Study of Some Lymphocyte Subsets in Children with Newly Diagnosed Primary Immune Thrombocytopenia

Thesis

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Amna Helmy Awad

Dedication

To the memory of my father Helmy Awad, you left fingerprints in my heart, you'll always be with me.

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List of Abbreviations

Abb.	Full term
APCS	*Antigen presenting cells*
CBC	*Complete blood count*
CD	*Cluster of differentiation*
CPGs	*Clinical practice guidelines*
CR	*Complete response*
CTL	*Cytotoxic T lymphocytes*
CTLA	*Cytotoxic T cell-associated antigen*
DC	*Dendritic cells*
EAE	*Experimental autoimmune encephalomyelitis*
EDTA	*Ethylene diamine tetra-acetic acid*
EGF	*Epidermal growth factor*
FOXp3	*Forkhead-box p3*
FSC	*Forward scatter*
GI bleeding	*Gastrointestinal bleeding*
GITR	*Glucocorticoid-induced tumour necrosis factor receptor*
GP	*Glycoprotein*
HCV	*HEPATITIS c virus*
HIV	*Human immunodeficiency virus*
I Tregs	*Induced Regulatory T cells*
ICH	*Intracranial hemorrhage*
ICIS	*International cooperative ITP study group*
ITP	*Immune thrombocytopenic purpura*
IgA	*Immunoglobulin A*
IgG	*Immunoglobuln G*
IgM	*Immunoglobulin M*
IL	*Interleukin*
INF	*Interferon*

List of Abbreviations Cont…

Abb.	Full term
ISTH BAT	*International society of thrombosis / scientific and standardization committee bleeding assessment tool*
IVIG	*Intra venous immunoglobulin*
mAbs	*Monoclonal antibodies*
M-CSf	*Macrophage colony stimulating factor*
MHC	*Major histocomptability complex*
MMR	*Measles –mumps-rubella*
MYH9	*Myisin heavy chain 9*
n Tregs	*Naturally occurring Regulatory T cells*
NAIT	*Neonatal alloimmue thrombocytopenia*
NR	*No response*
PC	*Portable computer*
PLN	*Proliferative lymphoid nodules*
R	*Response*
RH	*Rhesus factor*
SLE	*Systemic lopus erythromatosis*
SPSS	*Statistical package for Social Science*
T regs	*Regulatory T cells*
TAR	*Thrombocytopenia absent radius*
TCR	*T cell receptor*
Th	*T helper*
TNF	*Tumor necrosis factor*
TPO	*Thrombopoietin receptor*

Abstract

There was significant positive correlation between total leucocytic count at diagnosis and CD3,.And significant positive correlation between platelets after follow up and CD4 And high significant positive correlation between lymphocyte at diagnosis and CD3, CD4,CD8. And high negative significant correlation between lymphocytes after follow up and CD4/CD8 ratio.

There was no significant relation between $CD3^{+,}$ $CD8^{+}$,$CD4^{+}$ T lymphocytes and response to therapy, however it was observed that there is increase in expression of CD4+ T lymphocytes among the complete response compared with the response group but this was not significant, which may need further evaluation.

Understanding the role of T cell subsets will permit a better control of autoimmunity.

Keywords: *Regulatory T cells- T cell receptor- T helper - Tumor necrosis factor- Measles –mumps-rubella*

Introduction

Childhood immune thrombocytopenic purpura (ITP) is a common acquired bleeding disorder that is characterized by isolated thrombocytopenia (peripheral blood platelet count <100×103/μL) in the absence of other causes of thrombocytopenia. It is an autoimmune-mediated condition that results from antibody-mediated destruction of platelets and impaired megakaryocyte platelet production ***(Neunert , 2013).*** Newly diagnosed ITP may follow within a few weeks after an antigenic challenge such as infection or vaccination ***(Stasi and Newland, 2011).***

The trigger also may be a loss of tolerance due to molecular mimicry with cross-reaction of antibodies arising from infectious agents or drugs, genetic factors, and/or platelet Toll receptors. This loss of tolerance activates autoreactive effector B and T lymphocytes, which in turn initiates platelet destruction, mediated by cytotoxic T lymphocytes and the release of pro-inflammatory cytokines (IL-2/IL-17) by T helper (Th) cells (Th1/Th17). Th2 (anti-inflammatory) and regulatory B (Breg) and Treg cells are also inhibited (with decrease in IL-10/TGF-β), which leads to the disease becoming chronic. Some isotypes of autoantibodies may increase the bleeding risk ***(Perera et al., 2016).***

T cells have an important role in modulating the immune system's direction towards disease. Dysregulation of T cell

activity and cytokine abnormalities have been found to be a contributing factor to many autoimmune diseases, including ITP ***(Hu et al., 2012).***

The Th1/Th2 cytokine axis is critical for autoimmune reactivity. For example, the Th1/Th2 imbalance leading to autoreactive B cell differentiation seen in ITP was shown to be restored to a protective Th2 population after treatment with glucocorticoid ***(Guo et al., 2012).***

Management of newly diagnosed ITP consists of careful observation, regardless of platelet count ***(Schultz et al., 2014),*** Severe bleeding, which occurs in only 3%–5% of children, requires treatment with corticosteroids, intravenous immunoglobulin (IVIG), or anti-Rhesus-D immunoglobulin ***(Neunert et al., 2011).***

Most children with ITP have an acute presentation of purpura and bruising, and 80%–90% of the cases recover spontaneously or with therapy. However, in 10–20% of newly diagnosed children, ITP has a chronic course that persists beyond 12 months ***(Schultz et al., 2014).*** Because of the high impact of ITP on a child's everyday life and activities, identification of prognostic factors would be beneficial for reducing stress and improving quality of life for both these children and their parents ***(Heitink et al., 2014).***

Aim of the Work

To evaluate levels of CD3+ (T lymphocytes), CD4+ helper T lymphocytes and CD8+ cytotoxic T lymphocytes in patients with newly diagnosed immune thrombocytopenia and its impact on disease outcome.