

# **Case Study**

Andrew Beany M.D  
GI unit, Bnai Zion MC  
May 2016

# Case study

- D.Y., 66 year-old male
- Admitted on the 23.11.15 due to refractory nausea and vomiting
- Medical history
  - HTN
  - Chronic kidney disease (Cr=1.2)
- Chronic medication
  - Tritace comb® 5 mg /25 mg



## Differential diagnosis of nausea and vomiting

### Medications and toxic etiologies

Cancer chemotherapy  
Severe - cisplatin, dacarbazine, nitrogen mustard  
Moderate - etoposide, methotrexate, cytarabine  
Mild - fluorouracil, vinblastine, tamoxifen

Analgesics  
Aspirin  
Nonsteroidal antiinflammatory drugs  
Auranofin  
Antigout drugs  
Cardiovascular medications  
Digoxin  
Antiarrhythmics  
Antihypertensives  
Beta blockers  
Calcium channel antagonists

Diuretics  
Hormonal preparations/therapies  
Oral antidiabetics  
Oral contraceptives  
Antibiotics/antivirals  
Erythromycin  
Tetracycline  
Sulfonamides  
Antituberculous drugs  
Acyclovir  
Gastrointestinal medications  
Sulfasalazine  
Azathioprine  
Nicotine  
CNS active drugs  
Narcotics  
Antiparkinsonian drugs  
Anticonvulsants  
Antiblasthmatics  
Theophylline  
Radiation therapy  
Ethanol abuse  
Jamaican vomiting sickness  
Hypervitaminosis

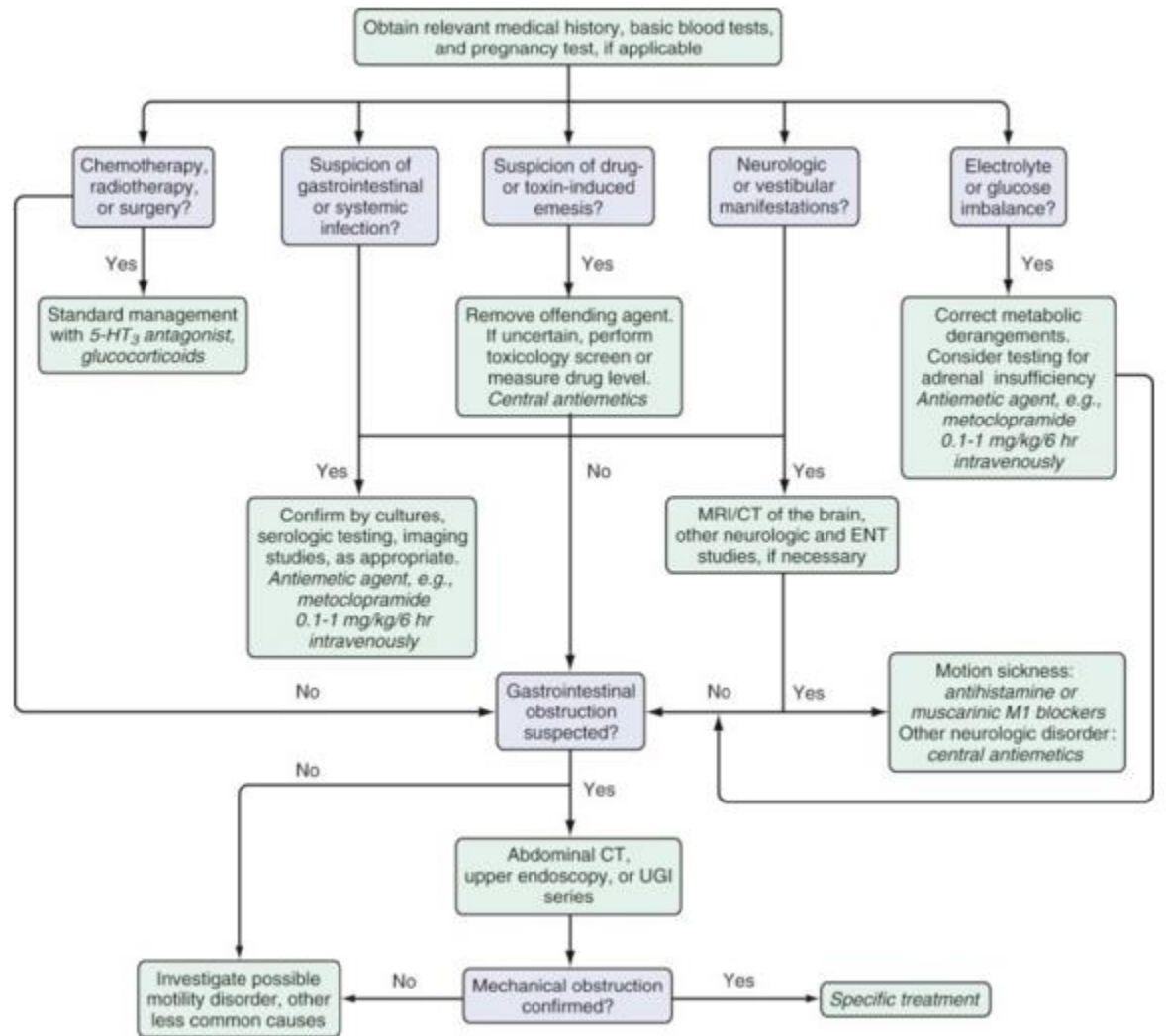
### Infectious causes

Gastroenteritis  
Viral  
Bacterial  
Nongastrointestinal infections  
Otitis media

### Disorders of the gut and peritoneum

Mechanical obstruction  
Gastric outlet obstruction  
Small bowel obstruction  
Functional gastrointestinal disorders  
Gastroparesis  
Chronic intestinal pseudo-obstruction  
Nonulcer dyspepsia  
Irritable bowel syndrome  
Organic gastrointestinal disorder  
Pancreatic adenocarcinoma  
Inflammatory intraperitoneal disease  
Peptic ulcer disease  
Cholecystitis  
Pancreatitis  
Hepatitis  
Crohn disease  
Mesenteric ischemia  
Retroperitoneal fibrosis  
Mucosal metastases

### CNS causes



Radiation therapy to the upper and lower chest

# History

- A month prior to admission the patient returned from a trip to China
- Upon his return, he started complaining of weakness, night sweating, decreased appetite, anorexia, nausea, vomiting and diarrhea
- No fever, abdominal pain or prominent respiratory complaints were reported



# No History of

- Blood transfusion
  - Smoking
  - Alcohol abuse
  - Aspirin or NSAIDs
  - Physical or mental stress
- 

# History

- Ambulatory CXR - susp. LLL consolidation
  - Treated with Cefuroxime and Roxithromycin
- 8.11.15 - CMV IgM - positive, IgG - 39
- 23.11.15 - CMV IgM – weak positive, IgG – 78

# Physical examination

- Weak and ill
- Vital signs- normal
- Scant petechial skin eruption
- Abdomen- normal

## ספירת דם - מכשיר

טווח	ת. ייחוס	יחידות	תוצאה	בדיקה
[.....]*	4.00 - 11.00	X10 <sup>3</sup> /MM <sup>3</sup>	11.10 H	WBC
[...*.....]	4.50 - 6.50	X10 <sup>6</sup> /MM <sup>3</sup>	5.10	RBC
[...*.....]	13.50 - 17.50	GR/DL	15.00	HGB
[...*.....]	40.00 - 52.00	%	46.00	HCT
[.....*..]	80.00 - 95.00	FL	90.20	MCV
[...*.....]	27.00 - 32.00	pg	29.40	MCH
[...*.....]	31.00 - 35.00	g/dl	32.60	MCHC
[...*.....]	11.50 - 14.50		11.90	RDW
[.....*..]	150.00 - 400.00	X10 <sup>3</sup> /MM <sup>3</sup>	341.00	PLT
*[.....]	7.00 - 10.00	FL	6.38 L	MPV
[.....*..]	40.00 - 75.00	%	68.50	NEUTRO%
[...*.....]	20.00 - 45.00	%	25.50	LYMPHO%
[...*.....]	2.00 - 10.00	%	5.37	MONO%
*[.....]	1.00 - 6.00	%	0.51 L	EOS%
[.....*..]	< 1.00	%	0.13	BASO%
		X10 <sup>3</sup> /MM <sup>3</sup>	7.57	Abs.Neutro.count
			---	IRF

## בדיקות קרישה

טווח	ת. ייחוס	יחידות	תוצאה	בדיקה
[...*.....]	70 - 120	%	90	PT %
[.....*..]	0.85 - 1.20	INR	1.07	PT-INR
[...*.....]	24.2 - 33.8	sec.	25.7	APTT
		R	0.86	PTTR

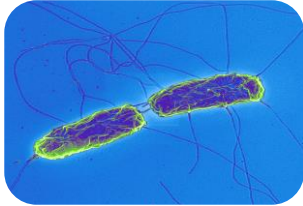
## BLOOD CHEMISTRY

בד"קה	תוצאה	יחידות	ת. ייחוס	טווח	
Glucose-B	100	MGR/DL	70 - 105	[.....*.]	
Urea-B	33	MGR/DL	15 - 40	[.....*.]	
Creatinine-B	1.4	H	MGR/DL	0.7 - 1.3	[.....]*
Sodium-B	137	MEQ/L	135 - 145	[.*.....]	
Potassium-B	5.1	MEQ/L	3.5 - 5.1	[.....*]	
Chloride-B	99	MEQ/L	98 - 107	[.*.....]	
Bilirubin, total-B	0.9	MGR/DL	0.2 - 1.2	[.....*..]	
AST(GOT)-B	16	U/L	8 - 38	[..*.....]	
ALT(GPT)-B	20	U/L	8 - 41	[..*.....]	
Alkaline Phosphatase-B	92	U/L	40 - 129	[.....*..]	
Gamma Glutmine Transaminase -B	21	U/L	11 - 50	[..*.....]	
Amylase-B	106	H	U/L	30 - 100	[.....]*
C-reactive protein-B	16.7	H	MGR/L	< 6.0	[.....]*

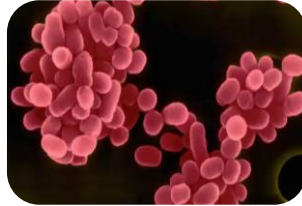
## BLOOD GAS

טווח	ת. ייחוס	יחידות	תוצאה	בדיקה
[....*....]	7.350 - 7.450		7.396	pH
[.*.....]	34.0 - 45.0	mmHg	36.3	pCO2
*[.....]	90.0 - 100.0	mmHg	12.7      L	pO2
[. *.....]	21.0 - 24.0	meq/l	21.8	HCO3 bicarbonate
	(-3) - (+3)	mmol/l	-4.6	ABE
*[.....]	95.0 - 100.0	%	13.9      L	sO2

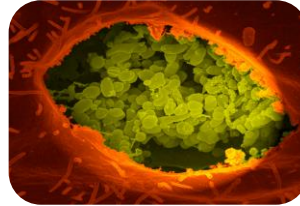




Typhoid



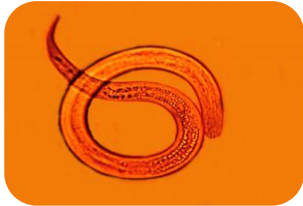
Brucella



Q Fever



Legionella



Strongyloides



Leptospira



Fasciola



Campylobacter



Yersenia



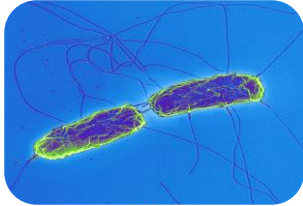
Other

# Course of Admission

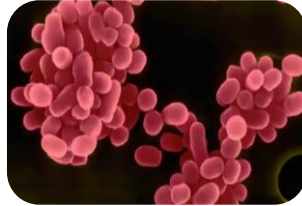
- Continuous and refractory vomiting
- 24.11.15 - Melena

# Upper GI endoscopy

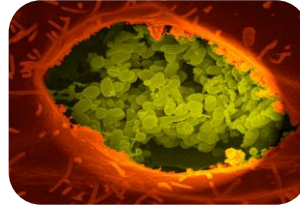




Typhoid



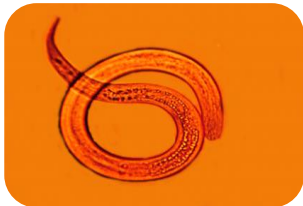
Brucella



Q Fever



Legionella



Strongyloides



Leptospira



Fasciola



Campylobacter



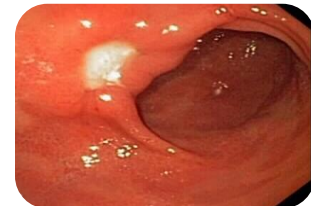
Yersenia



Gastric adenoca



Lymphoma

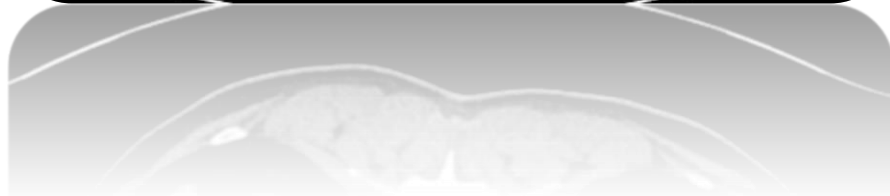
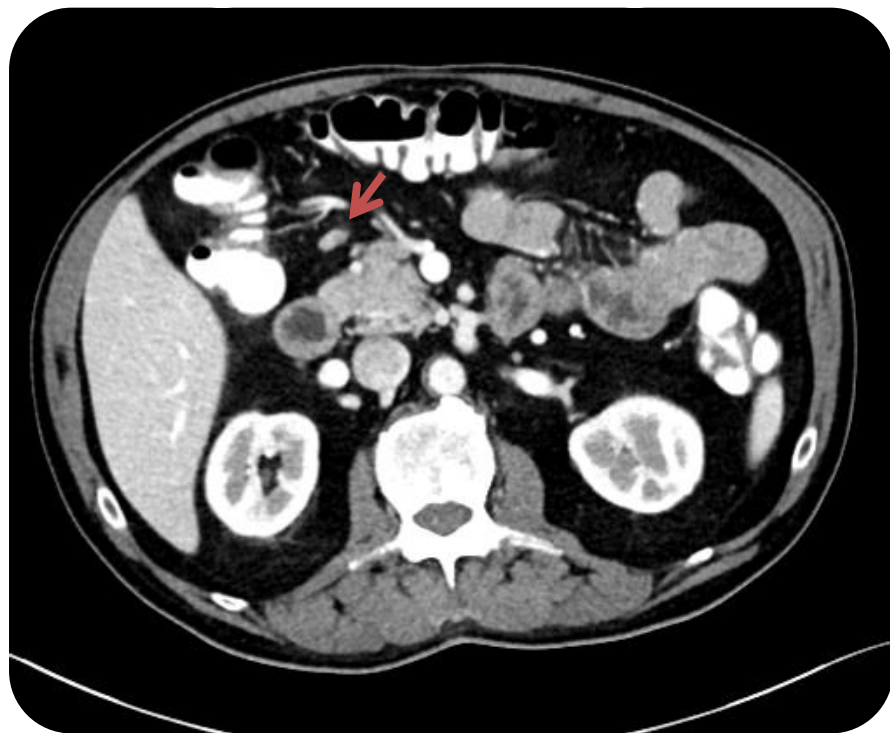


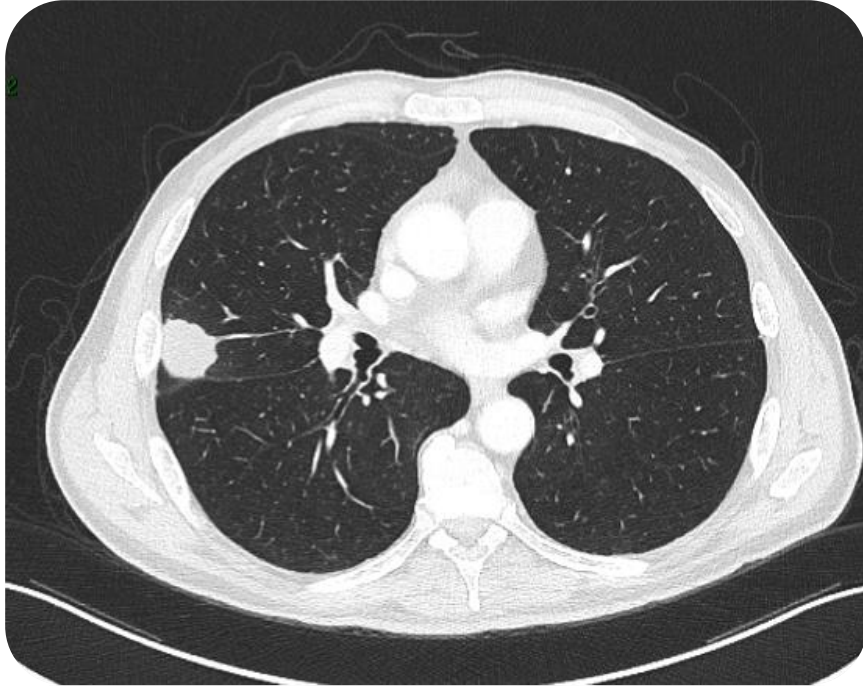
Peptic ulcer

GI Endoscopy

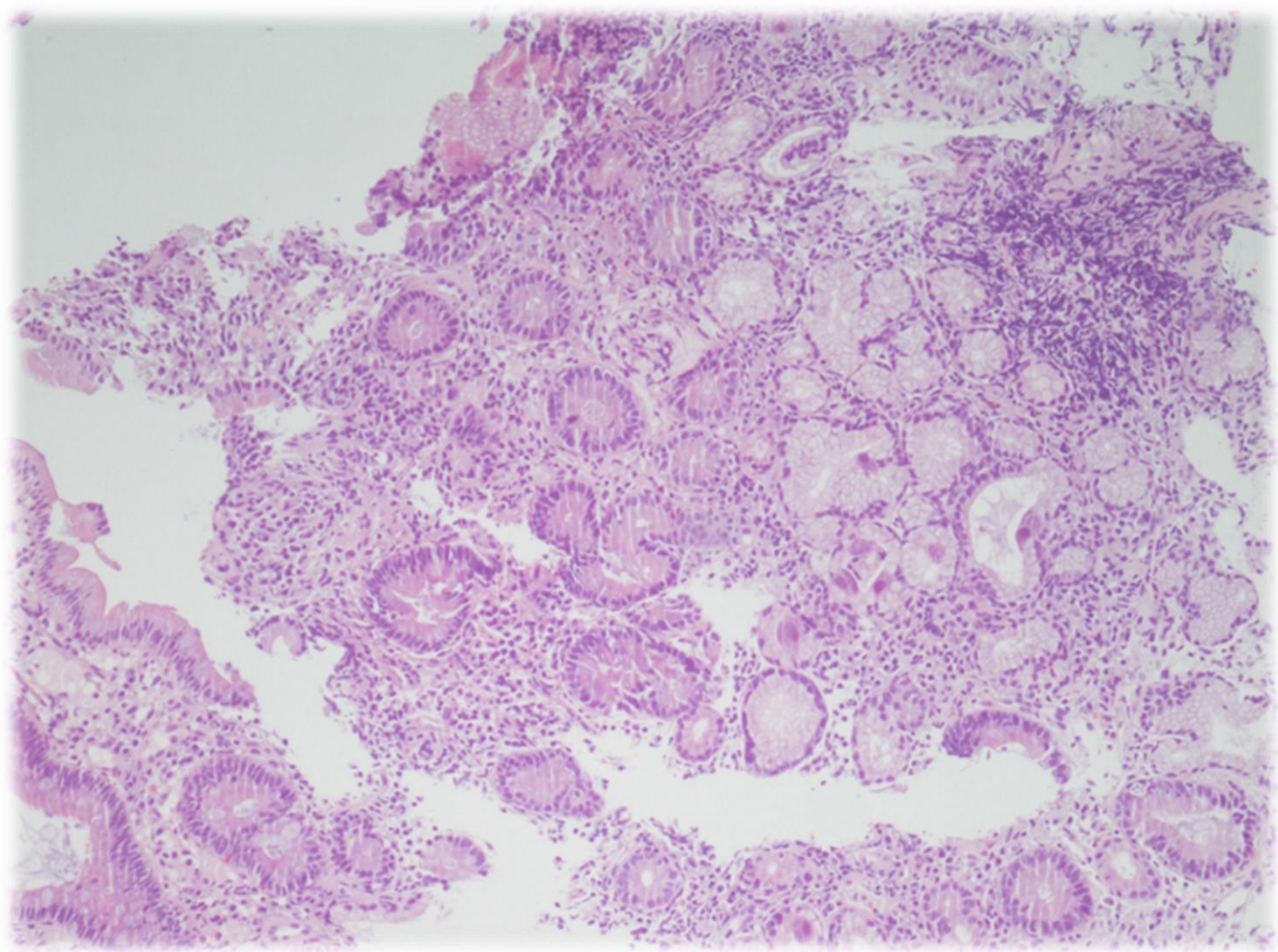


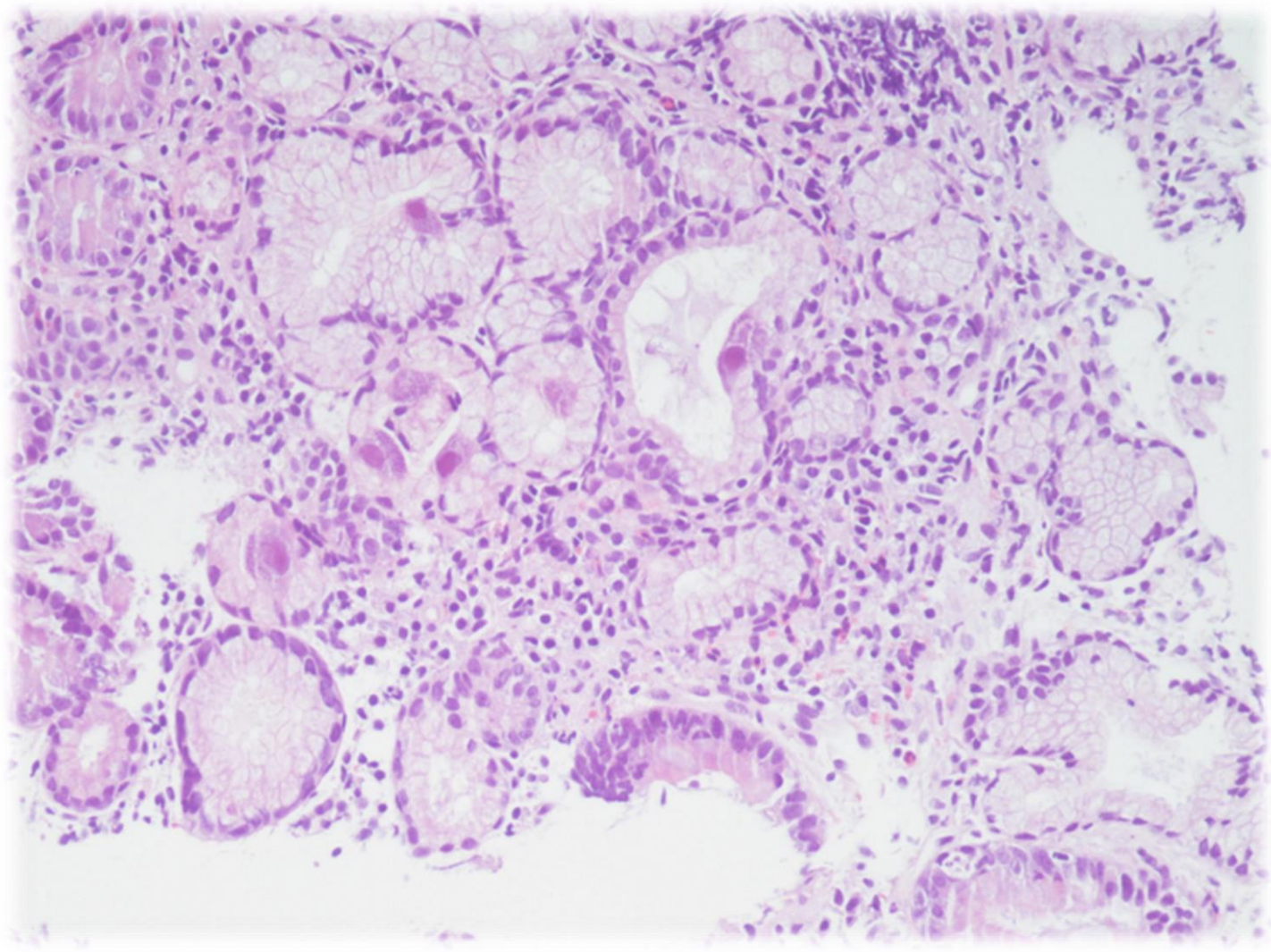
TB CT

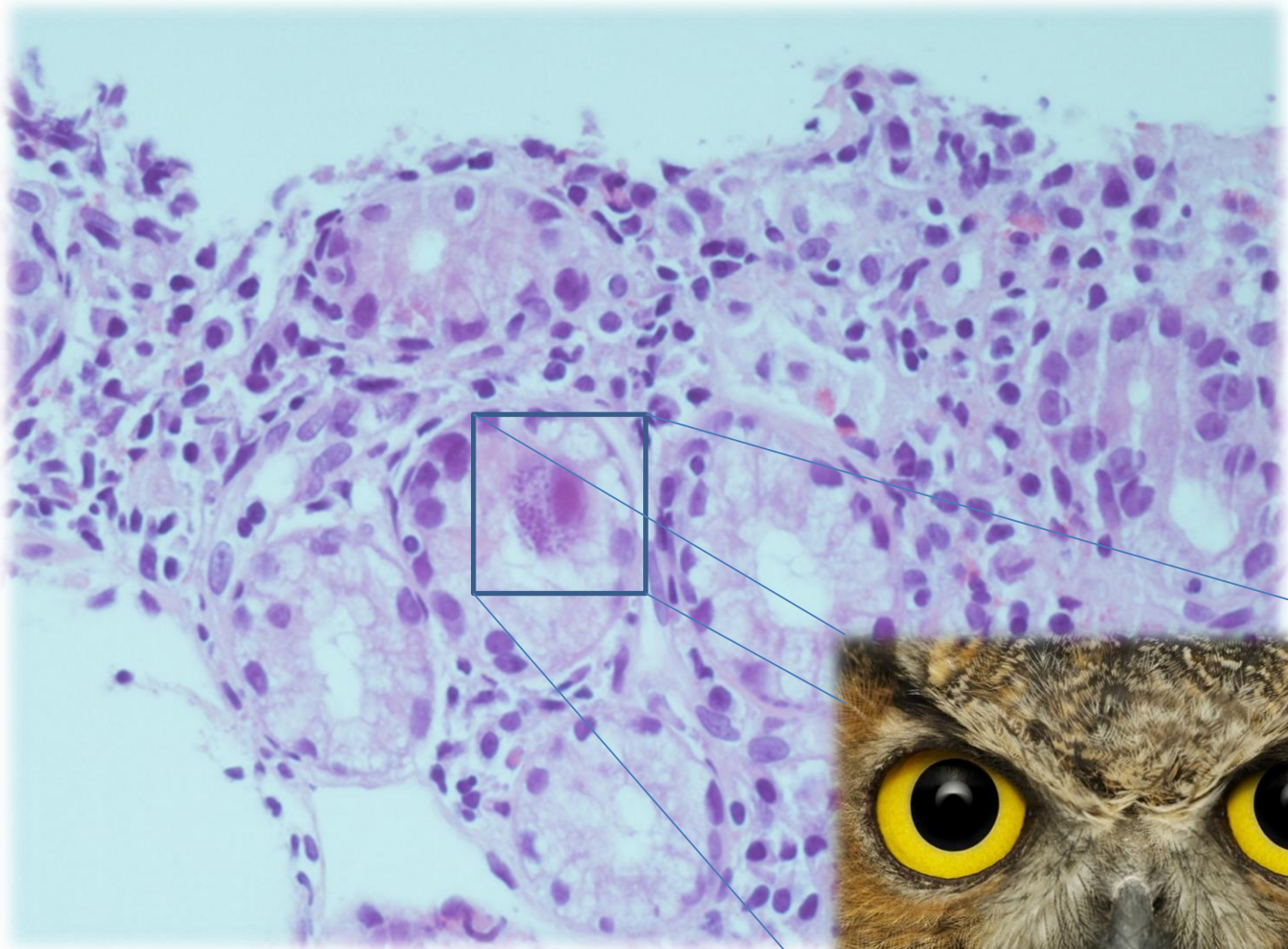


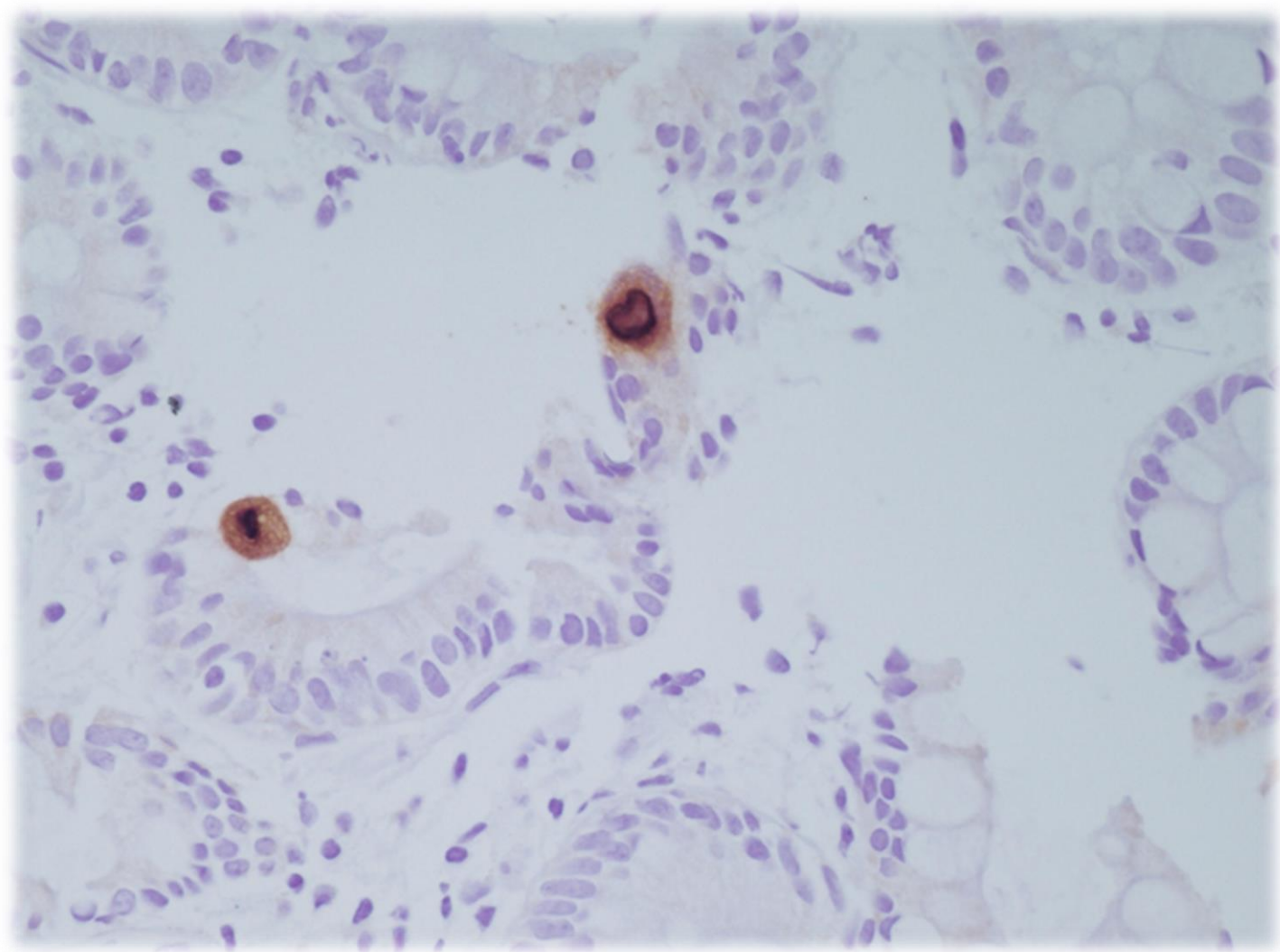












# Pathology

- Normal appearing gastric mucosa

Severe chronic active gastritis.  
Helicobacter pylori focally positive.  
See report 15-13991, 15-13992.

---

- Gastric ulcer

Severe chronic active gastritis with ulceration and scattered large cells with inclusions of CMV.  
Immunostain with CMV marker is positive.  
Immunostain with cytokeratin does not reveal additional findings.  
No tumor seen.  
Conclusion: CMV positive gastritis with ulceration.  
Helicobacter pylori focally positive.

---

- Duodenum

Duodenal mucosa with moderate scattered cells with inclusions of CMV.  
Conclusion: CMV related duodenitis.

---

Literature Review

# **CMV RELATED GASTRO-DUODENITIS IN AN IMMUNOCOMPETENT PATIENT**

# Spectrum of disease

## **Immunocompetent**

- Asymptomatic
- Mononucleosis syndrome
- Organ-specific complications- rare, mainly primary infection

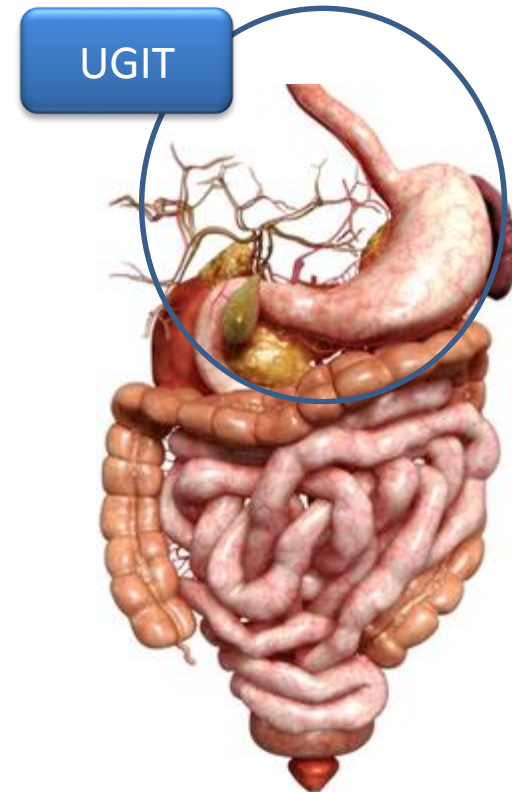
## **Immunocompromised**

- Substantial morbidity
- High mortality



# Organ specific complications

- Gastrointestinal
  - Colitis
  - Esophagitis
- Hepatic
- Neurologic
  - Encephalitis
  - Guillain-Barré syndrome
- Pulmonary
- Ocular
- Cardiovascular
  - Pericarditis and myocarditis
  - Atherosclerosis
  - Venous thrombosis



# CMV gastro-duodenal infection

- Mainly immunocompromised patients
  - Rarely reported in immunocompetent hosts

# CMV GD infection

## Endoscopic features

- Causes multiple gastric erosions and ulcers
  - Difficult to differentiate from *Helicobacter pylori*- or NSAID- related ulcers
- Irregularly shaped gastric ulcer accompanied by multiple erosions

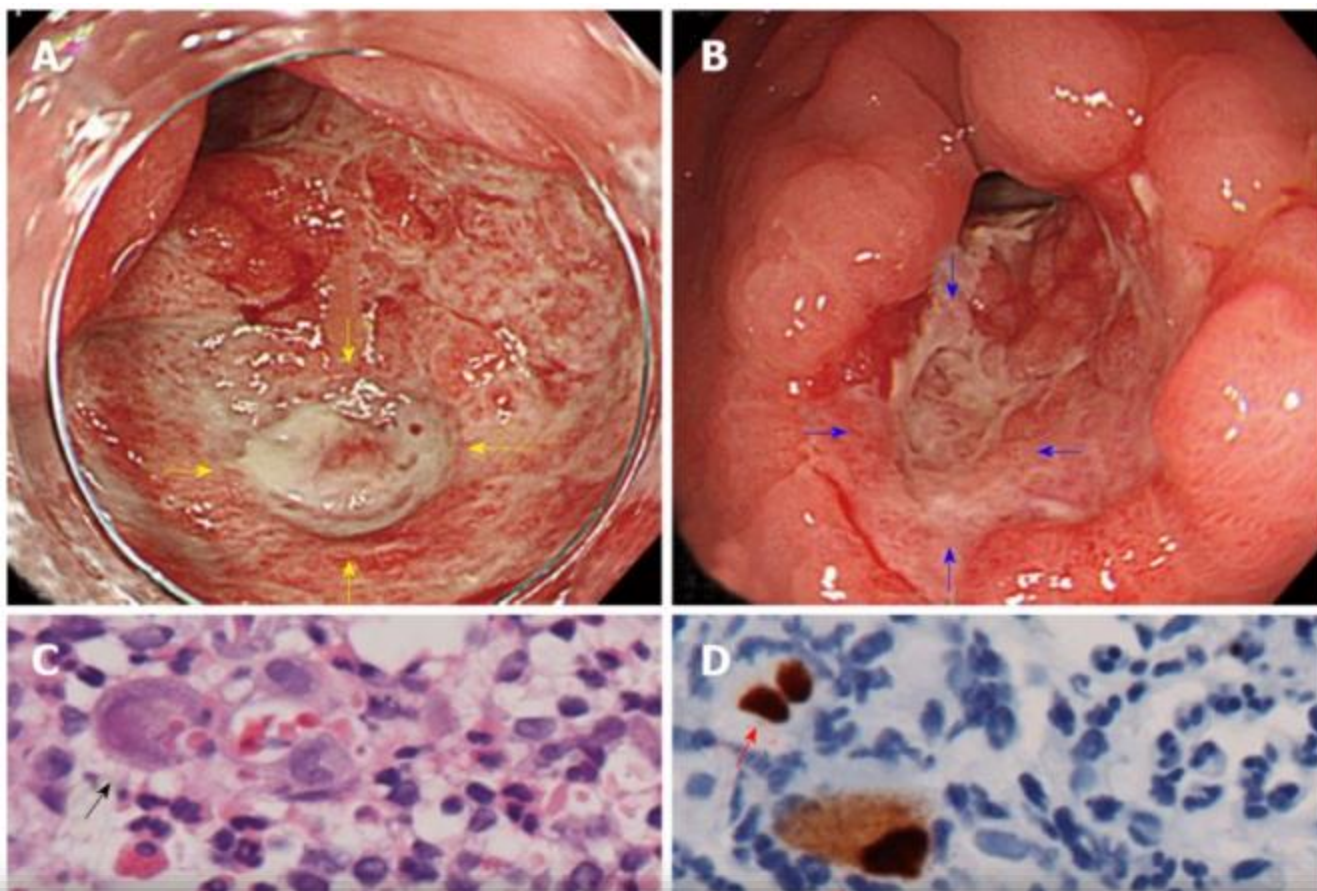
## **Obstructive Gastric Pseudotumor Caused by Cytomegalovirus in an AIDS Patient: A Case Report and Review of Surgical Treatment.**

Boteon YL<sup>1</sup>, Alves IP<sup>1</sup>, da Silva AP<sup>1</sup>, Terciotti Junior V<sup>1</sup>, Coelho Neto Jde S<sup>1</sup>, Lopes LR<sup>1</sup>, Ramos Mde C<sup>2</sup>, Andreollo NA<sup>1</sup>.

## **A giant gastric ulcer mimicking carcinoma in a renal transplant recipient with CMV infection.**

Lin CJ, Pan CF, Wu CJ, Chen HH, Kao CR, Lee CC.

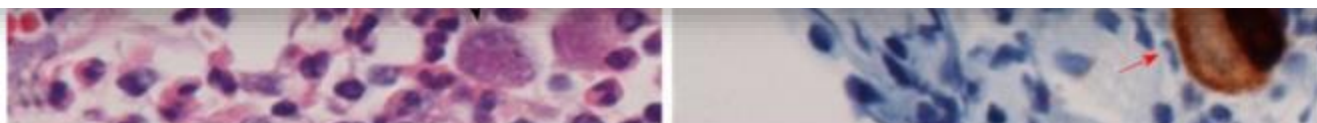




World J Gastroenterol. 2013 Feb 21;19(7):1143-6. doi: 10.3748/wjg.v19.i7.1143.

# **Cytomegalovirus-associated gastric ulcer: a side effect of steroid injections for pyloric stenosis.**

Mori H<sup>1</sup>, Fujihara S, Nishiyama N, Kobara H, Oryu M, Kato K, Rafiq K, Masaki T.



# CMV GD infection

## Pathogenesis

- Ill-defined
- "Cytomegalic vasculitis"
  - Endothelial cells are involvement causing an ischemic injury

Patra S, Samal SC, Chacko A, Mathan VI, Mathan MM. Cytomegalovirus infection of the human gastrointestinal tract. *J Gastroenterol Hepatol*. 1999;14(10):973-976.

Campbell DA, Piercey JR, Shnitka TK, Goldsand G, Devine RD, Weinstein WM. Cytomegalovirus-associated gastric ulcer. *Gastroenterology*. 1977;72(3):533-535.

# CMV GD infection

## Clinical features

- Most cases were accompanied by low grade fever, fatigue and other systemic inflammatory responses

[Gastroenterol Hepatol](#). 1998 Aug-Sep;21(7):332-4.

**[Gastric ulcers as the only manifestation of infection by cytomegalovirus in immunocompetent patients].**

[Article in Spanish]

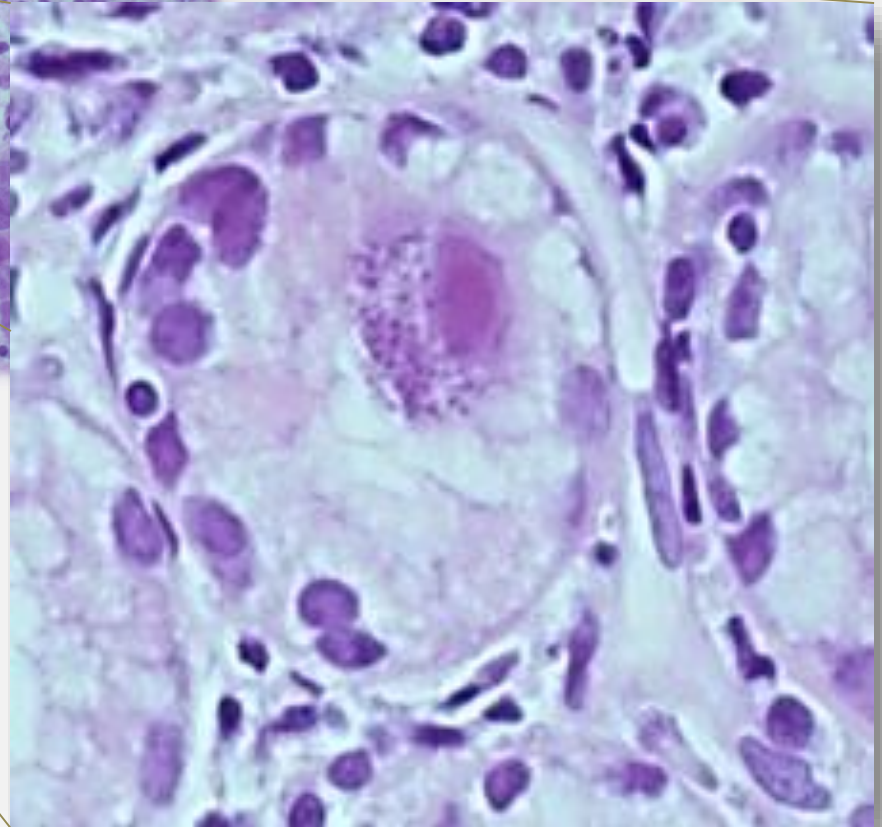
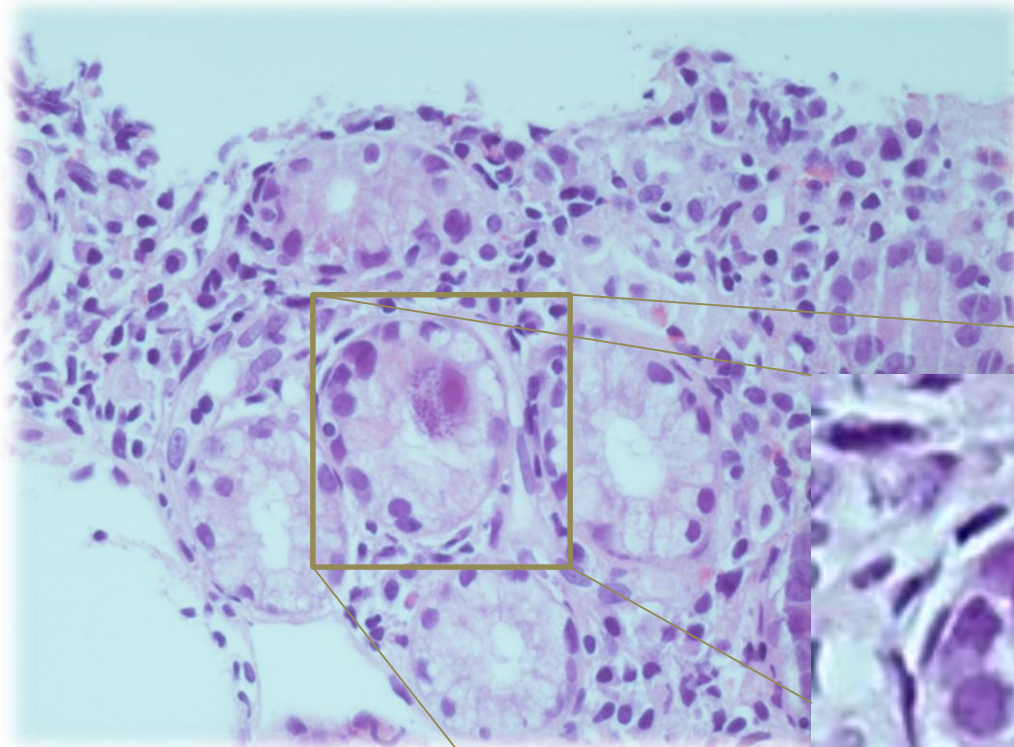
[Vergara M](#)<sup>1</sup>, [Herrero J](#), [de Torres I](#), [Armengol JR](#), [Saperas E](#), [Malagelada JR](#).

[Vergara M](#), [Herrero J](#), [de Torres I](#), [Armengol JR](#), [Saperas E](#), [Malagelada JR](#).

# CMV GD infection

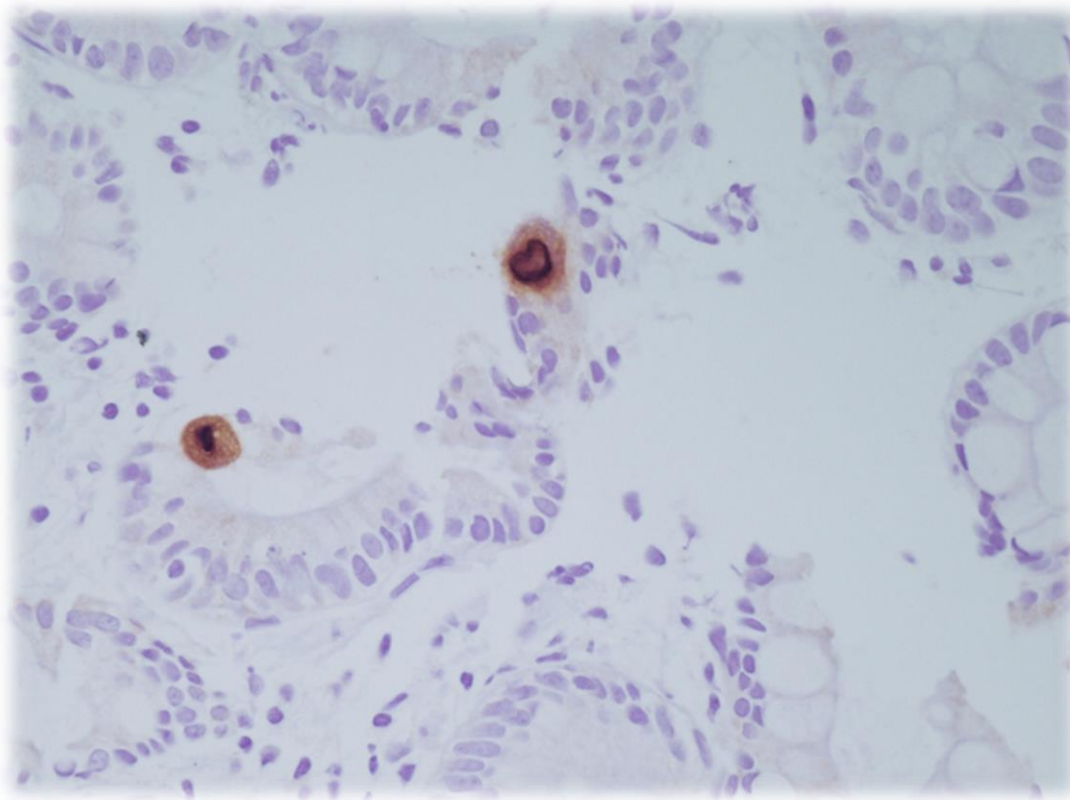
## Diagnosis

- Not easily ascertained
  - Rare
  - Absence of distinct morphological characteristics
- If CMV ulcers are suspected, it is important to examine the biopsy specimens for **inclusion bodies** using hematoxylin-eosin staining or CMV immunohistochemistry



### **Inclusion bodies**

- “Owl eye” appearance
- Aggregations of the virus particles
- Typically basophilic intranuclear
- Eosinophilic cytoplasmic inclusions may also be seen



Immunohistochemistry was found to have a higher sensitivity value than H&E staining

# CMV GD infection

## Differential Diagnosis

- H. Pylori
- NSAIDS
- Other
- Advanced gastric cancer
- Primary gastric lymphoma

- CMV causes the gastric ulcerations?
- CMV colocalizes the gastric lesions?

**Human herpesvirus 6 infection of the gastroduodenal mucosa.**

[Halme L](#)<sup>1</sup>, [Arola J](#), [Höckerstedt K](#), [Lautenschlager I](#).

- 31 immunocompetent patients who underwent UGI endoscopy because of dyspeptic symptoms
- No gastric CMV-infection was found
- 19% of duodenal biopsies revealed CMV-positive cells
- The histopathological findings were nonspecific and mild

J Clin Gastroenterol. 1994 Oct;19(3):198-201.

**Cytomegalovirus in upper gastrointestinal ulcers.**

Murray RN<sup>1</sup>, Parker A, Kadakia SC, Ayala E, Martinez EM.

- A prospective study
- Examined 38 immunocompetent patients with gastroduodenal ulcerations for the incidence of CMV infection
- Failed to document any evidence of CMV
  - By light microscopy, viral cultures, or monoclonal antibody testing
- Even within areas of previous mucosal injury induced by peptic factors or NSAIDs, no evidence of CMV "super-infection" was found

# CMV GD infection

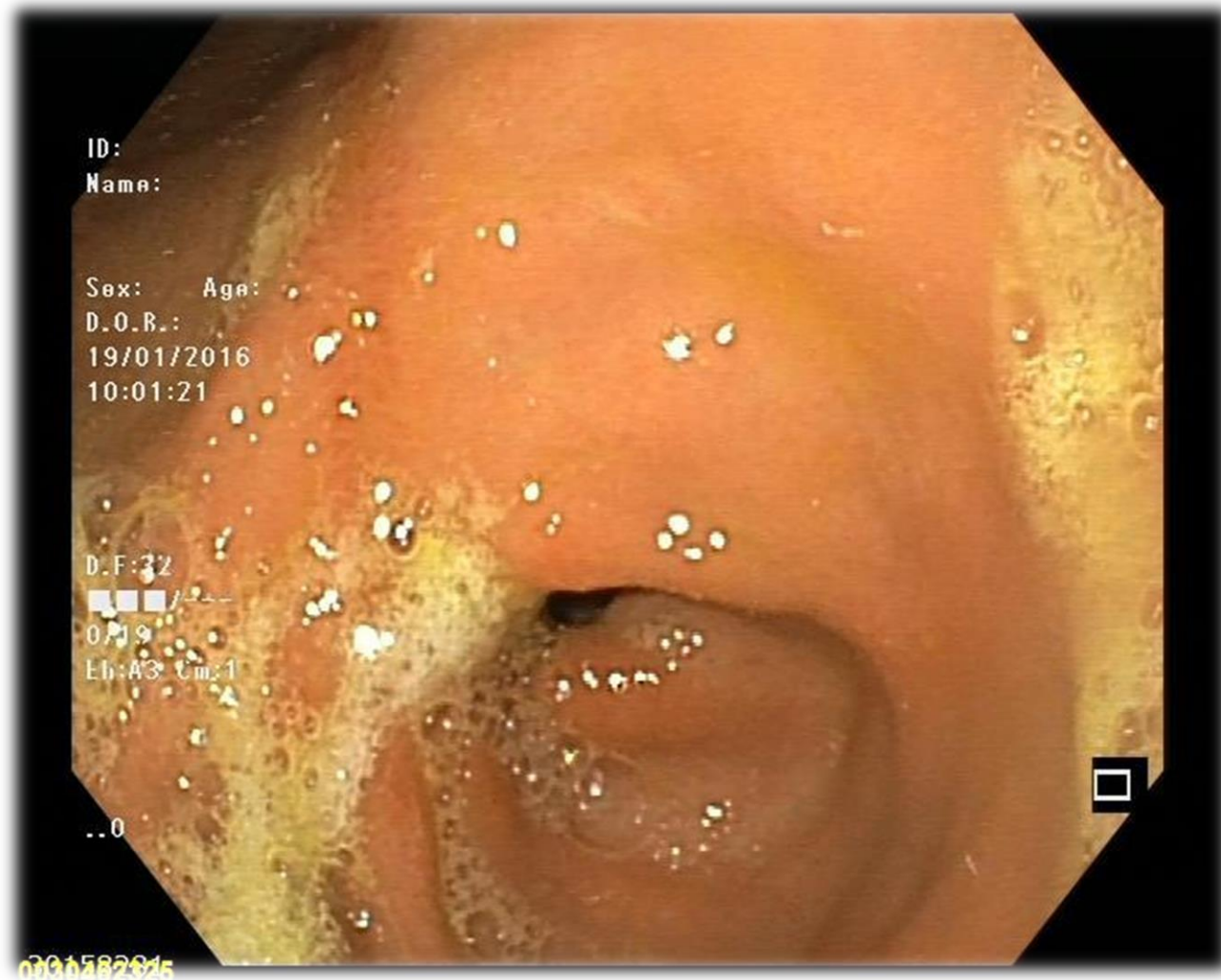
## Treatment and prognosis

- Self-limiting course in immunocompetent hosts
  - In contrast to the case in immunocompromised patients
- Ulcers were usually healed with oral PPI's
- Anti-viral therapy was not required
  - Except in one case of an ulcer refractory to anti-secretor treatment, and other case evolved to pyloric stenosis requiring surgery<sup>1</sup>
- The speed of healing was similar of H. pylori-related ulcers, ranging around 10 weeks<sup>2</sup>

(1) Vergara M, Herrero J, de Torres I, Armengol JR, Saperas E, Malagelada JR. [Gastric ulcers as the only manifestation of infection by cytomegalovirus in immunocompetent patients]. *Gastroenterol y Hepatol*. 21(7):332-334.

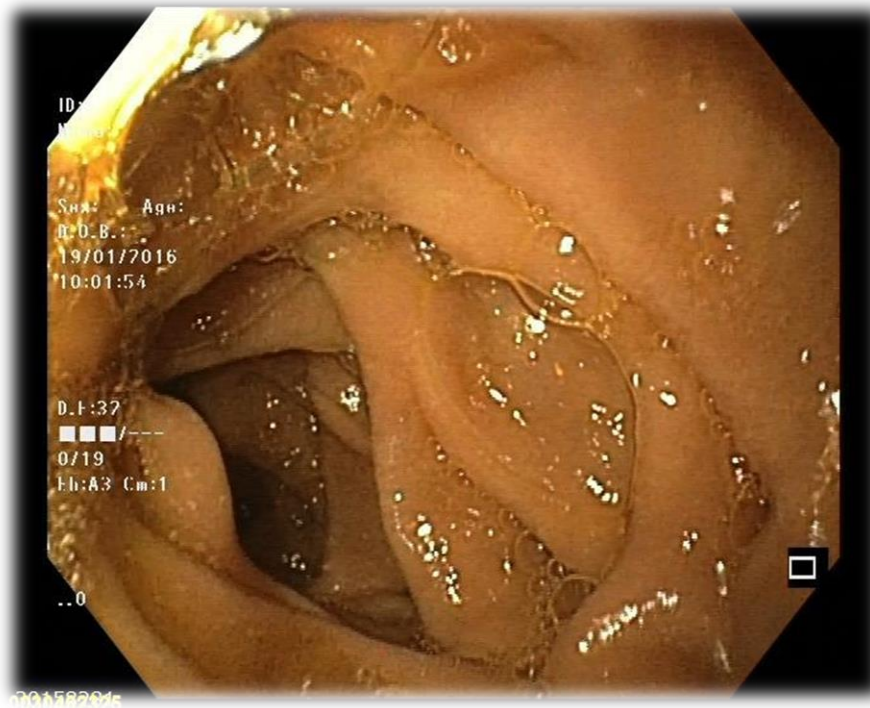
(2) Ebisutani C, Kawamura A, Shibata N, et al. Gastric ulcer associated with cytomegalovirus in an immunocompetent patient: method for diagnosis. *Case Rep Gastroenterol*. 2012;6(2):365-368. doi:10.1159/000339714.

# Follow-up endoscopy on day 50



Pathology: Gastric mucosa with chronic inflammation and foveolar hyperplasia

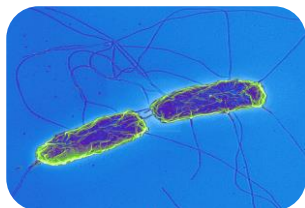
# Follow-up endoscopy on day 50



Pathology: Normal Duodenal mucosa

# In the present case

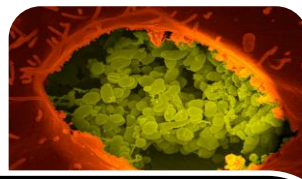
- We could not document any other potential causative agent
- The paucity of the *H. pylori* bacteriaceae in the gastroduodenal biopsies plays against its role in the pathogenesis of the ulcer
- Inclusion bodies had disappeared in the specimens obtained from the healing lesion
- Hence, we concluded that CMV infection itself contributed to the gastric ulceration



Typhoid



Leptospira



Fasciola



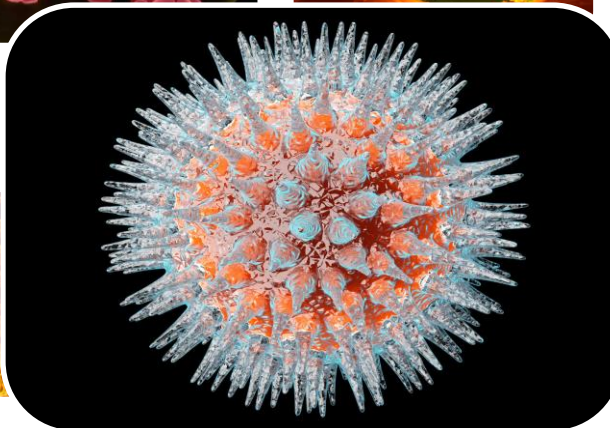
Legionella



Strongyloides



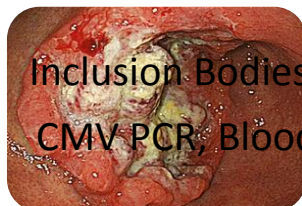
Campylobacter



## CMV



Yersenia



Gastric adenoca



Lymphoma



Peptic ulcer

Inclusion Bodies in Biopsies (H&E, IHC)  
CMV PCR, Blood - Positive 1278 IU/ml

- CMV-related gastro-duodenitis and gastric ulceration may rarely be encountered in healthy immunocompetent individuals
- Whether its discovery should lead to a search for an immunocompromised state is unknown
- It is usually a self-limited disease and PPI therapy was adequate for a complete healing in most cases



Time for

**DISCUSSION**