcers and normal mucosa although the test was negative for CMV, HSV and EBV. HIV serologic test was negative too.

We suspected viral esophagitis with CMV and we started treatment with Valganciclovir 900 mg/day for 21 days. The clinical course was favorable with no episode of rebleeding. The surprise has come from our pathology department which confirmed the presence of granular intracytoplasmic inclusion bodies imparting the characteristic of an “owl’s eye” appearance (Figure 2). The immunohistochemical studies confirmed the presence of CMV. The control endoscopy after one month showed healed esophageal ulcers with minimal residual lesions.

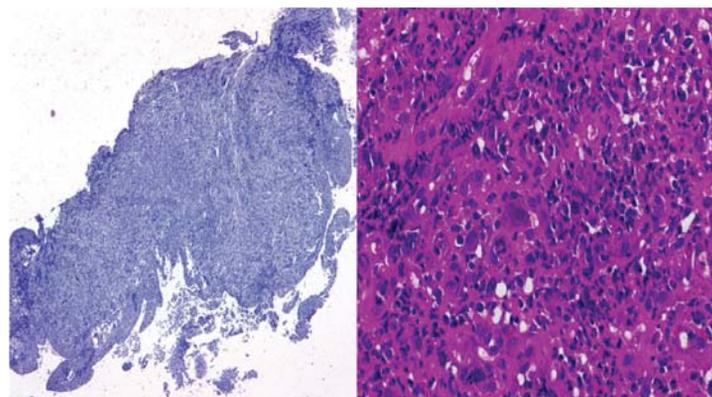
## DISCUSSIONS

The prevalence of viral esophagitis in immunocompromised patients has fallen in the past years because of the screening serology and antiviral prophylaxis performed especially in the population at risk, but severe life-threatening complications are still a major problem even in the immunocompetent patients<sup>12,13</sup>.

Since serology and conventional viral cultures cannot reliably differentiate past exposure to CMV from active infection in immunocompromised patients, the diagnosis of CMV infection is generally based on histologic examination of involved tissues. The following morphologic criteria are used to diagnose CMV infection by hematoxylin and eosin (H&E) staining: more than three times normal cellular enlargement; presence of homogeneous eosinophilic intranuclear inclusion bodies; and presence of granular intracytoplasmic inclusion bodies imparting the characteristic “owl’s eye” appearance to the cell. The presence of two of these criteria constitutes positivity by H&E staining in most studies<sup>14</sup>. The more sensitive method to detect CMV antigen is the immunohistochemical staining. Another way to predict CMV disease is the CMV quantitative



**Figure 1.** a, b) The initial endoscopy with massive clots in the esophagus; c, d) the second endoscopy after the repeated hemorrhage and removal of the clots with the snare – severe esophagitis with mucosal ulcers and erythema; E, f) the control endoscopy after one month showed healed esophageal ulcers with minimal residual lesions.



**Figure 2.** The first image showing nuclear reaction in rare cellular elements of granulation tissue and in the second image granulation tissue with rare endothelial cells with nuclear changes suggestive of CMV infection.

polymerase chain reaction or the CMV antigenemia assay; both are used in monitoring the efficacy of the treatment.

In this case the main challenge was initiation of antiviral treatment without confirmation of the diagnosis. The fact that the patient hasn't responded to the proton-pump inhibitor treatment, diabetes comorbidity and the endoscopic aspect different from reflux esophagitis, all these led to the suspicion of viral esophagitis. The antiviral treatment has been a major aid in the healing of esophageal lesions and saved the pati-

ent from a emergent esophagectomy which could have been fatal for him.

## CONCLUSIONS

Cytomegalovirus infectious esophagitis causing upper GI bleeding with hemorrhagic shock is rarely reported in the literature. We should consider this etiology in immunocompromised patients with non-peptic ulcerative esophagitis. Initiation of early antiviral treatment even without a histology result represents the key for a therapeutic success being lifesaving.

## References

1. Yamada's Textbook of Gastroenterology, sixth edition, 2016 by John Wiley & Sons Ltd., Esophageal infections and disorders associated with acquired immunodeficiency syndrome; 51: 943-945.
2. Sleisenger and Fordtran's Gastrointestinal and Liver diseases, 10th edition, 2016, Gastrointestinal Consequences of Infection with Human Immunodeficiency Virus; 34: 543-545.
3. Current Diagnosis and Treatment Gastroenterology, Hepatology and Endoscopy, Norton J. Greenberger, third edition, 2015 Gastrointestinal Manifestation in Immunodeficiency; 135:150.
4. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738092/> Severe Cytomegalovirus-Associated Esophagitis in an Immunocompetent Patient after Short-Term Steroid Therapy, Jan Weile,1,3,+\* Benjamin Streeck,2,+ Johannes Muck, 2Gerd Krebs,2 Karl-Heinz Jakobus, 2Cornelius Knabbe, 1 and Friedhelm Weber2
5. Rafailidis, P., E. G. Mourtzoukou, I. C. Varbobitis, and M. E. Falagas. 2008. Severe cytomegalovirus infection in apparently immunocompetent patients: a systematic review. *Virology*. 547. [PMC free article] [PubMed]
6. Atlas of Clinical Gastrointestinal Endoscopy, third edition, 2012, C. Mel Wilcox, Esophagus; Differential Diagnosis in Herpes Simplex Virus Esophagitis; 2:52-55.
7. Management of cytomegalovirus infection and disease in liver transplant recipients; 2014 Jun 27; Jackrapong Bruminhent and Raymond R Razonable.
8. Piiparinen H, Helanterä M, Lappalainen M, et al. Quantitative PCR in the diagnosis of CMV infection and in the monitoring of viral load during the antiviral treatment in renal transplant patients. *J Med Virol* 2005;76:367
9. LePage AK, Jager MM, Iwasenko JM, et al. Clinical aspects of cytomegalovirus antiviral resistance in solid organ transplant recipients. *Clin Infect Dis* 2013; 56:1018
10. Wiltshire H, Hirankarn S, Farrell C, et al. Pharmacokinetic profile of ganciclovir after its oral administration and from its prodrug, valganciclovir, in solid organ transplant recipients. *Clin Pharmacokinet* 2005;44:495.
11. Etiology, diagnosis and treatment of infectious esophagitis, 2013 Dec 30, Mariusz Rosołowski1 and Maciej Kierzkiewicz2
12. The immune response to human CMV, 2012 Mar 1; Corinna La Rosa and Don J Diamond
13. Gastric Ulcer Associated with Cytomegalovirus in an Immunocompetent Patient: Method for Diagnosis, 2012 Jun 14; Chikara Ebisutani,a,\* Akira Kawamura,a Norihito Shibata,a Masamichi Nasu,a Rei Ueno,a Keiko Mimura,b and Yoshikazu Kinoshita
14. The immunological footprint of CMV in HIV-1 patients stable on long-term ART, 2015 Oct 1; Jacquita S. Affandi, Jacinta Montgomery, Samantha J. Brunt, David Nolan, and Patricia Price.