Role of Bronchos copically Acquired Bronchoalveolar Lavage in The Diagnosis of Pulmonary Fungal Infections in Critically Ill Immunocompromised Egyptian Children

THESIS

Submitted in partial fulfillment for MD degree of Pediatrics **BY**

MERVAT GAMAL ELDIN MANSOUR

M.B.,B.Ch.,M.Sc.

Under Supervision of

DR. MAGID ASHRAF ABDEL FATTAH

Professor of Pediatrics Faculty of Medicine – Ain Shams University

DR. ALYAA AMAL KOTBY

Professor of Pediatrics Faculty of Medicine – Ain Shams University

DR. HADIA HUSSEIN BASIEM

Professor of Clinical Pathology Faculty of Medicine – Ain Shams University

DR. MALAK ALI HASSAN SHAHEEN

Lecturer of Pediatrics
Faculty of Medicine – Ain Shams University

DR. AHMED ABD ALGAWAD ELMASRY

Lecturer of Pulmonology Faculty of Medicine – Ain Shams University

Faculty of Medicine – Ain Shams University
Cairo - 2006

List of Contents

	Page
Introduction & aim of the work	1
Review of literature:	
Chapter 1	
Critically ill children & fungal infection	4
Chapter 2	
Medically important fungal infections in PICU	11
I- Aspergillus	
II- Candida	
Chapter 3	
Pediatric flexible bronchoscopy	57
Chapter 4	
Bronchoscopic anatomy	83
Patients & methods	96
Results	118
Discussion	163
Summary	194
References	199
Master tables	
Arabic summary	

List of Tables

		Page
Table 1	Different forms of serological diagnosis of invasive candidiasis.	53
Table 2	Indications for pediatric flexible bronchoscopy.	59
Table 3	Main drugs used for sedation for pediatric flexible bronchoscopy.	73
Table 4	Techniques to ensure adequate ventilation during anesthesia for pediatric flexible bronchoscopy.	75
Table 5	PSI score variables.	101
Table 6	PRISM score variables.	103
Table 7	Patients diagnoses and causes of PICU admission.	118
Table 8	Diagnoses and causes of PICU admission of patients with probable infection.	120
Table 9	Comparison of age and sex between the patients groups.	122
Table 10	Comparison of the critical illness of the patients groups by both PSI and PRISM clinical scorings.	123
Table 11	Comparison of the critical illness of the highly probable and the less probable subgroups by both PSI and PRISM clinical scorings.	125

Showing the results of blood fungal antigens.

149

Table 22

		Page
Table 23	Comparison of blood fungal antigen between patients groups.	150
Table 24	Comparison between fungal antigens in BAL and blood of the studied population.	151
Table 25	Comparison between BAL fungal culture and BAL fungal antigens in the studied population.	152
Table 26	Source of infection for fungal pneumonia.	154

List of Figures

		Page
Figure 1	Aspergillus	12
Figure 2	The clinical spectrum of conditions resulting from Aspergillus spore inhalation.	16
Figure 3	Chest-X ray showing collapse & consolidation of the Rt. middle lobe during ABPA.	18
Figure 4	CT scan demonstrating mild central bronchiectasis.	18
Figure 5	CT scan showing a highly characteristic air crescent sign in apical aspergilloma.	20
Figure 6	When to suspect invasive pulmonary aspergillosis.	22
Figure 7	Multiple slices of a high resolution CT of the halo sign.	25
Figure 8	Role of the host innate immunity against A. fumigatus.	29
Figure 9	The three components of diagnosing invasive candidiasis.	51
Figure 10	The proximal end of the FOB.	78
Figure 11	The mobile bronchoscopy unit.	80

		Page
Figure 12	Upper airway anatomy as it pertains to routes of insertion of FOB.	83
Figure 13	Important anatomic landmarks in the upper airway showing the laryngeal structures.	84
Figure 14	The length of the trachea in relation to age.	85
Figure 15	The inner diameter of the trachea at different levels.	86
Figure 16	The main carina.	87
Figure 17	The bronchial tree.	88
Figure 18	The Rt main bronchus and the entry of the Rt upper lobe.	89
Figure 19	Anatomy of the Rt upper lobe.	90
Figure 20	The divisions of the bronchus intermedius.	91
Figure 21	Anatomy of the Rt lower lobe.	92
Figure 22	The left main bronchus.	92
Figure 23	Divisions of the left main bronchus.	93
Figure 24	Anatomy of the left upper lobe.	94
Figure 25	Divisions of the lingula.	94
Figure 26	Anatomy of the left lower lobe.	95
Figure 27	Endotracheal tube.	108

		Page
Figure 28	Swivel Y connector.	109
Figure 29	Laryngeal mask airway.	109
Figure 30	Monitoring system of the patients during bronchoscopy.	109
Figure 31	Showing PENTAX FB-10X bronchoscope.	110
Figure 32	Showing germ tube production by Candida-albicans spp.	115
Figure 33	PSI and PRISM scores of both patients groups.	124
Figure 34	Comparison of PICU risk factors between the patients groups.	128
Figure 35	The comparison of both patients groups as regards drug risk factors.	131
Figure 36	The comparison of both patients groups as regards laboratory risk factors.	135
Figure 37	The number of risk factors in relation to the patients groups.	138
Figure 38	The fate of both groups.	139
Figure 39	Diagnostic modalities.	140
Figure 40	The distribution of fungal growth in BAL fluid of the studied population.	141

		Page
Figure 41	Growth of Candida on Sabouraud dextrose agar plate.	142
Figure 42	Growth of Aspergillus fumigatus on Sabouraud dextrose agar plate.	143
Figure 43	Microscopic picture of Aspergillus fumigatus.	143
Figure 44	Microscopic picture of Aspergillus niger.	144
Figure 45	Showing the results of BAL fungal culture in group (1).	145
Figure 46	Showing results of fungal culture of blood and BAL.	146
Figure 47	The distribution of fungal antigens detected in BAL fluid.	147
Figure 48	The results of BAL fungal antigen in group (1).	148
Figure 49	The results of blood fungal antigens in the studied population.	149
Figure 50	the results of serum fungal antigens in patients of group (1).	150
Figure 51	The interrelation between BAL and blood fungal antigen among the studied population.	151
Figure 52 (a, b)	Shows the interrelation between BAL fungal antigen and BAL fungal culture.	153

		Page
Figure 53	Source of infection for fungal pneumonia.	154
Figure 54	Shows summary of chest X- ray findings in the studied population.	155
Figure 55	Patient No 3: P-A chest X-ray.	157
Figure 56	Patient No 3: Bronch. view of the Rt. upper lobar bronchus.	157
Figure 57	Patient No 6: P-A chest X-ray.	158
Figure 58	Patient No 6: Bronch. view of the main carina.	158
Figure 59	Patient No 11: P-A chest X-ray.	159
Figure 60	Patient No 11: Bronch. view of upper division of the lingula.	159
Figure 61	Patient No 19: P-A chest X-ray.	160
Figure 62	Patient No 19: Bronch. view of upper division of the lingual.	160
Figure 63	Patient No 24: P-A chest X-ray.	161
Figure 64	Patient No 24: Bronch. view of the Lt. upper lobe.	161
Figure 65	Patient No 26: P-A chest X-ray.	162
Figure 66	Patient No 26: Bronch. view of the Rt. main bronchus.	162

List of Abbreviations

ABPA : Allergic bronchopulmonary aspergillosis

AIDS : Acquired Immune Deficiency Syndrome

ALT : Alanin transeferase

APACHE II: Acute Physiologic and Chronic Health

Evaluation II

AST : Aspartate transeferase

BAL : Bronchoalveolar lavage

BHI : Brain heart infusion

BMT : Bone marrow transplant

BUN : Blood urea nitrogen

C (a-v)O2 : Arterial to mixed venous oxygen content

difference

c3 : Complement3

CARS : Compensatory anti-inflammatory response

syndrome

CCD : Charge, Coupled Device

CGD : Chronic granulomatous disease

COPD : Chronic obstructive airway diseases

CRP: C- reactive protein

CVP : Central venous pressure

ECG : Electrocardiography

ELISA : Enzyme-linked immunosorbent assay

EPIC: The European Prevalence of Infections in

Intensive Care

ERS : European Respiratory Society

EUORTC/ MSG: European Organization for Research and

Treatment of Cancer/ Mycoses Study

Group.

FDA : Food and Drug Administration

FDPs: Fibrin degradation products

FIO2 : Fraction of inspired oxygen

FOB : Flexible fiberoptic bronchoscope.

FRC : Functional residual capacity

GVH : Graft versus host

HBV-FM: High-blood-volume fungal media

i Invasive aspergillosis

ICP : Intracranial pressure

iCU : Intensive Care Unit

IFN-✓ : Interferon gamma

IgE : Immunoglobulin E

IgG : Immunoglobulin G

IgM : Immunoglobulin M

IMA : Inhibitory Mould Agar

IPA : Invasive pulmonary aspergillosis

IV : Intravenous

KOH : Potassium hydroxide

mAb : monoclonal antibodies

MODS: Multiorgan dysfunction syndrome

NNIS : National Nosocomial Infections Surveillance

OR/ 95%CI : Odd ratio/ 95% confidence interval

PaCO2 : Partial arterial carbon dioxide concentration

PaO2/FIO2 : Partial arterial oxygen concentration/

Fraction of inspired oxygen.

PaO2 : Partial arterial oxygen concentration

PCWP : Pulmonary wedged capillary pressure

PEEP : Positive end-expiratory pressure

PICU : Pediatric intensive care unit

PIM : Pediatric Index of Mortality

PMN : Polymorph nuclear leucocytes.

PRISM III : Pediatric Risk of Mortality

PSI : Physiologic Stability Index

PT/PTT : Prothrombin time/ Partial Prothrombin time

RLL : Right lower lobe bronchus

RML : Right middle lobe bronchus

RUL : Right upper lobe

SAB : Sabouraud dextrose agar

SD : Standard deviation

SPSS : Statistical Package for the Social Science

TBB : Transbronchial biopsy

TPN: Total parenteral nutrition

WBC: White blood cells

WLB: White light bronchoscopy

INTRODUCTION

Pulmonary fungal infections represent a serious and a challenging problem for patients and physicians in the intensive care units (*Barth et al, 2000*).

The incidence of these infections is steadily increasing. Development of new effective immunosuppressive therapies for management of hematological and oncological diseases, wide use of strong broad spectrum antibiotics for treatment of bacterial infections and appearance of new virulent viruses are important factors claimed to explain the recent increase in the incidence of pulmonary mycosis (*Seyfarth et al, 2001*).

Pulmonary mycosis is an infectious process of the lungs by one or more of different fungal pathogens.

Opportunistic fungi (e.g. Candida species, Aspergillus species, Mucor species and Cryptococcus neoformans) tend to cause pulmonary infections in patients who have congenital or acquired defects in their host defense mechanisms. Infection can occur by inhalation of spores or by reactivation of a latent infection. Hematogenous dissemination through venous catheters is frequently encountered among immunocompromised patients in intensive care units (*Baughman*, 1999).

Mortality rate of opportunistic pulmonary mycosis is increasing among immunocompromised patients; it has been