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Fungal Infections following kidney transplantation

Essay

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Table of contents

| | |
|---|------------|
| Introduction | 1 |
| Aim of work | 4 |
| Review of literature | 5 |
| <u>Chapter1:</u> Immunology of kidney transplantation and immunosuppressive therapy | 5 |
| <u>Chapter2:</u> Infection Complications following kidney transplantation | 18 |
| <u>Chapter3:</u> Opportunist c infections in kidney transplant recipients | 30 |
| <u>Chapter4:</u> Fungal infections following kidney transplantation | 47 |
| • A-Identification and classification of fungi | 47 |
| • B-Overview and clinical presentation | 59 |
| • C-Diagnosis | 85 |
| • D-Prophylaxis and treatment | 102 |
| Summary | 130 |
| References | 132 |
| Arabic summary | |

List of abbreviations

| | |
|-------------|------------------------------------|
| % | Percentage |
| A. | Aspergillus |
| AFB | Acid Fast Bacilli |
| AIDS | Acquired Immunodeficiency 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

| | | |
|--------------------------|--|-----|
| <u>Figure 1:</u> | Three-signal model of alloimmune responses | 8 |
| <u>Figure 2:</u> | Individual Immunosuppressive Drugs and Sites of Action in the Three-Signal Model | 9 |
| <u>Figure 3:</u> | Temporal sequence of infections after organ transplantation | 25 |
| <u>Figure 4:</u> | Nocardia pneumonia. Bilateral hilar and perihilar thickenings of different density | 41 |
| <u>Figure 5:</u> | Timeline for Risk of Fungal Infections in Solid Organ Transplant Recipients | 62 |
| <u>Figure 6:</u> | Aspergillus pneumonia. Patchy consolidation with faded margins | 74 |
| <u>Figure 7:</u> | Disseminated histoplasmosis | 78 |
| <u>Figure 8:</u> | Pneumocystis carinii pneumonia | 84 |
| <u>Figure 9:</u> | The Saccharomyces cerevisiae ergosterol biosynthesis pathway | 104 |
| <u>Figure 10:</u> | Chemical structures and mechanisms of action for common antifungal drugs | 105 |

List of tables

| | | |
|-------------------------|--|------------|
| <u>Table 1:</u> | Classification of Immunosuppressive Therapies in Kidney Transplantation | 10 |
| <u>Table 2:</u> | Specific immunosuppressive drugs and infection | 22 |
| <u>Table 3:</u> | Temporal sequence of infections after organ transplantation | 26 |
| <u>Table 4:</u> | Simplified scheme illustrating major groups of the Kingdom Fungi | 51 |
| <u>Table 5:</u> | Clinical Data for the Main Agents of Invasive Fungal Infection | 58 |
| <u>Table 6:</u> | Fungal pathogens associated with invasive and/or disseminated infection in kidney transplant recipient | 60 |
| <u>Table 7:</u> | Factors Influencing the Net State of Immunosuppression | 65 |
| <u>Table 8:</u> | Serological tests for diagnosis of Candidal infection | 97 |
| <u>Table 9:</u> | Drug–drug interactions between antifungal agents and immunosuppressive agents | 123 |
| <u>Table 10:</u> | Pharmacokinetic and Pharmacodynamic Drug Interactions between the Azoles and Immunosuppressants. | 128 |

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 prophylaxis 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).