

Recent Advances in the Imaging of Multiple Myeloma

Essay

Submitted for partial fulfillment of Master Degree in
Radiodiagnosis

Presented by

Rami Mohammed Fouad Shaheen

M.B., B. Ch.
Faculty of Medicine
Ain Shams University

Supervised by

Dr. Aida El Shibiny

Professor of Radiology
Faculty of Medicine
Ain Shams University

Dr. Samer Malak

Assistant Professor of Radiology
Faculty of Medicine
Ain Shams University

***Faculty of Medicine
Ain Shams University
2011***

التطورات الأخيرة في تصوير المايلوما المتعددة

رسالة مقدمة من
الطبيب / رامي محمد فؤاد شاهين

توطئه للحصول على درجة الماجستير في الأشعة التشخيصية

تحت اشراف

دكتورة/ عايدة الشبيني
أستاذ الأشعة التشخيصية
كلية الطب – جامعة عين شمس

دكتور / سامر ملاك
أستاذ مساعد الأشعة التشخيصية
كلية الطب – جامعة عين شمس

كلية الطب
جامعة عين شمس
2011

List of figures

Figure	Contents	Page
1	Normal hematopoiesis in 10 year old girl	6
2	Normal conversion of hematopoietic marrow	7
3	Normal distribution of adult marrow	8
4	Epiphyseal marrow in 20 year old man	9
5	MRI of normal vertebral marrow	10
6	Normal coronal 18F FDG PET scan	12
7	FDG uptake of normal tonsils	13
8	FDG uptake of arytenoid muscles	15
9	FDG uptake of medial and lateral recti muscles	15
10	Coronal PET of normal thymus	16
11	PET scan after heavy meal	18
12	Sagittal PET and PET/CT of normal esophagus	19
13	Coronal PET and PET/CT of normal gastric wall	20
14	Coronal PET, CT and PET/CT of normal right colon	21
15	Physiological testicular FDG uptake	22
16	Benign ovarian FDG uptake	23
17	Ovarian corpus luteum cyst FDG uptake	24
18	Muscle FDG uptake	26
19	Brown adipose tissue FDG uptake	27
20	Effect of granulocyte CSF on FDG uptake	29
21	FDG uptake of long bone physes	30
22	Abnormal serum protein electrophoresis	34
23	Diffuse marrow infiltration	35
24	Isotropic voxels at two different fields of view	54
25	CTM and standard MRI in vertebral fractures	63
26	18 FDG PET/CT in activation of BAT	77
27	Typical radiographic appearance of flat bone lesions	81
28	Multiple cortical erosions and scalloping on X-ray	82
29	Diffuse osteopenia and vertebral collapse on X-ray	83
30	Persistent osteolytic lesions on X-ray	87
31	CT of lytic expansile mass in vertebral body	88
32	Osteolytic lesions in MDCT absent in radiography	90
33	MDCT versus radiography in staging MM	91
34	Significant finding on MDCT not found on RSS	92
35	CT showing no evidence of healing after remission	94
36	MRI of focal infiltration of the bone marrow	98

List of figures (Cont.)

37	MRI of diffuse infiltration of bone marrow	99
38	MRI of salt-pepper pattern of myeloma	101
39	MRI unmasking of focal lesions after chemotherapy	102
40	Avascular necrosis of left hip	103
41	ADC and DWIBS before and after treatment of MM	106
42	DCE-MRI before and after treatment	109
43	MRI of MM after treatment	110
44	MRI upstaging a stage I myeloma on radiography	113
45	Discordant findings between MDCT and MRI	114
46	Appearance of myeloma on FDG-PET	116
47	Breakout lesion and EMD on PET/CT	118
48	Examples of infection by FDG PET	119
49	Left humeral lesion in FDG-PET and radiography	121
50	MRI true positive and PET false negative findings	122
51	PET and MRI in demonstrating response to therapy	124
52	PET/CT showing extramedullary recurrence	125
53	MIBI versus MDP in evaluating myeloma	126
54	99mTc sestamibi in active multiple myeloma	127
55	Differentiation of diffuse MM from BM stimulation	130

List of tables

No	Title	Page
1	Durie and Salmon staging of multiple myeloma	37
2	Clinical features of multiple myeloma	38
3	Durie and Salmon staging of multiple myeloma	83
4	Recent Durie and Salmon PLUS staging system	105

List of Abbreviations

18F	Fluorine -18
3D	Three dimensional
99mTc	Technetium 99m
ADC	Apparent diffusion coefficient
AL	Amyloid light chain
BAT	Brown adipose tissue
BM	Bone marrow
BME-MAX	Bone marrow enhancement - maximum
CNR	Contrast to noise ratio
CNS	Central nervous system
cP	Centipoise
CSF	Colony stimulating factor
CT	Computer tomography
CTM	Continuous table movement
DCE-MRI	Dynamic contrast enhanced magnetic resonance imaging
DKK-1	Dickkopf-1
D-S	Durie and Salmon
DTPA	Diethylene-triamine-penta-acetic acid
DVT	Deep venous thrombosis
DWI	Diffusion weighted imaging
DWIBS	Diffusion weighted whole body imaging with background suppression
EPI	Echo planar imaging
ESR	Erythrocyte sedimentation rate
Fc	Fragment crystallizable
FDG	Fluorodeoxyglucose
FL	Focal lesion
FLE-MAX	Focal lesion enhancement - maximum
FOV	Field of view
Gd	Gadolinium
Ig	Immunoglobulin

List of Abbreviations (Cont.)

IGF-1	Insulin like growth factor-1
IL	Interleukin
IL-1	Interleukin-1
IL-6	Interleukin-6
kg	Kilogram
MBq	Megabecquerel
MC	M protein component
mCi	Millicurie
MDCT	Multi-detector computer tomography
MDP	Methylene diphosphate
MGUS	Monoclonal gammopathy of undetermined significance
MIP	Maximum intensity projection
MM	Multiple myeloma
mmol	Millimole
MPG	Motion probing gradient
MPR	Multiplanar reformatting
MRI	Magnetic resonance imaging
NFkB	Nuclear factor kappa B
NPO	Nil per os
OAFs	Osteoclast activating factors
OPG	Osteroprotegerin
PACS	Picture archiving and communication system
PET	Positron emission tomography
PET/CT	Positron emission tomography/computer tomography
POEMS	Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes
PTH	Parathyroid hormone
PTHrP	Parathyroid hormone related protein
RANKL	Receptor activator of nuclear factor kappa B ligand

List of Abbreviations (Cont.)

RBC	Red blood cell
ROI	Region of interest
RSS	Radiographic skeletal survey
SDF-1	Stromal derived growth factor-1
sestaMIBI	Sesta methoxy-iso-butyl-isonitrile
SNR	Signal to noise ratio
SPECT	Single photon emission computed tomography
STIR	Short time inversion recovery
TE	Time for echo
TGF-β	Transforming growth factor beta
TNF-α	Tumor necrosis factor alpha
TR	Time for repetition
TSE	Turbo spin echo
VEGF	Vascular endothelial growth factor
VIBE	Volumetric interpolated breath-hold examination
WBC	White blood cell
WB-MRI	Whole body magnetic resonance imaging

CONTENTS

Subject	Page
1. Introduction and Aim of the work.....	1
2. Relevant MRI and PET anatomy.....	4
3. Pathology of multiple myeloma.....	31
4. Technique of imaging modalities.....	52
5. Imaging criteria of multiple myeloma.....	80
6. Summary and conclusion.....	131
7. References.....	134
8. Arabic summary	

Chapter 1
Introduction
&
AIM OF THE WORK

Introduction

Multiple myeloma (MM) is a B cell neoplasm characterised by the proliferation and accumulation of plasma cells in the bone marrow and by the overproduction of monoclonal immunoglobulins that can be detected in serum and/or urine (***Nanni et al., 2006***). Multiple myeloma accounts for approximately 10% of haematological malignancies and shows a peak incidence during the seventh decade. Approximately 5%–10% of patients have a solitary plasmacytoma (***Schirrmeister et al., 2002***). The clinical presentation of MM includes bone pain, recurrent or persistent infections, anemia, weakness and renal impairment or a combination of these symptoms (***Ghanem et al., 2006***).

Determination of the total number of lesions is critical for staging purposes, as the treatment and prognosis is different for different types of myeloma, depending on precise staging. In the past, evaluation of the extent of osseous disease has relied primarily on the conventional radiographic skeletal survey (***Breyer III et al., 2006***) which was found to have limitations in evaluating early disease , and several studies have shown that multifocal disease may be present despite normal radiographs (***Bredella et al., 2005***). Conventional radiography also suffers from a relatively high false negative rate, leading to significant underestimation in diagnosing and staging of patients with multiple myeloma. Another disadvantage of radiographic technologies is that history and activity status of myeloma cannot be estimated (***Piekarek et al., 2009***).

➔ *Introduction and Aim of the Work*

As a result, new imaging modalities have been examined in the management of multiple myeloma aiming for better management of this condition.

Magnetic resonance imaging (MRI) was found to be sensitive and effective diagnostic method with an important impact on staging and further treatment of multiple myeloma (*Piekarek et al., 2009*). It was also found to have a prognostic significance; the number of lesions on MRI correlates very well with treatment outcome and overall survival of patients with multiple myeloma (*Lütje et al., 2009*).

Whole-body multi-detector computer tomography (MDCT) is superior to skeletal X-ray in detecting osteolytic lesions and in determining overall stage of multiple myeloma. Furthermore, additional findings could be seen detectable on whole body MDCT like emphysema, lymphadenopathy or hepatosplenomegaly that cannot be detected on conventional skeletal survey (*Lütje et al., 2009*).

Positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) was shown to be useful in assessment of response to therapy and as a prognostic indicator, especially in the setting of extramedullary disease (*Shortt et al., 2009*). It is also able to detect medullary involvement of multiple myeloma (*Bredella et al., 2005*).

Tc-99m sestamibi imaging is also being increasingly utilized in the staging of the disease process as well as determination of remission in patients with multiple myeloma following chemotherapy (*Kalaga et al., 2009*).

Aim of the Work

The aim of this work is to evaluate the recent advances in the imaging of multiple myeloma.

Chapter 2

Relevant MRI and PET Anatomy

Relevant MRI and PET Anatomy

MRI Anatomy of Bone Marrow

Normal Anatomy

The normal bone marrow has three primary components: osseous matrix, red marrow, and yellow marrow. The osseous components of the marrow are the trabeculae of cancellous bone, which provide the supporting framework for the red and yellow marrow elements. The red or cellular marrow is hematopoietically active, producing red blood cells (RBCs), white blood cells (WBCs), and platelet precursors. Hematopoietically inactive yellow marrow is composed of fat cells. These two types of marrow differ in their chemical composition. Recognition of these differences is important to understanding the MRI appearance of marrow. In infants and young children, red marrow consists of approximately 40% water, 40% fat, and 20% protein. As the individual ages, the fatty elements of hematopoietic marrow increase, and by age 70 years, red marrow is composed of approximately 60% fat, 30% water, and 10% protein. Yellow marrow contains approximately 80% fat, 15% water, and 5% protein. (Siegel, 2000)

MRI Appearance of Normal Marrow

The MR appearance of the bone marrow depends on the pulse sequence selection and the relative amounts of cellularity, protein, water, and fat within the