Study of Kappa to Lambda ratio in Multiple Myeloma as a predictor of outcome and prognostic factor in Egyptian patients

Thesis

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by

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Ibrahem Abd El-Hak El-saied

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List of Abbreviations

Abbreviations		Full term
AKI	:	Acute kidney injury
AL	:	Amyloidosis
BMT	:	Autologous bone marrow transplantation
BJP	:	Bence Jones protein
CG	:	Cytogenetic
CR	:	Complete response
CT	:	Computerized tomography
DM	:	Diabetes mellitus
FISH	:	Florescence in situ hybridization
FLCs	:	Free light chains
HB	:	Hemoglobin
IF	:	Immunofixation
IgA	:	Immunoglobulin A
IgD	:	Immunoglobulin D
IgE	:	Immunoglobulin E
IgG	:	Immunoglobulin G
IgM	:	Immunoglobulin M
IHD	:	Ischemic heart disease
IMWG	:	International Myeloma Working Group
ISS	:	International staging system

List of Abbreviations (Cont.)

Abbreviations		Full term
LCDD	:	Light chain deposition disease
LCMM	:	Light chain multiple myeloma
MGUS	:	Monoclonal gammopathy of undetermined significance
MM	:	Multiple myeloma
MRI	:	Magnetic resonant imaging
NCCN	:	National Comprehensive Cancer Network
NSMM	:	Non-secretory myeloma
PCR	:	Polymerase chain reaction
PD	:	Progressive disease
Plt	:	Platelet
POEMS	:	Osteosclerotic myeloma
PR	:	Partial response
S.Ca	:	Serum calcium
sCR	:	Stringent complete response
SD	:	Stable disease
SIFE	:	Serum immunofixation electrophoresis
SMM	:	Smoldering multiple myeloma
SPEP	:	Serum protein electrophoresis
TLC	:	Total light chains

List of Abbreviations (Cont.)

Abbreviations		Full term
UIFE	:	Urine immunofixation electrophoresis
UPEP	:	Urine protein electrophoresis
VCD	:	Velcade, cyclophosphamide, dexamethasone
VGP R	:	Very good partial response
VTD	:	Velcade, thalidomide, dexamethasone
WM	:	Waldenström's macroglobulinaemia
β2	:	Beta-2
κ/λ FLC ratio	:	Kappa : Lambda free light chain ratio

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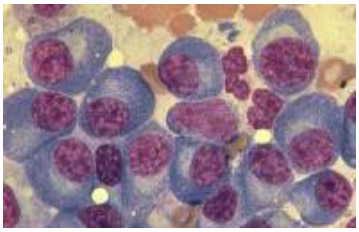
Introduction

Multiple myeloma (MM) is heterogeneous malignant neoplasm that occurs mainly in patients over 50 years of age characterized by neoplastic proliferation of a single clone of plasma cells (fig 1 a - b) producing a monoclonal immunoglobulin. This clone of plasma cells proliferates in the bone marrow and often results in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures. ***(Kyle RA, et al. 2004)***

The diagnosis of multiple myeloma is often suspected because of one or more of some clinical presentations as; bone pain with lytic lesions discovered on routine skeletal films, an increased total serum protein concentration and/or the presence of a monoclonal protein in the urine or serum, systemic signs or symptoms suggestive of malignancy, such as unexplained anemia, hypercalcemia, which is either symptomatic or discovered incidentally, is common, acute renal failure with a bland urine analysis or rarely the nephrotic syndrome due to concurrent primary amyloidosis. ***(Kariyawasan et al., 2007)***

It is important to distinguish multiple myeloma both from other causes of the clinical presentations above and other plasma cell dyscrasias for the purposes of prognosis and treatment. It is also important to evaluate patients suspected of having multiple myeloma in a timely fashion since a major delay in diagnosis has been associated with a negative impact on the disease course.

Most patients with MM present with signs or symptoms related to the infiltration of plasma cells into the bone marrow, kidney damage or other organs from excess light chains. ***(Kariyawasan et al., 2007***)



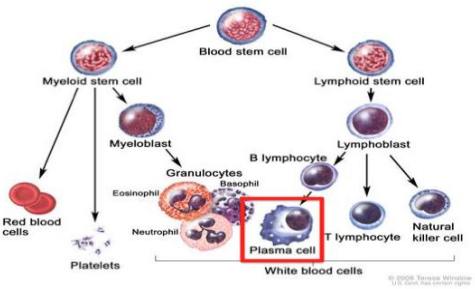


Fig. (1:a-b) microscopic pictureof plasma cell (a) and stages of plasma cell proliferation (b)) (***Kyle RA et al. 2004)***

EPIDEMIOLOGY

MM accounts for approximately 1 percent of all cancers and slightly more than 10 percent of hematologic malignancies in the United States (US).The annual incidence in the US is approximately 4 to 5per 100,000. A similar incidence has been reported in the South Thames area of the United Kingdom and in European general. (***Kyle. RA, et al., 2004)*** The median age at diagnosis is 66 years.

MM occurs in all races and all geographic locations. The incidence varies by ethnicity; the incidence in African Americans and blacks from Africa is two to three times that in whites ***(Huang SY, et al., 2007)***

A small but unknown fraction of cases are familial. The risk of developing MM is approximately 3.7-fold higher for persons with a first-degree relative with MM. MM has been reported in clusters of two or more first-degree. ***(Lynch. HT, et al., 2001)***

In Egypt the data are limited to determine the actual incidence rate but there is study done To determine the clinical and laboratory characteristics and survival of diagnosed Egyptian multiple myeloma patients admitted to

the Haemato-Oncology Department between 2000 and 2010. Records of all patients in whom multiple myeloma was diagnosed at the Kasr Al Aini Hospital between 2000 and 2010 were included in this retrospective study. The mean age of patients was 58.5 years (range, 27-80 years). Fifty-nine percent were males. The majority of patients (73 %) had an immunoglobulin G monoclonal band and 70 % were Kappa chain-positive. Mean overall survival was 37.5 months (range, 1-84 months). ***El Husseiny N, et al (2013)***

Survival analysis was statistically insignificant with respect to age, sex, International Staging System and type of treatment ($p > 0.05$). Our records were largely comparable to those reported in Chinese studies but different from those noted in Western and Arabic countries. ***(Qiu L, et al., 2008)***.

Detection of monoclonal free light chains (FLCs) (fig 2) is important for diagnosis and monitoring of monoclonal gammopathies. Although FLCs are especially important in light-chain diseases, such as light-chain myeloma, primary systemic (AL) amyloidosis, and light-chain deposition disease, FLC abnormalities occur in as many as 97% of plasma cell disorders, including 95% of