

Role of Nuclear Medicine In Management of Relapsing Lymphoma

Essay

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In nuclear medicine

By

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Abstract

The use of unlabelled immunotherapy (rituximab) in treatment of relapsed NHL proven by many studies done a high efficiency rate with a relatively fewer side effects compared to other conventional therapeutic modalities. Thus rituximab therapy has substantially changed the practice of lymphoma treatment. Although rituximab on its own has a relatively low complete response rate (6%) and overall response rate (48%), it is an effective therapy.

The two other approved radiopharmaceuticals which are currently used are Zevalin and Bexxar. Both Zevalin and Bexxar therapies are safe and effective in the treatment of NHL when used as directed and must be considered when standard treatments are ineffective. They are efficacious in patients who had failed rituximab therapy.

Key words

Zevalin- Bexxar-Non-hodgkin lymphoma

List of content

1- Introduction and aim of the work	1
2- Pathology of lymphoma	4
3- Role of Gallium scan in lymphoma	15
4- PET and PET/CT in lymphoma	28
5- Evaluation of lymphoma using other radiopharmaceuticals	57
6- Relapsing lymphoma.	64
7- Therapy of Non Hodgkin lymphoma	69
8- Immuno and radioimmunotherapy of lymphoma.	76
9- Summary and conclusion.	127
10- References.	131
11- الملخص العربي.	

List of figures

Fig no	Title	Page
1	Mechanism of FDG uptake	31
2	Biodistribution of FLT	32
3	Whole body FDG- PET and MET-PET scans in stage 4 low grade NHL	34
4	Detection of recurrent lymphoma within a residual mass by PET/CT.	37
5	¹⁸ F-FDG accumulations of lymphadenopathy and an incidental nodular uptake in the left pelvis. In contrast, ⁶⁷ Ga scintigraphy showed almost no abnormal findings except for slightly increased left hilar ⁶⁷ Ga uptake (physiological).	39
6	Characterization of FDG uptake in a hyperplastic thymus by PET/CT	41
7	Differentiating brown fat uptake from sites of disease by PET/CT.	42
8	Intense marrow activation by PET scan following granulocyte stimulating factor	43
9	Detection of extranodal lymphoma on PET/CT	44
10	PET/CT used for the differential diagnosis between a malignant and benign etiology in left pelvic increased FDG uptake.	47

List of figures

11	Abdominal para-aortic lymph node involvement. Improved staging with the use of PET/CT.	50
12	Diagrammatic presentation of the structure of the antibody	78
13	Monoclonal antibodies production	80
14	CD20 binding sites	89
15	Mechanisms of action of rituximab	90
16	Diagrammatic presentations of common side effects of rituximab	95
17	Different cells expressed on lymphoma antigens	97
18	¹¹¹ In-labeled ibritumomab tiuxetan images	100
19	Schematic diagram represent the schedule administration of Zevalin	103
20	Rationale for antibody predosing	115
21	Schematic representation of Bexxar MAB administration	116

List of tables

NO	Title	Page
1	World Health Organization (WHO): classification system of the Lymphomas	6-7
2	Common β^+ emitters of clinical importance	28

List of Abbreviation

ADCC	antibodies dependent cytotoxicity
AHSCT	autologous hematopoietic stem cell transplantation
ANC	absolute neutrophilic count
BMT	bone marrow transplantation
CD	Clusters of differentiation
CDC	cell dependent cytotoxicity
CDRs	complementarily defining regions
CL	constant-region domain of light chain
CR	Complete Response
CRu	Complete remission—unconfirmed/uncertain
CT	Computer Tomography
DLBCL	diffuse large B-cell lymphoma
ESR	Erythrocyte sedimentation rate
Fab	fragment antigen binding
Fc	fragment crytallizable
FDA	food and drugs administration
FDG	Fluro deoxy glucose
FLT	flurothymidine

List of abbreviation

Ga	Gallium
GIT	gastrointestinal tract
GLUT	glucose transporters
GS	Gallium scan
HD	Hodgkin's disease
Kev	Kilo electron volt
HACA	human antichimeric antibodies
HAMA	human antimouse antibodies
IL-2	interleukin-2
IPI	international prognostic index
LDH	lactate dehydrogenase
mAbs	monoclonal antibodies
MALT	mucosa-associated lymphoid tissue
mCi	milli Curie
MCL	Mantle cell lymphoma
MET	Methionine
MRI	Magnetic resonance imaging
mSv	Milli sievert
MTD	maximum tolerated dose
NHL	Non Hodgkin lymphoma
NPV	negative predictive value

List of abbreviation

ORR	over all response rate
OS	overall survival
PBSCT	peripheral blood stem cell transplantation
PD	Progressive disease
PET	Positron emission tomography
PFS	progression-free survival
%R	Percentage of retention
PPV	positive predictive value
PR	Partial response
REAL	Revised European-American Classification of Lymphoid Neoplasm
RES	reticuloendothelial system
RIC	radio-immunoconjugate
RIS	Radio immuno scintigraphy
RIT	Radio- immunotherap
SD	Stable disease
SPD	sum of the products of the diameter
SPECT	Single photon emission tomography
SRS	Somatostatin receptor scintigraphy
SSKI	saturated solution potassium iodide

List of abbreviation

TBI	total body irradiation
TfR	Transferrin receptor
TLS	Tumor lysis syndrome
TSH	thyroid stimulating hormone
TTP	time to progression
VH	variable heavy chain
VL	variable light chain
WHO	World Health Organization

Introduction and aim of work

Introduction

Lymphomas are a diverse group of cancers that affect a type of white blood cell lymphocytes - immune cells, account for over 3% of Cancers occurring world wide. About 85% of lymphomas are of B-cell origin, and 15% of T-cell origin. B-cells originate and mature and differentiate in the bone marrow. T-cells also start in the bone marrow, but they differentiate and mature in the thymus gland. Lymphoma is generally divided into two groups: Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL). Hodgkin's lymphoma accounts for one-sixth of all lymphomas represent about 11.5 percent of all lymphomas diagnosed in 2007. Non-Hodgkin's lymphoma (NHL) is the 6th leading cause of cancer death in the United States (*Eleanor et al. 2007*).

Nearly all patients with indolent lymphomas relapse after initial treatment, Successful retreatment is possible, but disease-free periods become increasingly shorter with each subsequent treatment. And more than half of patients with aggressive lymphomas are cured, while about 20% progress and the other 30% relapse after a disease-free period. Among those who relapse, many can still be cured with aggressive treatments (**Horning et al, 1993**).

Early detection of recurrence is clinically important, constitutes an important challenge in modern medical imaging and can improve the prognosis and survival of patients with cancer. CT considered the primary method of investigation because of its low cost and widespread availability provides high-resolution anatomic details but may underestimate the actual tumor burden by overlooking small tumor clusters in areas of distorted anatomy after treatment (**Gossmann A et al, 2005**).

Introduction and aim of work

FDG-PET whole body scan provided an important tool in its early diagnosis after achieving a complete response even in asymptomatic patient as well as it is better than other imaging modalities that depend mainly on the anatomy such as CT, as the former image the physiological and metabolic rate of the tumor which appears earlier before the anatomical changes develop especially when a residual non- tumoral mass is present after therapy (**Malik et al, 2006**).

PET/CT has been shown to be the most effective tool in the assessment of recurrent lymphoma as it provide a unique combination of the cross-sectional anatomic information provided by CT and the metabolic information provided by PET and has a higher sensitivity and specificity than CT and MRI combined (**Malik E et al, 2005**).

In general (NHL) is sensitive to chemotherapy and radiation therapy, In spite of this, management of patients with relapsed NHL is considered difficult because of chemo-resistance (**Shioyama et al., 2000**). Biological therapies (Immunotherapy) use substances similar to those naturally produced by the immune system but are made in a laboratory. These substances may kill lymphoma cells, slow their growth, or activate the patient's own immune system to more effectively overcome the lymphoma, such as monoclonal antibodies which are normally produced by the immune system to help to fight infections and can be made in the laboratory. After years of research, several monoclonal antibodies are now being used as treatments for relapsing lymphoma and often results in surprisingly high response rates compared with those expected from estimated absorbed radiation doses (**Ora Israel et al, 2007**).

Introduction and aim of work

The first monoclonal antibody approved by the FDA for treatment was rituximab (Rituxan). This antibody recognizes and attaches to a substance called CD20 that is found on the surface of some types of lymphoma cells (*Christine et al, 2003*).

Other approved radio immunotherapy by the FDA was ibritumomab tiuxetan (Zevalin), which is the rituximab antibody that has radioactive ⁹⁰yttrium and tositumomab (Bexxar), which is an antibody with radioactive iodine attached (*Christine et al, 2003*).

AIM OF WORK

The aim of this work is to provide a review of literature about the potential role of nuclear medicine in all phases of management of relapsing lymphoma; starting from diagnosis, treatment and assessment of response. Also provide a review of the basic concepts of RIT, the milestones leading to its current emergence as a treatment option for patients with relapsing lymphoma, alone and in combination with other treatment modalities. Discussion of its basic principles as production (Hybridoma , Recombinant), applications (monoclonal antibodies for treatment (Chimeric and humanized antibodies) are also included.