Multiple Myeloma: A retrospective Analysis of the Patients Treated at Ain Shams University Clinical Oncology Department with a Review of the Literature

Thesis

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Moushira Esmail

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List of Abbreviations

Abb.	Full term
ASCT	Autologous stem cell transplantation
BMA	Bone marrow aspirate
BMB	Bone marrow biopsy
BMPCs	Bone marrow plasma cells
CA	Chromosomal abnormalities
CAMDR	Cell adhesion-mediated drug resistance
CBC	Complete blood count
CT	Computed tomography
CXCR	CXC-chemokine receptor type 4
DCE	Dynamic contrast-enhanced
DFCI	Dana-Farber Cancer Institute
DWI	Diffusion-weighted imaging
FDA	Food and Drug Administration
FLC	Free light chain
HLC	Heavy/light chain
iFISH	interphase FISH
IFM	Intergroupe Francophone du Myelome
IMWG	International Myeloma Working Group
IRd	Ixazomib, lenalidomide, dexamethasone
ISS	International Staging System
KRD	Carfilzomib (Kyprolis)- Lenalidomide-Dexamethasone
LDH	Lactate dehydrogenase
MGUS	Monoclonal gammopathy of undetermined significance
miRNA	microRNA
MM	Multiple myeloma
MP	Melphalan, prednisone

List of Abbreviations Cont..

Abb.	Full term
MPT	Melphalan, prednisone, thalidomide
MRI	Magnetic resonance imaging
NCCN	National Comprehensive Cancer Network
OS	Overall survival
PET	Positron emission tomography
PFS	Progression free survival
RANKL	Receptor activator of nuclear factor-κB ligand
Rd	Lenalidomide plus dexamethasone
R-ISS	Revised ISS
SLAMF7	Signaling lymphocytic activation molecule F7
SMM	Smouldering MM
SUV	Standardized uptake value
SWOG	Southwest Oncology Group
TTP	Time to progression
VCD	Bortezomib (Velcade)- cyclophosphamide-dexamethasone
VEGFA	Vascular endothelial growth factor A
VRD	Bortezomib (Velcade)- lenalidomide (Revlimid)- dexamethasone
VTD	Bortezomib (Velcade)- Thalidomide-Dexamethasone
ECOG	Eastern Cooperative Oncology Group
G-CSF	Granulocyte stimulating factor
MDS	Myelodysplastic syndrome
VMP	Bortezomib (Velcade) – Melphalan – Prednisone
VMPT	Bortezomib (Velcade) – Melphalan – Prednisone Thalidomide

List of Abbreviations Cont..

Abb.	Full term
TRM	Transplantation-related mortality
GVHD	Graft-versus-host disease
MRC	Medical research council
BIPN	Bortezomib _induced Peripheral neuropathy
SDS	Salmon-Durie staging system
SD	Stationary disease
PR	Partial response
CR	Complete response
PD	Progressive disease
CTCAE	Common Terminology Criteria for Adverse Effects
^{18}F-FDG	^{18}F-fluorodeoxyglucose
CRP	C-reactive protein
LDH	Lactate dehydrogenase
ISS	The International Staging System
MDEs	Myeloma-defining events
TD	Thalidomide-Dexamethasone
Pom/Dex	Pomalidomide-Dexamethasone
VD	Bortezomib-Dex
VMP	Bortezomib-Melphalan-Prednisone
CyBorD	Bortezomib- Cyclophosphamide- Dexamethasone
CCyD	Carfilzomib- Cyclophosphamide- Dexamethasone

Abstract

Multiple Myeloma: Aretrospective analysis of the patients treated at Ain Shams University Clinical oncology department with a review of the literature.

Purpose/Objective: This study aims at analysis the epidemiological data of the patients treated from multiple myeloma at Ain Shams University together with reviewing the different lines of management according to recent recommendations.

Patients and methods: This retrospective analyses of 62 patients with multiple myloma data recorded at their files with follow up and reviews of the recent advances in the management of multiple myeloma.

Results: among 62 patients involved in the present study we found that 96.8% of patients showing clinical improvement after treatment on other hand only 3.2% deteriorated, 61.35 of patients were alive,9.7% died and 29% lost follow up, the mean time to DFS was 22.55 months, mean OS was 63.2 months with 87.8% of patients survived at the end of the study,as regard mean PFS was 54.9 months with PFS at end of study was 74.9% of patients, there was insignificant differences between OS and demographic data,laboratory studies, there was insignificant differences between PFS and demographic data,laboratory studies.

Conclusion: Multiple myeloma (MM) is a heterogeneous hematologic malignancy involving the proliferation of plasma cells derived by different genetic events contributing to the development, progression, and prognosis of this disease.

Key words: Multiple myeloma –Kahler's disease – Egypatian patients – prognostic factors.

INTRODUCTION

Multiple myeloma (MM) is a malignant neoplasm of plasma cells that accumulate in bone marrow leading to bone destruction and marrow failure ***(Siegel et al., 2017).***

Most cases of multiple myeloma also feature the production of a para protein (an abnormal antibody) which can cause kidney problems. Bone lesions and hypercalcemia are also often encountered ***(Dimopoulos et al., 2011).***

Multiple myeloma accounts for about 1.8% of all cancers and slightly over 17% of all the hematologic malignancies in the United States. Myeloma is most frequently diagnosed among people aged from 65 to 74 years with median age 69 years. About 30,280 new myeloma cases have been estimated in the United States in 2017 with an estimated 12,590 deaths ***(Siegel et al., 2017).***

It is more common in men and for unknown reasons, is twice as common in African Americans as it is in White Americans. With conventional treatment, median survival is 3–4 years, which may be extended to 5–7 years or longer with advanced treatments ***(Ocio et al., 2008).***

AIM OF THE WORK

This study aims at analysing the epidemiological data of the patients treated from multiple myeloma at Ain Shams University together with reviewing the different lines of management according to recent recommendations.

Chapter 1

MULTIPLE MYELOMA INCIDENCE AND EPIDEMIOLOGY

Almost all patients with **M**ultiple **M**yeloma (MM) evolve from an asymptomatic pre-malignant stage termed monoclonal gammopathy of undetermined significance (MGUS). MGUS progresses to MM at a rate of 1% per year. In some patients, an intermediate asymptomatic but more advanced pre-malignant stage termed smouldering (or indolent) multiple myeloma (SMM) can be recognised. SMM progresses to myeloma at a rate of 10% per year over the first 5 years following diagnosis, 3% per year over the following 5 years, and 1.5% per year thereafter ***(Rajkumar et al., 2014).***

Multiple myeloma accounts for approximately 1.8% of all cancers and slightly >15% of hematologic malignancies in the United States. Myeloma is most frequently diagnosed among people aged 65 to 74 years, with the median age being 69 years. In 2016, the American Cancer Society estimated that 30,330 new cancer cases occurred in the United States, with an estimated 12,650 deaths ***(Siegel et al., 2017).***

Egyptian data from national population-based cancer registry, MM represented 0.53% of cancers in males and 0.34% of cancers in females at period from (2008-2011) with peak age of diagnosis from 60 to 65 years in males and from 70 to 75