

Recent Updates in Neuropsychiatric Complications of Organ Transplantation and their Management

Essay

*Submitted For Partial Fulfillment of the Master Degree in
Neurology and Psychiatry*

By

Wael El Sayed Abdel Hak El Said
MB, B.CH. (2002)

Supervised by

Prof. Dr. Taha Kamel Taha Alloush

*Professor of Neuropsychiatry
Faculty of Medicine - Ain Shams University*

Prof. Dr. Ayman Mohammad Nassef

*Professor of Neuropsychiatry
Faculty of Medicine - Ain Shams University*

Dr. Lobna M. El-Nabil El-Sayed

*Assistant Professor of Neuropsychiatry
Faculty of Medicine – Ain Shams University*

**Ain Shams University
Faculty of Medicine
2015**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقَدْ أَعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
وَرَسُولُهُ وَالْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (١٠٥)



*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

*My profound thanks and deep appreciation to **Prof. Dr. Taha Kamel Taha Alloush**, Professor of Neuropsychiatry, Faculty of Medicine, Ain Shams University for his great support and advice, his valuable remarks that gave me the confidence and encouragement to fulfill this work,*

*I am also thankful to **Prof. Dr. Ayman Mohammad Nassef** Professor of Neuropsychiatry, Faculty of Medicine, Ain Shams University for his valuable supervision, co-operation and direction that extended throughout this work,*

*I would like to direct my special thanks to **Dr. Lobna M. El-Nabil El-Sayed**, Assistant Professor of Neuropsychiatry, Faculty of Medicine, Ain Shams University, for her invaluable help, fruitful advice, continuous support offered to me and guidance step by step till this essay finished.*

*I am deeply grateful to **my family** who directed and encouraged me during the preparation of this work,*



Wael El Sayed Abdel Hak El Said

List of Contents

	Page
Acknowledgment	--
List of Abbreviations	i
List of Figures	ii
List of Tables	v
Introduction	1
Aim of The Work	4
Review of Literature	5
Chapter 1 : Organ transplantation	5
Chapter 2 : Infections	13
Chapter 3 : Malignancies	32
Chapter 4 : Cerebrovascular	43
Chapter 5 : Epilepsy	59
Chapter 6 : Other Neurological Complications	71
Chapter 7 : Psychiatric Complications	86
Discussion	106
Summary	124
Conclusion	127
Recommendations	128
References	129
Arabic Summary	-

List of Abbreviations

AED	: Antiepileptic drug
Allo-BMT	: Allogeneic bone marrow transplantation
APPT	: Activated partial prothrombin time
BMT	: Bone marrow transplantation
CABG	: Coronary artery bypass grafting
CADP	: Chronic acquired demyelinating polyneuropathies
CMV	: Cytomegalovirus
CNI	: Calcineurin inhibitor
CNS	: Central nervous system
CPM	: Central pontine myelinolysis
CSF	: Cerebrospinal fluid
CT	: Computerized tomography
CVD	: Cerebrovascular diseases
CVST	: Cerebral venous sinus thrombosis
DM	: Diabetes mellitus
EBV	: Epstein-Barr virus
EEG	: Electroencephalography
ELISA	: Enzyme-linked immunosorbent assay
GVHD	: Graft-versus-host disease
HIE	: Hypoxic-ischemic encephalopathy
HLA	: Human leukocyte antigen
HSCT	: Hematopoietic stem cell transplantation
HSV-1/2	: Herpes viruses 1 and 2
IQ	: Intelligence quotient
ICH	: Intracranial hemorrhage
KS	: Kaposi's sarcoma
LDLT	: Living-donor liver transplantation
LOC	: Level of consciousness
LP	: Lumbar puncture
LT	: Live transplantation

List of Abbreviations (Cont.)

NCC	: Neurocysticercosis
NMSCs	: Nonmelanoma skin cancers
NPCs	: Neuropsychiatric complications
OLT	: Orthotopic liver transplantation
PCKD	: Polycystic kidney disease
PCR	: Polymerase chain reaction
PIQ	: Performance Intelligence Quotient
PML	: Progressive multifocal leukoencephalopathy
PRES	: Posterior reversible encephalopathy syndrome
PT	: Prothrombin time
PTLD	: Posttransplant lymphoproliferative disease
PTSD	: Post-traumatic stress disorder
RPLS	: Reversible posterior leukoencephalopathy syndrome
SOT	: Solid organ transplantation
SSRIs	: Selective serotonin reuptake inhibitors
TIA	: Transient ischemic attack
TIA	: Transient ischemic attacks
VIQ	: Verbal Intelligence Quotient
VNS	: Vagus nerve stimulation
VZV	: Varicella-zoster virus
WNV	: West Nile virus

List of Figures

Fig.	Title	Page
1	The phases in the “timetable of infections” according to time elapsed since transplantation	16
2	Brain biopsy specimens from transplant patient with PTLN.	38
3	(a) Cerebral hemorrhage in an 8-year-old boy 6 weeks after bone marrow transplantation for acute myeloid leukemia. (b) Intraocular hemorrhage in a 7-year-old boy 2 months after bone marrow transplantation for aplastic anemia.	51
4	(a) Subdural hemorrhage in a 21-month-old boy 1 month after bone marrow transplantation for thalassemia. (b) Cerebral infarcts in an 8-year-old boy 4 weeks after bone marrow transplantation for acute myeloid leukemia.	52
5	55-year-old woman with venous sinus occlusion on 72nd day after hematopoietic stem cell transplantation (HSCT).	55
6	31-year-old woman with spinal infarction presented with sudden-onset paralysis of right upper and lower extremities on 440th day after HSCT.MRI was performed 7 hours after onset.	56
7	Algorithm for treatment of seizures in transplant patients	70
8	A 50-year-old woman 6 months post liver transplant experienced a generalized seizure and unresponsiveness.	76
9	A 48-year-old woman with acute myelogenous leukemia status post allogenic BMT had a seizure 19 days after transplantation.	77

List of Figures (Cont.)

Fig.	Title	Page
10	Algorithm for the evaluation of a patient with posttransplant encephalopathy, including failure to awaken from surgery	122
11	Algorithm for the management and evaluation of a patient with seizures after transplantation	123

List of Tables

Table	Title	Page
1	Incidence of neurologic complications after solid organ transplantation.	7
2	Opportunistic infections affecting transplant recipients	31
3	Type of Cerebrovascular Complications	48
4	Drugs : use, available formulations, standard dosage, main drug interactions, typical adverse effects and cost	66
5	Cause of posttransplant encephalopathy	72
6	Neurologic Consultation: The Encephalopathic Solid Organ Transplant Recipient	74

Introduction

Organ transplantation as a treatment of choice has increased in recent years due to concurrent advances in medical science. Patients successfully receive transplanted solid organs - kidney, heart, liver, pancreas, lungs, and intestines - and transplanted bone marrow and stem cells. The United Network for Organ Sharing (UNOS) reports more than 100,000 patients waiting for a transplant, with most waiting for a kidney or liver. That number sharply contrasts with the number of transplants completed during 2009: 28,462, of which approximately 21,000 were donations from a deceased donor and the remainder from a living donor. Because of the dramatic need for donors and the necessary immediacy of donor and recipient information, UNOS has established an online database (UNet) which provides access to information concerning waiting patients (*UNOS, 2010*)

Organ donation presents a range of practice issues for the psychologist. The transplant recipient has been historically identified as the patient who is the subject of both accurate assessments before transplant to determine appropriateness of the procedure and ongoing psychological interventions after transplant. However, as attention to organ donation has increased, other important patients have been identified. Because most donors are deceased, decision making about donation falls to family members at a time of significant grief and distress. These donor families are also important patients in the donation process. Additionally, families of patients eligible to receive organ donation experience many concerns during the waiting period and after transplantation, and thus form an additional patient population. Although the majority of this article focuses on patients receiving transplants, the other patients are also considered. Psychosocial issues are present before, during, and after transplantation. Patients who hope to receive a donor organ typically try to increase their

medical knowledge before the transplantation process takes place. With this knowledge, however, come additional sources of anxiety, including transplant evaluation outcome, the shortage of organs, the uncertainty of donation, and increased understanding that having a transplant may not offer a cure (**Engle, 2001**).

Psychosocial stressors change during the transplant process. These changes result from relocation to the transplant center, guilt over knowing that a donor death occurred in order to procure a donor organ, coping with the medical regimen, body image concerns, and exposure to loss. Diagnosable disorders among patients during hospitalization have been identified, including anxiety disorders, cognitive impairment, depression, and even posttraumatic stress disorders (**Bunzel et al., 2005**).

After the transplant procedure, psychosocial concerns tend to revolve around readjustment to a new lifestyle. These concerns include anxiety at discharge, perhaps due to loss of security or fear of adjustment; sadness or guilt from leaving relationships formed with other transplant patients; estrangement from family and community during readjustment to family and work roles; and increased physical and functional impairment (for reviews of psychosocial issues in organ transplant (**Olbrisch et al., 2002**).

The posttransplantation clinical course is generally complicated by dysfunction of various organ systems, and early or delayed neurologic complications may develop in 30-60% of patients (**Zivkovic and Abdel-Hamid, 2010**). Because of the constantly changing protocols of transplantation and immunosuppression, the nature of neurologic complications has changed over time. Improved survival of patients undergoing transplant also shifts the focus of neurologic complications towards long-term complications.

Timing of neurologic events provides significant guidance on which causes to consider; for example, most cases of metabolic encephalopathy and seizures occur in the first few weeks after transplantation, whereas most opportunistic infections occur 1 month or more after transplant. Drug toxicity tends to occur early (contributing to the high rate of seizures and altered mental status observed after transplant) but can occur at any point while the patient is on immunosuppressant therapy. The total rate of complications is variable because investigators include a variety of other neurologic symptoms, including headache, tremor, and peripheral nervous system dysfunction in **(Munoz et al., 2010)**.

Serious complications occur in roughly 10% to 30% of transplant recipients. The spectrum of neurologic morbidity may also be shifting, with a declining incidence of severe acute complications with refined operative techniques and postoperative care (including lower-intensity immunosuppressive regimens); as transplant patients survive longer, they become more at risk for delayed complications such as opportunistic infections and malignancies. Encephalopathy remains the most common complication in these series, with rates as high as 43% (generally highest after liver, intestinal, and lung transplant); it predominantly occurs in the immediate postoperative period, out until hospital discharge and often extending length of stay **(Saner et al., 2007)**.