Role of Cytomegalovirus DNA Measurement in Diagnosis and Monitoring of active infection in patients receiving immunosuppressive therapy

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INTRODUCTION

Cytomegalovirus (CMV) is among the most common and potentially lethal infectious agents in immunocompromised patients. Quantification of CMV load in blood has become the mainstay of clinical management allowing for direct deployment of antivirus therapy, assessment of the response to therapy and recognition of cases with drug resistance.

OBJECTIVES

In the present study, we implemented a Quantative Polymerase Chain Reaction (Q-PCR) assay for measuring CMV-DNA and we also investigated clinical characteristics and outcome among patients receiving immunosuppressive therapy.

MATERIALS & METHODS

A total of 156 hospitalized patients with clinical suspicion of CMV infection, were enrolled in this study.

Of them:

- 146 had hematological malignancies
- 10 had solid-organ malignancies
- 25 were transplanted patients

Analysis methods:

- In all patients, plasma samples were processed with Q-PCR (Light Cycler, CMV Quant, Roche Diagnostics)
- In CMV-DNA positive patients, serum CMV antibody (IgG and IgM) titers were measured via microparticle enzyme immune assay (AxSYM, Abbott).

The association between viral load in plasma and clinical data was also investigated.

RESULTS

Positive cases detected by:

- Serology IgM (+): one kidney transplanted patient [IgM was negative in all other PCR positive cases]
- PCR (+): 28 patients
  - 16 with haematological malignancies (87.5% had chronic lymphocytic leukemia)
  - 2 with solid malignancies
  - 10 transplanted patients

Among patients with CMV disease, pneumonitis was the most common clinical presentation (71%). Other opportunistic infections were noted in 14% patients, all with a hematological malignancy. CMV viral load in different clinical conditions shown in Fig 1.

Different patients settings	median blood CMV viral load [range] Fig 1.
Overall	1840 [351-58700] copies/ml.
hematological malignancies	1970 [362-58700] copies/ml
solid-organ malignancies	622 [351-893] copies/ml
transplanted patients	2355 [351-10200] copies/ml

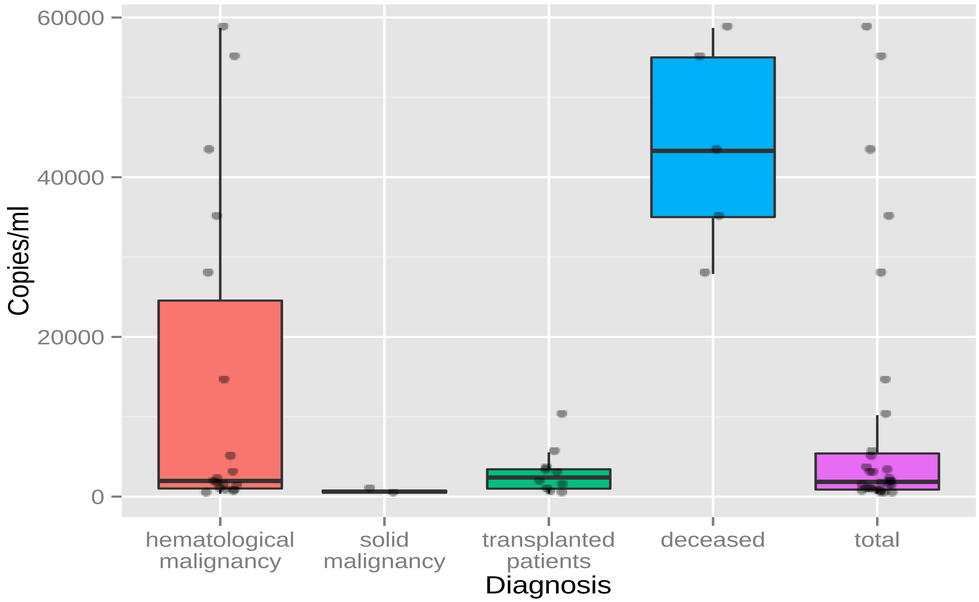

Fig 1. The estimated CMV viral load in different clinical conditions

The overall mortality rate was 18% and the major causes of death were respiratory failure and sepsis. All patients who died had hematological malignancies with a high viral load (median: 43300 copies /ml).

All CMV PCR positive patients received ganciclovir. The treatment led to a marked decrease in CMV DNA copy number. The length of treatment needed to control CMV replication and obtain a negative result via PCR method, after implementation of treatment, were 27 (range 13-45) days.

CONCLUSIONS

The spectrum of CMV infections for immunosuppressive patients is expanding and diagnosis has increased due to the advent of new molecular diagnostic techniques. Furthermore, the time lag between primary infection and IgM production, as well as the failure of immunosuppressive patients to produce IgM antibody significantly decreased the clinical utility of serology in diagnosing CMV disease. So, CMV quantification will continue to have a crucial role in delivering individualized patient management in a variety of clinical settings.

References

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