



## Case report

# A case report of small bowel perforation secondary to cytomegalovirus related immune reconstitution inflammatory syndrome in an AIDS patient



Eva María Gutiérrez-Delgado <sup>a</sup>, Hiram Villanueva-Lozano <sup>a</sup>, Miguel J. García Rojas-Acosta <sup>b</sup>, Ivett C. Miranda-Maldonado <sup>c</sup>, Javier Ramos-Jiménez <sup>a,\*</sup>

<sup>a</sup> Infectious Diseases Service, Internal Medicine Department, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Mexico

<sup>b</sup> Ophthalmology Service, Clínica Cuauhtémoc Moctezuma, Monterrey, Mexico

<sup>c</sup> Department of Pathological Anatomy and Cytopathology, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Mexico

## HIGHLIGHTS

- Cytomegalovirus (CMV) is the main etiology of non-traumatic perforation of the small bowel in immunocompromised individuals.
- We describe a case of CMV associated Immune reconstitution inflammatory syndrome.
- To our knowledge this is the first case of small bowel perforation due to IRIS related CMV.
- It is of importance for the clinician to consider CMV related IRIS as a cause of acute abdomen.

## ARTICLE INFO

## Article history:

Received 14 August 2016

Received in revised form

6 November 2016

Accepted 6 November 2016

## Keywords:

Small bowel

Intestinal perforation

Non-traumatic perforation

Cytomegalovirus

IRIS

## ABSTRACT

Non-traumatic small bowel perforation is rare in adults but carries a high morbidity and mortality. The diagnosis is made on clinical suspicion, and the most common causes in developing countries are infectious diseases, being cytomegalovirus infection in immunocompromised patients the main etiology. We describe a patient with a recently diagnosed advanced stage HIV infection and an intestinal perforation associated with cytomegalovirus immune reconstitution inflammatory syndrome after highly active antiretroviral therapy initiation.

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## 1. Introduction

Non-traumatic small bowel perforation is rare, both in the general population and in patients with HIV [1]. Immune reconstitution inflammatory syndrome (IRIS) is a condition seen in some

cases of AIDS or other immunosuppressive conditions, in which the recovery of the immune system causes an exaggerated inflammatory response to a previously acquired opportunistic infection. Among its causes are cytomegalovirus infection and manifestations of IRIS. Cytomegalovirus (CMV) infection usually presents in immunocompetent patients as a mononucleosis-like syndrome which almost always is self-limiting but in immunocompromised patients it commonly causes organ-specific damage such as retinitis, polyradiculopathy, meningoencephalitis, esophagitis, and colitis. All of these can cause disability or even death if they are not treated promptly and adequately [2].

In this report we describe a case of small bowel and colon perforation due to CMV related IRIS, which is not a entity frequently

\* Corresponding author. Francisco I., Madero y Av., Gonzalitos, Mitras Centro, Monterrey, Nuevo León, Mexico.

E-mail addresses: [evagutierrez\\_84@hotmail.com](mailto:evagutierrez_84@hotmail.com) (E.M. Gutiérrez-Delgado), [dr.villanueval@hotmail.com](mailto:dr.villanueval@hotmail.com) (H. Villanueva-Lozano), [drgaroaretina@gmail.com](mailto:drgaroaretina@gmail.com) (M.J. García Rojas-Acosta), [imiranda77@hotmail.com](mailto:imiranda77@hotmail.com) (I.C. Miranda-Maldonado), [javramos31@hotmail.com](mailto:javramos31@hotmail.com) (J. Ramos-Jiménez).

thought for the clinician in the differential diagnosis of intestine perforation, highlighting the importance of consider IRIS as a cause of acute abdomen complication in the AIDS patient after the initiation of antiretroviral therapy, specially those with baseline low CD4<sup>+</sup> count.

## 2. Presentation of case

The patient, a 40-year-old male who has sex with men, entered the hospital in July 2015 due to severe diffuse abdominal pain. He was diagnosed with HIV-1 two months prior with CD4<sup>+</sup> baseline level of 54 cells/mm<sup>3</sup>. Antiretroviral regimen was started one month before admission consisting of tenofovir disoproxil fumarate, emtricitabine, and efavirenz. Also, one month before hospitalization, he was treated with oral valganciclovir because of CMV retinopathy diagnosis, manifested as a decrease in visual acuity. In this occasion on physical exploration, the patient presented abdominal pain on gentle palpation, rebound tenderness, and abdominal wall rigidity. On a CT of the abdomen splenomegaly, multiple lymphadenopathy and free fluid in the abdomen were found. On admission, blood tests showed a CMV viral load in total blood of 10 copies/mL and an undetectable HIV viral load (<20 copies/mL); the leukocyte count was 12,000 cells/ $\mu$ L. At the ophthalmologic exploration, chorioretinitis and macular edema were found. Subsequently, optical coherence tomography of both eyes showed a normal central retina with a central macular thickness of 264  $\mu$ m, while in the left eye a diffuse macular thickening of 744  $\mu$ m at the center point with the presence of intraretinal cysts in all layers of the retina was observed; this changes compatible with macular edema. No data of retinitis or cell inflammation in the vitreous cavity were found; something we would expect in a case of CMV retinitis.

The patient was taken to the operating room and an exploratory laparotomy was performed. A perforation one meter distal to the Treitz angle in the jejunum was found, so a side-to-side anastomosis of the small bowel was performed and vancomycin, caspofungin, levofloxacin and ganciclovir were started. Acute and chronic inflammation was found in histopathological sections with cytopathic changes consisting of cells with enlarged nuclei surrounded by a clear halo (Fig. 1), these were associated to acute peritonitis and lymphoid hyperplasia of Peyer's patches. Areas of recent bleeding, ulceration, and erosion zones with granulation tissue were also seen CMV presence in the tissue was confirmed by immunohistochemistry (Fig. 2). The patient was discharged home 17 days after surgery and seven days later antiretrovirals were

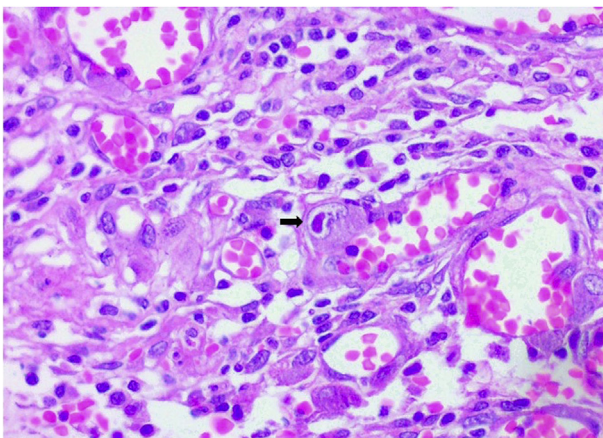


Fig. 1. Arrow indicates cytoplasmic inclusion in cytomegalovirus-infected cell.

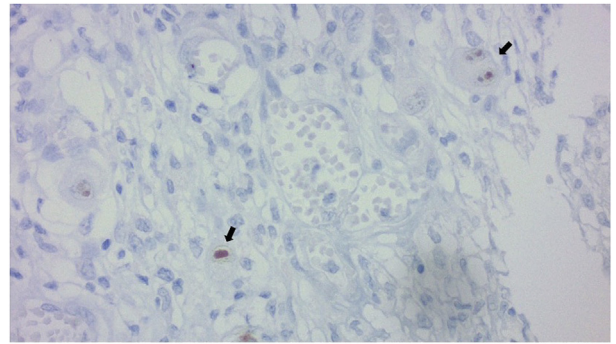


Fig. 2. Cytomegalovirus infected cells evidenced by immunohistochemistry.

reinitiated and CMV treatment was switched from ganciclovir to oral valganciclovir.

The patient was readmitted 15 days later after sudden, severe, generalized abdominal pain. Rebound tenderness was found on exploration, therefore a new exploratory laparotomy was done finding multiple adhesions, and dissection of the colon at the splenic angle flexure. A colonic perforation without local abscesses was detected and intestinal resection, colostomy and a mucocutaneous fistula were done. A second histopathology study described a perforated wall and ulcerated colon associated with a mixed inflammatory process with a foci of granulomatous reaction and cytopathic changes suggestive of CMV. Subsequently, the patient was restarted on intravenous ganciclovir until the oral route was feasible after that, oral valganciclovir was given.

## 3. Discussion

Small bowel perforation in adults can result from obstruction that causes gangrene, hernia strangulation or trauma [3]. Traumatic small bowel perforation is not uncommon but can be fatal, subsequent peritonitis can lead to multi-organ failure and death unless prompt therapy is established [1]. Furthermore, perforation of the terminal ileum should be considered as a possibility in the case of dark peritonitis [4]. Non-traumatic perforation of the small intestine is rare, with an incidence of 1 case per year per 350,000 inhabitants with a mortality of 15–39%; some authors attribute this to a non-specific clinical picture resulting in a delayed diagnosis [5].

The clinical picture of small intestine perforation is non-specific [1]. Wani et al. published in 2006 a review of 79 cases. All patients had abdominal pain but only 32% presented rigidity. Also, only 57% had fever, and leukocytosis was present in 29% of cases [4]. The diagnosis was mainly clinical with imaging studies showing free gas with a low diaphragm in some cases (17–37% are evident on radiography, but generally, the cause is established after surgical treatment) [1,3,5].

Sometimes perforation is contained because of its retroperitoneal location, with development of an abscess, and an insidious clinical picture. This is in contrast with free perforation in which the clinical picture is more spectacular and sudden [3].

Causes of non-traumatic perforation of the small bowel can be divided into inflammatory (eg. Crohn's disease); infectious, associated with drugs such as indomethacin; congenital (Meckel's diverticulum); metabolic (homocystinuria); vascular (granulomatous arteritis); and due to primary and secondary malignancies [3]. The most common causes in the general population in developing countries are tuberculosis and typhoid disease, while in developed countries, the main etiologies are Crohn's disease and neoplasms [1].

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