Cytomegalovirus Infections in Patients With Multiple Myeloma

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Background

- Substantial progress in the treatment of multiple myeloma (MM) has led to improved patient outcomes and prolonged survival of patients.
- These therapeutic advances have resulted in increased cumulative immunosuppression leading to increased susceptibility to opportunistic infections including CMV infection.
- The significance of CMV infection in MM patients is not well understood.
- We sought to describe the clinical characteristics and outcomes of patients with MM who develop CMV infection.

METHODS

- Retrospective chart review of MM patients at Mount Sinai Hospital in NY who had CMV DNA PCR sent.
- The Mount Sinai Multiple Myeloma Database was utilized to identify patients who developed CMV viremia, defined as CMV DNA PCR>500 IU/mL
- Demographic, clinical and laboratory data were abstracted from electronic medical records. IRB approval was obtained.

Statistical Analysis

- Factors associated with 30-day mortality by univariate analysis were evaluated using Fischer's exact and Wilcoxon rank-sum test.

Table 1: Patient Characteristics

Variable	N (%)
Age, median (range)	59 (33-74)
Sex (male)	27 (58%)
MM disease status	
Stringent complete response or complete response	2 (4%)
Very good partial response or partial response	7 (15%)
Minimal Response or Stable Disease	2 (4%)
Progressive Disease	20 (43%)
Chemotherapy within 30 days	42 (91%)
Steroids within 30 days	39 (84.7%)
Median steroid dose (weekly dexamethasone equivalent, mg)	19.5 (0-262)
History of ASCT	33 (71.7%)
Number of lines of chemotherapy, median (range)	5 (1-14)
Lymphopenia (ALC < 1.0 x 10^3/uL)	32 (69.5%)
Hypogammaglobulinemia	39 (84.7%)

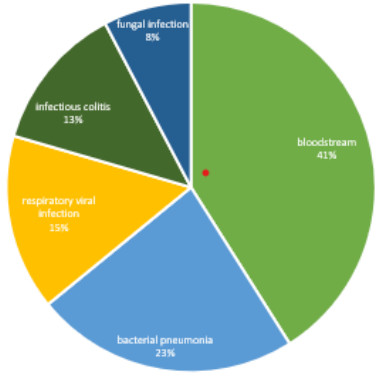
Table 2: CMV Infection Characteristics

CMV Infection Characteristics	N (%)
Symptomatic CMV Infection	22 (47%)
CMV disease	8 (17%)
Proven	1 (12.5%)
Suspected	7 (87.5%)
CMV treatment	33 (71%)
Ganciclovir	14 (30%)
Valganciclovir	26 (56%)
Foscarnet	4 (8%)
Duration of viremia, days, median (range)	19 (1-202)
Peak CMV VL, IU/mL, median (range)	2186 (529- 1119191)

Table 3: Univariate analysis of risk factors for 30-day mortality

Variable	OR (95% CI)	P value
Age >60	0.58 (.12-2.71)	0.711
Progressive disease	3.28 (0.70-15.2)	0.149
Lines of chemotherapy (median)	—	0.476
>3 lines of chemotherapy	2.96 (0.32-26.7)	0.421
History of ASCT	0.74 (0.15-3.54)	0.698
Chemotherapy within 30d	0.70 (0.64-3.20)	1.000
Steroids within 30d	1.54 (0.16-14.7)	1.000
Steroid dose, mg/week, median (range)	**—**	**0.065**
Lymphopenia (ALC < 1.0 x 10^3/uL)	0.84 (.17-4.0)	1.00
Hypogammaglobulinemia		0.316
Coinfection	2.38 (.43-13.1)	0.450
Peak CMV PCR >1000 IU/mL	**0.09 (0.18-0.51)**	**0.008**
Peak CMV PCR >10,000 IU/mL	0.77 (0.13-4.35)	1.00
Peak CMV Value, IU/mL, median (range)	—	0.170
Symptomatic CMV Infection	0.28 (.05-1.59)	0.243

Co-Infections



RESULTS

Demographics

414 MM patients had CMV PCR sent at least once. Forty-six cases of CMV infection were identified.

CMV Infection Characteristics

- Forty-six patients were found to have CMV viremia, defined as PCR>500 IU/mL. Twenty-two (47%) had symptomatic infection.
- In 8/46 (17%) patients, CMV end-organ disease was suspected. Twenty (43%) patients had progressive disease status, 73% had prior history of autologous stem cell transplant and 85% had received steroids within 30 days of CMV infection.
- Twenty-nine (63%) patients had concurrent infections within 30 days of CMV infection, including bloodstream infection (n=16), bacterial pneumonia (n=9), respiratory viral infection (n=6), infectious colitis (n=5), and fungal infection (n=3).

Outcomes

- 9/46 (19%) patients died within 30 days of CMV infection and 12/46 (26%) required ICU admission during that hospitalization.
- In univariate analysis of risk factors associated with mortality, higher weekly steroid dose approached statistical significance (p=0.06) and peak CMV PCR >1000 IU/mL (p.008) was associated with lower mortality.

CONCLUSION

CMV infection is associated with morbidity and mortality in MM patients. Prospective studies are needed to better assess the clinical significance of CMV reactivation in this population.