CMV COLITIS IN SOLID ORGAN TRANSPLANT PATIENTS

Ozan Yildiz[1], Hande Arslan[1], Gonca Ozgun[2], Nuredtin Suna[3], Ozlem Yilmaz[1], Emre Karakaya[4], Mehmet A. Haberal[4]

[1]Department of Infectious Disease and Clinical Microbiology, Baskent University
[2]Department of Pathology, Baskent University
[3]Department of Gastroenterology, Baskent University
[4]Department of General Surgery, Division of Transplantation, Baskent University
Ankara/Turkey

Introduction

- The predictive value of CMV DNAemia, in end organ disease particularly in gastrointestinal involvements, has become a subject of debate
- Defining and deciding on the treatment duration in end organ disease has become challenging in this patient group
- In this case series, demographic data of 11 patients diagnosed with CMV colitis through pathology, as well as findings that may be relevant for diagnosis and treatment, are shared

Method

- A retrospective study of patients with CMV colitis diagnosis through pathological results from November 2014 to January 2024 at Baskent University Hospital (Ankara, Turkey)
- Data were obtained from medical records
- Inclusion criteria comprised SOT patients who had a pathology diagnosis for CMV colitis (In case of repeated positive results, the first time patient was diagnosed was included)
- We evaluated laboratory ,colonoscopic, endoscopic , pathological findings and other information about the patients that may be relevant for diagnosis and treatment.

Results-1

- 11 Renal transplant patients diagnosed as CMV colitis ;
  - Mean age was 46
  - Male ratio was 54%
  - The median diagnosis time after transplantion was 1054 days.
- Diagnosis period of CMV infection:
  - 4/11 patients were diagnosed < 200 days (within the 100 days after valganciclovir prophylaxis)
  - 5/11 patients were diagnosed after 5 years
  - 5 patients developed CMV colitis in the 6 month period after undergoing rejection treatment (Two of these patients had their transplantation 5 years ago)
- Concurrent infections
  - 2/11 had concurrent bacterial infections
  - 1/11 had both bacterial and fungal infections

Results-2

- Viremia
- 8/11 had viremia at the time of pathology diagnosis

  For 8 patients who had viremia
  - The median viral load:2634 IU/ml
  - The highest viral load:40,400 IU/ml
  - The lowest viral load: 239 IU/ml
- Treatment
- All (11) patients were treated by either ganciclovir or valganciclovir
- Treatment durations was determined with negative blood test(CMV-PCR) in the patients with viremia or the improvement of symptoms in the patients without viremia (Table1)

Table1:Demographic Information and Relevant Findings

	Age	Gender	Time after Transplant	Viremia (Iu/ml)	First negative blood test after treatment (Weekly checks)	Treatment Time and dosage	Relaps	Rejection Treatment 6 month before cmv colit diagnosis	Co Infection During Cmv colitis	6 month Surival after Cmv colitis
Case 1	57	Male	193 days	4.570	1 week	2 weeks of 1x250mg iv ganciclovir Daily	No relaps	Pulse steroids, Rituximab	E.coli Klebsiella	Exitus
Case 2	28	Female	1899 days	20.000	2 weeks	14 days of 1x130mg iv ganciclovir	No relaps	None	No Co-infection	Alive
Case 3	56	Male	178 days	1.070	No follow up blood test	No treatment	No relaps	None	No Co-infection	Alive
Case 4	46	Female	189 days	40.400	1 month	1 month of 2x900mg po valganciclovir	No relaps	Pulse steroids, plasmaphresis	E.coli Aspergillus	Alive
Case 5	57	Female	2935 days	274	No follow up blood test	1 day of 1x250mg Ganciclovir	No relaps	Pulse steroids	Klebsiella	Exitus
Case 6	57	Male	115 days	Negative	-	1 month of 2x250mg iv Ganciclovir	No relaps	None	No Co-infection	Exitus
Case 7	39	Female	4291 days	Negative	-	10 days of 1x220mg iv ganciclovir	Colitis Relaps	Pulse steroids	No Co-infection	Alive
Case 8	64	Female	1054 days	698	2 weeks	1 month of 1x450mg po Valganciclovir	Colitis Relaps	None	No Co-infection	Alive
Case 9	41	Male	4211 days	239	1 month	2 weeks of 2x150mg iv ganciclovir, 2 weeks of 2x900mg po Valganciclovir	Viremia Relaps	None	No Co-infection	Alive
Case 10	36	Male	553 days	586	No follow up blood test	2 weeks of 1x450mg po Valganciclovir	No Relaps	Pulse steroids, Plasmaphresis Rituximab	No Co-infection	Alive
Case 11	44	Male	5636 days	Negative	-	3 weeks of 1x150mg iv Ganciclovir	Colitis Relaps	None	No Co-infection	Alive

Results-3

Survival

- The 6-month survival after the diagnosis of CMV colitis was 72%.
- 3/11 patients died within 6 months from the CMV colitis diagnosis
  - 1/3 had the third highest viral load
  - 1/3 had the second lowest
  - 1/3 did not have viremia

Relaps

- 4/11 had relaps episodes (Table2)

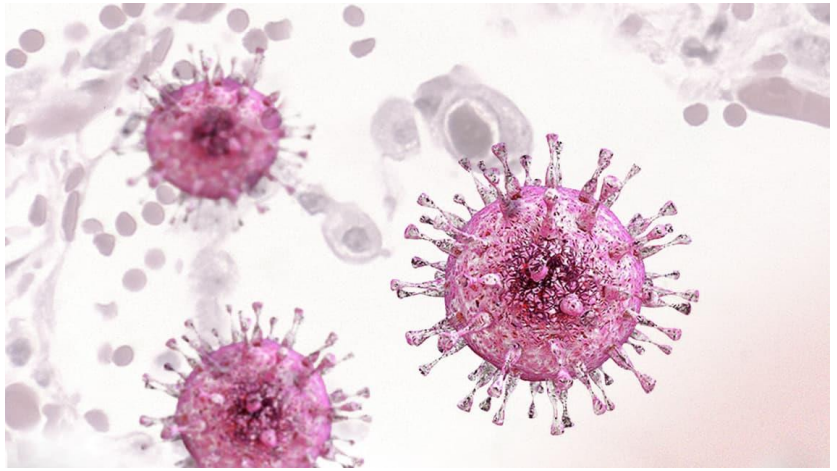
Relaps Case	Viremia at the time of first cmv colitis diagnosis (Iu/ml)	First negative blood test after treatment (Weekly checks)	Treatment Time and dosage	Relaps Type	New Pathology Findings
Case7	Negative	-	10 days of 1x220mg iv gansiklovir	Colitis	Ulcer - ulcer base. Active inflammatory granulation tissue. **CMV-positive cells have been observed immunohistochemically in the ulcer base.**
Case8	698	2 weeks	1 month of 1x450mg po valgansiklovir	Colitis	Active colitis. **The presence of staining with CMV antibody and positive CMV-PCR (DNA) findings suggest that the case is diagnosed as "CMV colitis."**
Case 9	239	1 month	2 weeks of 2x150mg iv gansiklovir, 2 weeks of 2x900mg po valgansiklovir	Viremia	---
Case11	Negative	-	3 weeks of 1x150mg iv gansiklovir	Colitis	**CMV colitis with severe active chronic colitis findings.** Mild crypt distortion, minimal crypt loss, focal cryptitis, and crypt abscess formation have been observed. Erosion is present on the surface. Moderate lymphoplasmacytic inflammation with eosinophilic leukocytes

Table2:Relaps Cases Findings

Table3:Colonoscopy,Endoscopy and Pathology Findings

	Colonoscopy	Endoscopy	Pathology
Case1	Pancolitis, İleocecal valve ulcer	Esophagitis, pangastritis, Bulbitis	Mild inflammatory cell infiltration, including edema, congestion in lamina propria. **Staining was observed with CMV.**
Case 2	Pancolitis,İleocecal valve ulcer	Esophagitis, pangastritis	Minimal distortion in the crypts. Cryptitis and crypt abscesses Congestion, edema, and mononuclear inflammatory cell infiltration in the lamina propria .Diffuse active colitis . **Morphological and immunohistochemical findings compatible with CMV colitis.**
Case 3	İleocecal valve ulcer	Esophageal ulcer, Atrophic gastritis,Bulbitis	Active colitis characterized by ulcers.**Widespread staining was observed in the ulcer area with CMV.**
Case 4	İleocecal valve ulcer, hyperemic and erosive colon	No simultaneous endoscopy was perfomed.	Focal cryptitis and crypt abscess formations have been observed.There is significant edema and mild active inflammation in the lamina propria. **Scattered positive reactions were observed in the endothelium and crypt epithelial cells with CMV staining.**
Case 5	Pancolitis	Laceration in esophagus, gastric ulcers	Active colitis.**Positive reaction has been observed in a few cells with CMV.**
Case 6	Widespread ulcers in colon	Atrophic erythematous gastropathy	Ulceration in the crypts. Mixed type inflammatory cell infiltration including edema in the lamina propria, cryptitis, and crypt abscesses were seen. **CMV antibody is positive in immunohistochemical study.**
Case 7	Ulcer in the terminal ileum	Erythematous gastropathy	Ulcer and its base inflammatory granulation tissue**.CMV staining was observed in the nucleus of one cell at the base of the ulcer.**
Case 8	Polips in sigmoid colon	Erosive pangastritis	Active colitis.**The inclusions specific to CMV were positively stained with CMV dye.**
Case 9	Ulcer in ascending colon	Normal endoscopy	Findings of fibrosis in a focal segment of the colon wall. Minimal signs of inflammation in the small intestine mucosa. **As a result of immunohistochemical examination,CMV antibody positivity was detected.**
Case 10	Hyperemic areas in sigmoid and ascending colon	Erosive gastropathy and deudonal ulcer	Erosion, mixed-type inflammatory cell infiltration rich in eosinophils in the tunica propria, cryptitis, crypt abscess, minimal crypt distortion, loss of mucus, as well as significant reparative/regenerative changes were observed, alongside desquamation in glandular epithelium. **Staining was observed with CMV.**
Case 11	Pancolitis	Erythematous gastropathy	Erosion and focal neutrophilic leukocyte infiltration in the surface epithelium. Focal cryptitis, crypt abscess formation, and sporadic crypt destruction, along with occasional cytoplasmic eosinophilia and characteristic cystic appearance, consistent with crypt atrophy. Diffuse reactive/regenerative changes in the epithelium. **In the immunohistochemical study, positivity was observed in a small number of cells with CMV.**

Conclusion



- Known as an opportunistic infection, CMV is expected to occur particularly in the first year after transplantation, while in our study, the median onset time was 1932 days
- Only five patients had recently received rejection treatment
- The development of the disease in other patients without any known predisposing condition was noteworthy