Is Traumatic Lumbar Puncture A Risk Factor For CNS Relapse In Children With Acute Lymphoblastic Leukemia ?

Thesis

Submitted For Partial Fulfillment Of Master Degree In

Pediatrics

By

ABD EL HAMID MOSTAFA EL MESIRY

MBBCH

Supervisors

PROF. DR MOHSEN SALEH EL ALFY
Professor Of Pediatrics
Ain Shams University

PROF. DR. MANAL HASHEM AHMED
Professor Of Clinical Pathology
Ain Shams University

Dr. MOHAMED ABO EL ASRARE MOHAMED EL BIOMY AFIFY
Lecturer Of Pediatrics
Ain Shams University

Faculty Of Medicine

Ain Shams University

2006

دراسة علاقة الوخز القطني الإصابي بإنتكاسة الجهاز العصبي المركزي عند الأطفال مرضي سرطان الدم الحاد

رسالة

توطئة للحصول على درجة الماجستير فى طب الأطفال

مقدمة من

الطبيب/ عبد الحميد مصطفي المسيري

بكالوريوس الطب والجراحة

تحت إشراف

الاستاذ الدكتور/ محسن صالح الألفي

أستاذ طب الأطفال

كلية الطب – جامعة عين شمس

الأستاذ الدكتور/ منال هاشم أحمد

أستاذ الباثولوجيا الإكلينيكية

كلية الطب – جامعة عين شمس

الدكتور/ محمد أبو الأسرار محمد البيومي عفيفي

مدرس طب الأطفال

كلية الطب – جامعة عين شمس

كلية الطب – جامعة عين شمس

2006

بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما
علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

البقرة آية: (٣٢)

ACKNOWLEDGEMENT

First and fore most thanks are due to **Allah** the beneficent and merciful of all.

I would like to express my deep gratitude and appreciation to PROF. DR MOHSEN SALEH EL ALFY, Professor Of Pediatrics, Ain Shams University, for his continuous help and unlimited support.

I am greatly indebted and grateful to PROF. DR. MANAL HASHEM AHMED, Professor Of Clinical Pathology and Dr. MOHAMED ABO EL ASRARE MOHAMED EL BIOMY AFIFY, Lecturer Of Pediatrics, Ain Shams University for their continuous encouragement to bring this work to the attempted goal.

This work wouldn't come to light without the help of my family members, their patience and co-operation.

Special appreciation is devoted to my faithful fiancé for her care and support.

Lastly, but not the least, I would like to express a lot of thanks to all patients included in our study.

ABD EL HAMID MOSTAFA EL MESIRY

2006

List of abbreviations

ALL	Acute lymphoblastic leukemia
AML	acute myelogenous leukemia
BFM	Berlin-Frankfurt-Munster
BMT	Bone marrow transplantation
CCG	Children's Cancer Group
CNS	central nervous system
CSF	Cerebrospinal fluid
EFS	event-free survival
FAB	French-American-British
FISH	fluorescence in situ hybridization
FLT-3	FMS-like tyrosine kinase-3
HHC	hereditary hemochromatosis
HSC	Hematopoietic Stem Cells
IGFBP	Insulin-Like Growth Factor Binding Protein
IT MTX	intrathecal methotrexate
ITDs	internal tandem duplications
ITTT	intrathecal triple therapy
MLL	mixed lineage leukemia
MPO	Myeloperoxidase
MRD	minimal residual disease
PDGFR	platelet-derived growth factor receptor
RT-PCR	reverse transcriptase-polymerase chain reaction
TCCSG	Tokyo Children’s Cancer Study Group

TdT	deoxynucleotidyl transferase
TLP	traumatic lumbar puncture
UKCCS	United Kingdom childhood cancer study
WBC	white blood cell
WHO	World Health Organization

CONTENTS

List of tables

List of figures

INTRODUCTION

Acute lymphoblastic leukemia is at risk for CNS relapse(5-10%) ***(Swaiman et al, 1999).***

Central nervous system involvement among children with ALL has been defined by either ; the presence of at least 5 leukocytes per microliter or the presence of cranial nerve palsy on physical examination ***(Pinkel et al,1994).***

Patients with T-cell ALL are at higher risk for relapse in CNS ***(Shrappe et al,1998).***

Central nervous system relapse has been observed in patients with leukocytic count >100 × $10^{(9)}$/L in B-cell precursor and 50 × $10^{(9)}$/L in T-cell immunophenotype ***(Pui et al,1998).***

Central nervous system leukemia occurs commonly in infants and preschool children than adolescents and adults because a higher proportions of their vasculature in the leptomeningies ***(Pinkel et al,1994).***

Traumatic lumbar puncture can adversly affect the outcome of children with ALL via iatrogenic introduction of leukemic blast cells into the CSF ***(Gjjar et al.,2000).***

Traumatic lumbar punctures are defined as those in which the CSF contained at least 10 RBCs per microliter while bloody LPs are defined as those in which the CSF contained at least 500 RBCs per microliter ***(Burger et al., 2003).***

AIM OF WORK

The aim of this work is to determine whether a traumatic LP is a risk factor of CNS relapse in children with ALL or not and to determine the other risk factors for CNS relapse.

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN CHILDREN

Acute lymphoblastic leukemia (ALL) is an aggressive neoplasm that has been defined by the presence of more than 30% lymphoblasts in the bone marrow or peripheral blood in the French-American-British (FAB) Cooperative Group classification system ***(Bennett et al., 1981)***. In the recently proposed World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissues, a blast count above 20% is sufficient for a diagnosis of acute leukemia ***(Harris et al, 1999).***

INCIDENCE:

Acute lymphoblastic leukemia (ALL) is the most common malignant disorder in childhood, representing nearly one third of all pediatric cancers ***(Ek et al., 2004).***

Annual incidence of ALL is about 30 cases per million people, with a peak incidence in patients aged 2-5 years. In the US, each year, 2000-2500 new cases of childhood ALL are diagnosed. Internationally, **t**he incidence rate is thought to be similar throughout the world to that in the United States ***(Rubnitz, 2005).***

ETIOLOGY:

Childhood leukaemia is a biologically diverse disease, so several pathways to its development are possible. All probably combine genetic susceptibility and exposure to external risk factors at a time when the child is vulnerable. Many external factors have been reported as associated with an increased risk of childhood leukaemia. Some may be causal, but some may merely be correlated with the actual cause. Other apparent associations may be due to chance or bias ***(Dickinson, 2005).***

Environmental Factors

Draper et al., (2005) investigated whether there is an association between distance of home address at birth from high voltage power lines and the incidence of leukaemia in children in England and Wales. They concluded that there is an association between childhood leukemia and proximity of home address at birth to high voltage power lines, and the apparent risk extends to a greater distance than would have been expected from previous studies.

The United Kingdom childhood cancer study (UKCCS) in a large population based case-control study supported the hypothesis that reduced exposure to infection in the first few months of life increases