Value of CD133-2 (AC141) Expression Analysis in Acute Leukemia

Thesis

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By

Heba Mostafa Abo El Sood

(M.B.,B.Ch)

Ain Shams University

Supervised by

Professor / Manal Hashem Ahmed Fayek

Professor of Clinical and Chemical Pathology
Faculty of Medicine, Ain Shams University

Doctor / Mona Ahmed Ismail

Assistant Professor of Clinical and Chemical Pathology
Faculty of Medicine, Ain Shams University

Doctor / Reem Abd El Khalek Khattab

Assistant Professor of Clinical and Chemical Pathology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University

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List of abbreviations

5-TM	5-Transmembrane
ABC	ATP-binding cassette transporter protein
AC-133	Monoclonal antibody of CD133
AC-141	Monoclonal antibody of CD133
AL	Acute leukemia
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
AML-MRC	AML with myelodysplasia-related changes
AP	Acid phosphatase
APL	Acute promyelocytic leukemia
BAL	Biphenotypic acute leukemia
BCRP1	Breast cancer resistance protein1
BCSH	British Committee for Standards in Haematology
BM	Bone marrow
CBC	Complete blood count
CBF ß	Core-binding factor ß
CD	Cluster of differentiation
cDNA	Complementary DNA
Chk	Checkpoint kinase
CR	Complete remission
CSCs	Cancer stem cells
cyt	Cytoplasmic
del	Deletion

DL	Dichronic lenses
DNA	Deoxyribonucleic acid
EDTA	Ethylene diamine tetra-acetic acid
FAB	French-American-British
FACS	Fluorescence-activated cell sorting
FCM	Flow cytometry
FISH	Fluorescence in-situ hybridization
FITC	Fluorescein isothiocyanate
FLT-3	Fms-like tyrosine kinase-3
FS	Forward angle scatter
GPA	Glycophorin A
Hb	Hemoglobin
HCC	Hepatocellular carcinoma
HLA-DR	Human leukocytic antigen
HPC	haematopoietic progenitor cell
HSC	Hemopoietic stem cell
ICC	Immunocytochemistry
IHC	Immunohistochemistry
Inv	Inversion
ISH	In situ hybridization
kb	Kilobase
Kda	Kilodalton
K-EDTA	K-ethylene diamine tetra-acetic acid
LSC	Leukemic stem cell

NPM	Nucleophosmin
NSE	Non specific esterase
MDR	Multidrug resistance
MDS	Myelodysplastic syndrome
MDS/MPD	Myelodysplastic/ Myeloproliferative disease
MIC-M	Morphologic-immunologic- cytogenetic-molecular genetic
MLL	mixed lineage leukemia
MoAb	Monoclonal antibody
MPD	Myeloproliferative disorder
MPN	Myeloproliferative neoplasms
MPO	Myelo-peroxidase
MRD	Minimal residual disease
mRNA	Messenger ribonucleic acid
MYH11	smooth muscle myosin heavy chain
PAS	Periodic acid Schiff
PB	Peripheral blood
PBS	Phosphate buffered saline
PCNA	Proliferating cell nuclear antigen
PCR	Polymerase chain reaction
PE	Phycoerythrin
PNH	Paroxysmal nocturnal hemoglobinuria
PML	Promyelocytic leukemia
PMTs	Photomultiplier tubes

List of abbreviations (Cont.)

PROM1	Prominin (mouse)-like 1
RAR α	Retinoic acid receptor α
RNA	Ribonucleic acid
RT-PCR	Reverse transcriptase-polymerase chain reaction
SBB	Sudan black-B
SD	Standard deviation
SDF-1	Stromal-derived factor-1
SE	Specific esterase
sIg	Surface immunoglobulin
Sig	Significance
Sm	Surface membrane
SPSS	Statistical package for Social Science
SS	Side scatter
t	Translocation
t-AML	Therapy related AML
TCR	T-cell receptor
TdT	Terminal deoxynucleotidyl transferase
TLC	Total leukocytic count
UCB	Umbilical cord blood
WBC	White blood cells
WHO	World Health Organization
X^2	Chi-square test

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INTRODUCTION

Acute leukemia displays characteristic patterns of surface antigen expression (CD antigens), which facilitate their identification and proper classification and hence play an important role in instituting proper treatment plans ***(Kaleem et al., 2003).***

Acute leukemias are derived from either malignant, transformed, uncommitted multipotent stem cells or lineage-restricted progenitor cells. So far, CD34 is the most commonly used antigen to define immature hematopoietic progenitor cells ***(Wuchter et al., 2001).***

Immunophenotypical studies of acute leukaemia patients have shown that the CD34 antigen is expressed in a relatively high proportion of cases, ranging from 30 to 60% in acute myeloid leukaemia (AML) and from 60 to 70% in acute lymphoblastic leukaemia (ALL) ***(Sperling et al., 1995)***.

CD 133 (human Prominin-1) is a new stem cell marker which may be an alternative to the usual CD34 positive monoclonal antibody selection system ***(Ebner et al., 2000)***.

It is a cell-surface glycoprotein which is expressed on several types of stem cells, including hematopoietic stem cells, endothelial progenitor cells, progenitor cells in human fetal liver, bone marrow, cord blood and peripheral blood, as well as to a small proportion of CD34-negative cells in these tissues ***(Piechaczek, 2001).***

The CD133 surface antigen was originally discovered as the target of a monoclonal antibody, ***AC133***, that was generated to bind the CD34+ population of hematopoietic stem cells ***(Bidlingmaier et al., 2008).*** Which reacts with an epitope on the extracellular domain of the five-transmembrane protein of CD133, described firstly by **Yin et al. 1997.**

CD133-2 (AC141), the next became available and recognizes the same antigen as AC133 but by a different epitope ***(Yu et al., 2002).*** AC141 may be an informative marker for the detection and further characterization of immature AML cells ***(Guenova and Balatzenko, 2008).***

AIM OF THE WORK

The aim of this study is to assess the diagnostic value of CD133-2 clone (AC141) of anti-CD133 monoclonal antibody in acute leukemia, also to evaluate its correlation with the different clinical and laboratory data and response to therapy.

ACUTE LEUKEMIA

Acute leukemias are characterized by a relentless accumulation of immature, abnormal hematopoietic cells in the bone marrow and peripheral blood. It has been postulated that leukemias result from a clonal disorder involving the malignant transformation of early hematopoietic progenitors, and is maintained by the leukemia stem cells and, hence, may be organized in a similar way to normal hematopoiesis ***(Guenova and Balatzenko, 2008).***

Acute leukemias are broadly classified into non lymphoblastic (myeloid) and lymphoblastic categories based on the cell origin ***(Clovin et al., 2003).***

Acute myeloid leukemia (AML) represents a group of clonal hematopoietic stem cell disorders in which both failure to differentiate and over proliferation in the stem cell compartment result in accumulation of non functional cells termed myeloblasts ***(Stone et al., 2004).***

Acute lymphoblastic leukemia (ALL) is a malignant disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal marrow hematopoietic cells resulting in suppression of hematopoiesis and, thereafter, anemia, thrombocytopenia, and neutropenia. Lymphoblast can accumulate in various extramedullary sites, especially the

meninges, gonads, thymus, liver, spleen and lymph nodes ***(Sarkodee-Adoo et al., 2003).***

Incidence:

Although the incidence of acute leukemias accounts for less than 3% of all cancers, these diseases constitute the leading cause of death due to cancer in children and persons aged less than 39 years ***(Deschler and Lubbert, 2006).***

AML is the most common type of leukemia in adults, as it accounts for approximately 25% of all leukemias in adult in the Western world ***(Greenlee et al., 2001).***

It continuously shows 2 peaks in occurrence in early childhood and later adulthood, with an incidence of 3.7 per 100,000 persons and an age-dependent mortality of 2.7 to nearly 18 per 100,000 persons ***(Deschler and Lubbert, 2006).***

AML has increasing frequency with age (median 64 years) with incidence 35/100,000 at age 90. It is infrequent in children under 15 years ***(Provan et al., 2004)***, as it forms a minor fraction (10-15%) of leukemias in childhood (Fig. 1) ***(Hoffbrand et al., 2006).***