

Cytomegalovirus in Immunocompetent Individuals and Immunocompromised Patients

Essay

Submitted in Partial Fulfillment of the Requirements
Master Degree In Internal Medicine

By

Ahmed Abd EL Aziz Mohamed Said Ahmed

(M.B B.Ch).

Faculty of Medicine - Tanta University

Supervised By

Prof. Dr. Essam Abd EL Wahed Hassan

Professor of Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

Prof. Dr. Hany Mohamed Abd Aallah Hegab

Assistant Professor of Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

Dr. Mohamed Mahmoud Moussa

Lecturer in Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

**Faculty of Medicine
Ain Shams University
2010**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا
مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة آية
(32)



Firstly, I am extremely grateful and thankful to Allah who gave me the ability and the power to finish this work.

I am really happy to grasp this opportunity to express my sincere appreciation & deep gratitude to [Prof. Dr. Essam Abd EL Wahed Hassan](#), Professor of Internal Medicine and Haematology, Faculty of Medicine Ain Shams University, for his faithful guidance & supervision during the course of this work. It is a pleasure to record my thanks for his continuous help and encouragement throughout this research.

My sincere thanks and gratitude to [Prof. Dr. Hany Mohamed Abd Aallah Hegab](#), Assistant Professor of Internal Medicine and Haematolog, Faculty of Medicine-Ain Shams University, for his supervision, valuable advises and scientific help.

Thanks to [Dr. Mohamed Mahmoud Moussa](#), Lecturer in Internal Medicine and Haematology, Faculty of Medicine-Ain Shams University, for his supervision and participation in this work.

Also, I wish to thank every body who helped me throughout this research. Finally, great thanks to my family who supported me during this work, specially my father, my mother, my wife, my brothers and finally my daughter Nadeen.

List of Contents

<i>Title</i>	<i>Page</i>
Chapter 1: Human cytomegalovirus	1
Chapter 2: CMV in immunocompetent individuals	44
Chapter 3: CMV infection in immunocompromised patients	79
Discussion	118
Recommendations	129
References	131
Arabic summary	

List of Abbreviations

ab	Antibody
AIDS	Acquired immunodeficiency syndrom
AMP	Adenomonophosphate
BMT	Bone marrow transplantation
CD4+	Cluster of differentiation 4
CDV	Cidofovir
CID	Cytomegalic inclusion disease
CMV-IGIV	CMV-intravenous immunoglobulin
CNS	Central nervous system
CPE	Cytopathic effect
CTL	Cytotoxic lymphocyte
D+	Donor seropositive
DNA	Deoxyribonucleic acid
E	Early (CMV protein)
EBV	Epstein-Barr virus
ERGIC	Endoplasmic reticulum-golgi intermediate compartment
FDA	Federal Drug Adminstration
gB	Glycoprotein B
GCV	Gancyclovir

gH	Glycoprotein H
GIT	Gastrointestinal tract
gL	Glycoprotein N
gM	Glycoprotein M
gN	Glycoprotein N
gO	Glycoprotein O
G0	Gape 0/growth arrested
HAART	Highly active anti-retroviral treatment
HCMV	Human cytomegalovirus
HCMV DB	HCMV dense bodies
HHV-6	Human herpes virus 6
HHV-7	Human herpes virus 7
HIV	Human immunodeficiency virus
IE	Immediate early (CMV protein)
IFN- γ	Interferon γ
IgG	Immunoglobulin Gamma
IgM	Immunoglobulin Mu
IL	Interleukin
Kda	Kilodalton
KSHV	Kaposi's sarcoma-associated herpes virus
L	Late (CMV protein)

MHC	Major histocompatibility complex
MIE	Major immediate early
Mrna	Messenger ribnucleic acid
NF-NB	Nuclear factor B
NK	Natural killer
PBL	Peripheral blood leukocytes
PCR	Polymerase chain reaction
PFA	Pyrophosphate analog foscarnet
PP65	Phosphoprotein of 65 KD
PTLD	Post-transplant lymphoproliferative disease
R-	Recipient seronegative
RNA	Ribonucleic acid
TNF	Tumour necrosis factor
UL	Unique long (gene product)
VZV	Varicella zoster virus

List of Tables

Table	Title	Page
Table (1)	Review of case reports of sever CMV infections in immunocomptent patients.	61
Table (2)	Incidence of CMV disease in solid organ transplant recipients.	85
Table (3)	Definition and diagnosis of CMV infection and disease in solid organ transplant recipients.	94

List of Figures

Figure	Title	Page
Figure (1)	Schematic of the HCMV virion.	5
Figure (2)	Overview of the HCMV life cycle.	11, 12
Figure (3)	Typical time course for development of CMV-specific-IgG and IgM from a primary infection.	23
Figure (4a)	CMV oesophagitis.	80
Figure (4b)	CMV ventriculoencephalitis.	80
Figure (5)	Risk factors for development of late CMV disease.	97
Figure (6)	CMV retinitis in patients with AIDS.	117

Cytomegalovirus in Immunocompetent Individuals and Immunocompromised Patients

Essay

Submitted in Partial Fulfillment of the Requirements
Master Degree In Internal Medicine

By

Ahmed Abd EL Aziz Mohamed Said Ahmed

(M.B B.Ch).

Faculty of Medicine - Tanta University

Supervised By

Prof. Dr. Essam Abd EL Wahed Hassan

Professor of Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

Prof. Dr. Hany Mohamed Abd Aallah Hegab

Assistant Professor of Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

Dr. Mohamed Mahmoud Moussa

Lecturer in Internal Medicine and Haematology
Faculty of Medicine-Ain Shams University

**Faculty of Medicine
Ain Shams University
2010**

INTRODUCTION

Cytomegalovirus (CMV) is a member of betaherpesvirinae in the subfamily herpesviridae. CMV infection is found worldwide. over 50% of adult population have serological evidence of latent infection, although infection is symptomless. (1)

Humoral immunity and Cellular immunity play an important role in CMV infection. the specific T-cell response against CMV is based on their memory function, including their ability in mediating, effectors, proliferation, and secretion of chemokines. The combination of CD4&CD8 response is critical for the infection control. (2)

Congenital CMV infection is the leading non genetic cause of neurosensory hearing loss in developed countries. although central nervous manifestations at birth in children with symptomatic congenital CMV infection predict cognitive and motor deficits, they do not predict hearing loss. (3)

Primary CMV infection in immunocompetent persons has been associated with Prolonged fever, more or less typical infectious mononucleosis, biochemical or clinical hepatitis, skin rash, colitis, pneumonitis, adenitis, myocarditis, and, rarely, Encephalitis or other involvement of the CNS. (4)

A hall mark of CMV infection is life-long latency after primary infection. Although evidence of CMV reactivation has been demonstrated in immunocompetent individuals and in patients with severe sepsis or other forms of stress. The clinical relevance of such reactivation is unclear and it probably has no therapeutic consequences. (5)

CMV infection in humans is a major cause of morbidity and mortality in immunocompromised hosts. Among bone marrow and solid organ transplantation recipients, active infection is related to [1] the presence of late CMV infection in the donor or recipient [2] the organ transplanted, and [3] the intensity of immunosuppressive therapy. (6)

CMV has both direct and indirect effects on transplant graft and native organ function. Direct effects include bone marrow suppression, pneumonitis, myocarditis, encephalitis, hepatitis, nephritis, retinitis, enteritis and pancreatitis. The major indirect effects include graft rejection, secondary bacterial or fungal infections, development of Epstein-Barr virus associated post-transplant lymphoproliferative disease, accelerated atherosclerosis. (7)

AIM OF THE STUDY

Comparison between cytomegalovirus in immunocompetent individuals and immunocompromised patients.

REFERENCES

- (1) Kumar & Clark, Clinical Medicine 2002 15th edition, chapter 2, page 49.
- (2) Alexandre Harari, Simone C. Zimmerli and Giuseppe Pantaleo. cytomegalovirus (CMV)-specific cellular immune response. Human Immunology 2004;65:500-506.
- (3) Rivera LB, Bopp SB, Flower KB, Britt WJ, Stagno S, Pass RF. Predictors of children with symptomatic congenital cytomegalovirus infection. Pediatrics 2002;110:762-767.
- (4) Sandra M. Arend and Aloys C.M. Kroes, Look and Ye Shell Find... cytomegalovirus infection in immunocompetent patients. Clinical Infectious Diseases. Chicago J.37;12,1607-1608.
- (5) Loenen WA, Bruggeman CA, Wiertz EJ. Immune Evasion by human cytomegalovirus: Lessons in immunology and cell biology Semin immunol 2001;13:41-49
- (6) Fishman JA, Rubin RH. Infection in organ-transplantation recipients. N Engl J Med 1998;338:1741-1751.
- (7) Gilberto Torres-Mardiz and Helen W. Boucher, Perspectives in the Treatment and Prophylaxis of cytomegalovirus Diseases in Solid-Organ transplant Recipients, Clinical Infectious Diseases Society of America. 2008;47:702-711.

فيروس السيتوميكاليو فى الاشخاص ذوى الكفاءة المناعية
والمرضى ذوى نقص المناعة
رسالة
مقدمة توطئة للحصول على درجة الماجستير فى الامراض الباطنة

مقدمة من

أحمد عبدالعزيز محمد سيد أحمد
بكالوريوس الطب والجراحة
كلية طب- جامعة طنطا

تمت اشرافه

الاستاذ الدكتور/عصام عبد الواحد حسن
استاذ الامراض الباطنة وامراض الدم
كلية الطب-جامعة عين شمس

الاستاذ الدكتور/هانى محمد عبدالله حجاب
استاذ مساعد الامراض الباطنة وامراض الدم
كلية الطب-جامعة عين شمس

الدكتور/محمد محمود موسى
مدرس الامراض الباطنة وامراض الدم
كلية الطب-جامعة عين شمس

كلية الطب
جامعة عين شمس

2010