العدوى الفطرية بعد زراعة الكلى

بحث مقدم توطئة للحصول على درجة الماجستير فى الامراض الباطنة

مقدم من

محمد مصطفى درويش مصطفى

بكالوريوس الطب والجراحة-جامعة عين شمس

تحت اشراف

أ.د. ياسر سليمان احمد

استاذ الباطنة العامة وامراض الكلى

كلية الطب- جامعة عين شمس

د. وليد انور عبد المحسن

مدرس الباطنة العامة وامراض الكلى

كلية الطب- جامعة عين شمس

كلية الطب- جامعة عين شمس

٢٠٠٩

Fungal Infections following kidney transplantation

Essay

Submitted for partial fulfillment of master degree in internal medicine

Presented by

Mohamed Mustafa Darwish Mustafa

M.B.,B.Ch

Ain Shams University

Supervised by

Prof. Dr. Yasser Soliman Ahmed

Professor of Internal medicine and Nephrology

Faculty of Medicine-Ain Shams University

Dr. Waleed Anwar Abdel Mohsen

Lecturer of Internal Medicine and Nephrology

Faculty of Medicine-Ain Shams University

Faculty of Medicine

Ain Shams University

2009

Acknowledgment

First and foremost, I thank God for helping and guiding me in accomplishing this work.

I would like to express my sincere gratitude to ***Prof. Dr. Yasser Soliman Ahmed***, Professor of internal medicine and nephrology, Ain Shams University, for his great support and stimulating views. His active, persistent guidance and overwhelming kindness have been of great help throughout this work.

I must extend my warmest gratitude to ***Dr. Waleed anwar Abdel Mohsen***, Lecturer of internal medicine and nephrology, Ain Shams University, for his great unlimited help and faithful advice throughout this work.

Last but definitely not least, I would like to thank my family for always being there for me.

Table of contents

List of abbreviations

%	Percentage
A.	**Aspergillus**
AFB	Acid Fast Bacilli
AIDS	Acquired Immunedeficiency Syndrome
AmB	Amphotericin B
ATG	Antithymocyte globulin
BAL	bronchoalveolar lavage
C.	Candida
CMV	Cytomegalovirus
CNS	central nervous system
CSF	cerebrospinal fluid
CT	Computed tomography
DFA	direct fluorescent antibody
DIF	Direct immunofluorescence
EBIs	Ergosterol biosynthesis inhibitors

EBV	Epstein–Barr virus
ERG.	Ergosterol
F.	Fusarium
H.	Histoplasma
HBV	Hepatitis B virus
HCV	Hepatitis C virus
IFDs	Invasive fungal diseases
IV	Intravenous
K	Potassium
MAP	Mitogen activated protein
mg	Milligram
mm	millimeter
MMF	Mycophenolate Mofetil
MRI	Magnetic resonance imaging
μm	Micrometer
P.	Pseudallescheria
PC	Pneumocystitis carinii

PCP	Pneumocystitis carinii pneumonia
PTLD	post transplant lymphoproliferative disorder
Spp.	species
TB	Tuberculosis
vs.	versus
VZIG	varicella zoster immunoglobulin
VZV	Varicella Zoster Virus

List of figures

List of tables

Fungal Infections Following Kidney Transplantation

Introduction

Kidney transplantation has become the treatment of choice for both the quality of life and survival in patients with end stage renal disease **(Ciancio G, et al., 2005).** In the last decade, infection related mortality among renal transplant recipients has not decreased ,and invasive fungal infections remain important causes of mortality in this Population **(Linares L, et al., 2007).**

Immunosuppressive therapy after renal transplantation can lead patients to suffer severe infections that can be life threatening **(Kutinova A, et al., 2006)**. The morbidity and mortality rates associated with renal transplantation and the use of immunosuppressive medications, are high **(Mischitelli M, 2008).**

The incidence of fungal infections in renal transplant recipients is less than that reported for other organ transplant recipients. The mortality is related to the pathogenicity of the organism, site of infection,impaired inflammatory response, limited diagnostic tools, rapid clinical progression, failure to recognize high risk patients, and co-morbid diseases **(Kubak B,**

et al., 2005). After the first month, patients are exposed to opportunistic infections, mainly invasive viral and fungal infections, this risk persists until 6 months post transplant, but late opportunistic infections occur among high risk patients **(Linares L, et al., 2007).**

The most common fungal infection in the renal transplant recipients is Candidiasis, with Candida albicans the most frequent isolated pathogen. Suppression of gut flora by antibiotics,metabolic derangement (Diabetes and corticosteroids), and perturbation of host barriers with intravenous lines and bladder catheters, all enhance growth of candidal species **(Silkensen J, 2000).**

Abbott K et al conducted a study, analyzing 33420 renal transplant. Fungal infection were most commonly associated with esophagitis, pneumonia, meningitis, and urinary tract infection, led by candidiasis, Aspergillosis, cryptococcosis, mucormycosis, and zygomycosis **(Abbott K, et al., 2001).**

The diagnosis of fungal infection remains problematic and frequently leads to delays in clinical recognition. Isolation of candida from cultures occurs commonly, and does not

necessarily imply infection. Diagnosis of Aspergillus infection depends on high clinical suspicion, isolation, and typical radiographic findings. Galactomannan assays may aid in early diagnosis of invasive Aspergillosis in the high risk settings **(Kubak B, et al., 2005).**

Targeted prophylaxix for patients at high risk, aggressive treatment using broad spectrum antifungal agents, are recommended **(Linares L, et al., 2007).** The correct treatment of invasive fungal infection is often challenging **(Veroux m, et al., 2007).** It is recommended to monitor serum levels of immunosuppressive drugs closely (e.g. Cyclosporine A, tacrolimus, sirolimus) in patients receiving concomitant antifungal agents, because of the interaction between them **(Munksgaard B, 2004).**

In summary, infection related mortality among renal transplant recipients is an important issue, with a trend towards a high incidence of mortality associated with invasive fungal infections **(Linares L, et al., 2007).**

Aim of the Work

The aim of this review is to focus on fungal infections in kidney transplant recipients, recognition of high risk patients, methods of diagnosis, prophylaxis, treatment of common and emerging fungal infections, and overall morbidity and mortality of post transplant fungal infections.

Immunology of transplantation and immunosuppressive therapy

The central issue in kidney transplantation remains suppression of allograft rejection. Thus, development of immunosuppressive drugs is the key to successful allograft function. Immunosuppressive agents are used for induction (intense immunosuppression in the initial days after transplantation), maintenance, and reversal of established rejection. The following model of alloimmune response illustrates how these immunosuppressive drugs act **(Halloran P, 2004).**

three-signal model of alloimmune responses

Alloimmune responses involve both naive and memory lymphocytes, including lymphocytes previously stimulated by viral antigens cross-reacting with HLA antigens. In the graft and the surrounding tissues, dendritic cells of donor and host origin become activated and move to T-cell areas of secondary lymphoid organs. There, antigen-bearing dendritic cells engage alloantigen-reactive naive T cells and central memory T cells that recirculate between lymphoid compartments but cannot enter peripheral tissues(Figure 1).