CARDIAC CHANGES IN ACUTE CHILDHOOD LEUKAEMIA

THESIS

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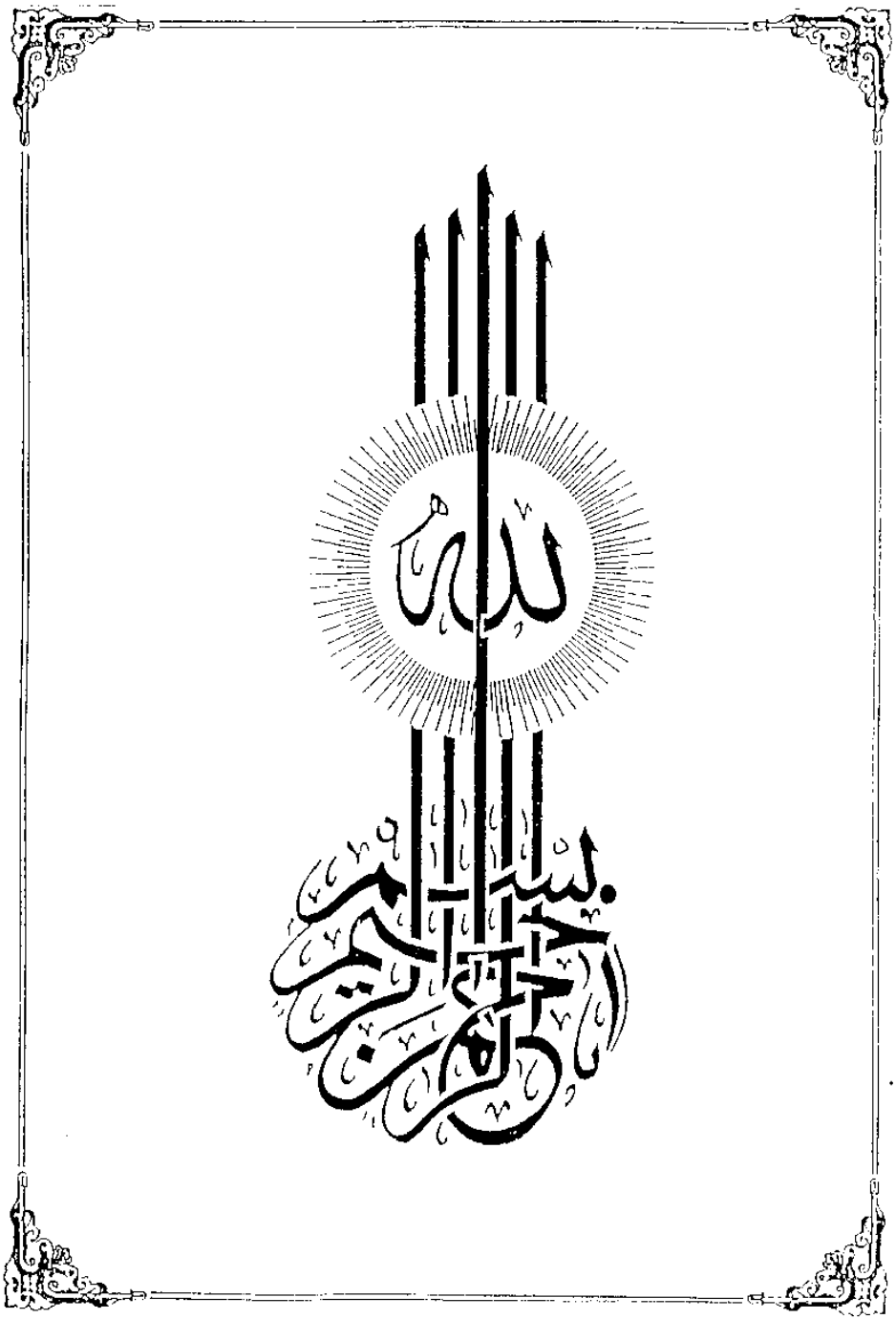

Table of Contents

* List of Abbreviations
* Introduction and Aim of Work 1
* Review of Literature 2
  - Acute Leukaemia
    . Incidence and Prevalence 2
    . Classification 4
    . Prognosis 11
    . Affection of Various Organs 17
  - Cardiac Manifestations in Acute Leukaemia
    . Pericardial Involvement 27
    . Arrhythmias and ECG Changes 35
    . Cardiomegaly and Congestive Heart Failure 37
    . Heart Murmurs 37
    . Endocarditis 38
  - Cardiac Toxicity of Antineoplastic Agents 41
  - Echocardiography in Paediatric Cardiodiagnosis ... 55
* Material and Methods 59
* Results 64
* Discussion 73
* Summary and Conclusion 84
* References 88
* Arabic Summary

LIST OF ABBREVIATIONS

ALL	:	Acute lymphoblastic leukaemia.
ANLL	:	Acute non lymphoblastic leukaemia.
B.M.	:	Bone marrow.
CHF	:	Congestive heart failure.
CNS	:	Central nervous system.
C/O	:	Complaint.
Cond.	:	Conduction.
CSF	:	Cerebrospinal fluid.
ECG	:	Electrocardiogram.
EDD	:	End diastolic dianeter,
EDV	:	End diastolic volume.
EF	:	Ejection fraction.
ESD	:	End systolic diameter.
ESV	:	End systolic volume.
FAB	:	French American British (classification)
F Sh	:	Fractional shortening.
Hb%	:	Haemoglobin percentage.
HS	:	Highly significant.
Ig	:	Immunoglobulin.
Lt. Vent.	:	Left ventricle.
NS	:	Non significant.
PAS	:	Periodic acid Schiff stain.
PE	:	Pericardial effusion.
RVD	:	Right ventricular diameter.
Rt. Vent.	:	Right ventricle.
S	:	Significant.
S.V.	:	Stroke volume.
Volt.	:	Voltage.
W. th.	:	Wall thickness.

INTRODUCTION

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AIM OF THE WORK

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Acute leukaemia is one of the most serious diseases that may attack the child. It may involve any tissue of the body, but because of its universal involvement of the bone marrow and its greatest concentration there, even in the earliest cases, bone marrow involvement is the sine qua non of the disease (Simone et al., 1982).

Cardiac metastasis are usually a late phenomenon in most malignancies, but in view of the prolonged remissions now obtained frequently, it is becoming increasingly important to prevent, detect and treat these complications (Rosenthal et al., 1984). Cardiac infiltration, often microscopic, is frequently found at autopsy (Gunz and Henderson, 1983) occurring in 34% of cases reported by Kirshbaum and Preuss (1943), 30% in the more recent series of Javier et al. (1967) and 37% in that of Roberts et al., (1968).

That is why, it was tempting to study the heart condition in Egyptian infants and children suffering of acute leukemia in a trial to delineate the extent of the problem in our country.

REVIEW OF LITERATURE

ACUTE LEUKAEMIA

DEFINITION AND PREVALENCE

Leukaemia is a protean group of diseases of unknown cause that have in common a high fatality rate due to complications of bone marrow failure or infiltrations of tissues. This results from generalised proliferation of immature or abnormal leukocytes.

The incidence of leukaemia varies between 3.86 and 8 per 100,000 as reported in different countries around the world (Khalifa et al., 1982). Leukaemias are considered the most common form of childhood cancer accounting for one third of such cases in the United States. The acute lymphoblastic leukaemias account for 76% of the total, with acute non-lymphocytic leukaemias and chronic myelocytic leukaemias accounting for 21 and 3% respectively. Only few cases of chronic lymphocytic leukaemia have been reported in children (Riemenschneider, 1983).

In a trial to evaluate the behaviour of acute lymphoblastic leukaemia in Egypt, Khalifa et al. (1982) found that the incidence of acute leukaemia among outpatients attending the Children's Hospital, Ain Shams University, Cairo, in the 7 years period from 1974-1981, happened to be 23.3 / 100,000. About 77% of the cases were of the acute lymphoblastic variety & the male to female sex ratio in the acute lymphoblastic group

was 2: 1 and the peak incidence was found in the 3-5 years age group. On the other hand, in the acute non- lymphoblastic group the sex ratio was 1.88 : 1 & no special age prediliction was observed.

In another study in Egypt,the leukemias rank second to lymphomas as regards childhood cancer & they constituted about one fourth (24.9%) of childhood malignant tumours in 1976, and approximately one fifth (18.7%) in 1978. The acute lymphatic leukaemias accounted for 81.5% of total childhood leukemias in 1976 and 65.8% in 1978. (Cancer Research, Faculty of Medicine, Cairo University, Progress Report, 1976 and 1978).

CLASSIFICATION

* Acute Lymphoblastic Leukemia (A.L.L.) :

Acute lymphoblastic leukaemia is a progressive malignant infilteration of the bone marrow and lymphatic organs by immature cells that closely resemble lymphoblasts. The precise derivation of these cells is not known with certainty. Although there is increasing evidence based on membrane receptors that these cells are indeed lymphoid in origin, there is enough heterogeneity within these non myelocytic forms of acute leukaemia on morphologic, cytogenetic, immunologic and cytochemical grounds to discourage attempts to provide a definitive subclassification at the present time (Henderson and Jones, 1982).

I- Morphology (FAB Classification) :

A group of French, American and British (FAB) hematologists introduced morphologic criteria for the classification of ALL in 1976 (Bennet et al., 1976). The FAB classification defined 3 types of lymphoblasts, L_1, L_2 and L_3, based on cell size, nuclear chromatin pattern and shape, proninence of nucleoli, and cytoplasmic characteristics, including amount of basophilia and vacuolization.

The morphologic classification was modified in 1981, the new scoring system for L_1 and L_2 blasts was based on nuclear/ cytoplasmic ratio, number of nucleoli, nuclear membrane regularity & cell size (Bennet et al., 1981) (table 1).

Some, but not all, laboratories agreed that the FAB classification was prognostic and that L_1 morphology carried a more favourable prognosis (Wagner & Baehner, 1979). Others were unable to confirm the prognostic importance of FAB morphology (Greaves et al., 1981). Miller et al. (1981) reported that children with > 25% L_2 lymphoblasts had a significantly higher relapse rate & significantly poorer survival.

* Uncommon morphologic variants :

- Hand mirror cells : They have distinctive elongated tails, or uropods, that most likely reflect the dynamic state of cell motility. The biological significance of hand mirror cell is unknown but it is active in immunologic intracellular complexes, endocytosis & immune complexes (Soderberg & Coons, 1978).

In a large study performed by the children's cancer study group, only 5.9% had more than 10% hand mirror cells. A significantly greater proportion of this group was 10 years of age or older, had a haemoglobin level of over 10 g/dl & had L_2

morphology. Disease-free survival & overall survival were significantly worse in children with the hand mirror cell type ALL (Miller et al., 1983).

- Inclusion body ALL : it is a rare and unclassifiable morphologic variant, speculated by some investigators to be viral particles & by others as basophilic granules. (Miller, 1984).

- Convoluted cell ALL : They have no diagnostic or prognostic proved significance (Miller, 1984).

- Biphenotypic leukaemias : Mosaicism in ALL is not unexpected. Examples are the mixed L_1/L_2 patterns, the emergence of the L_2 type of ALL at the time of relapse of leukaemia originally diagnosed as L_1 and the coexistence of ALL and ANLL at the time of diagnosis or during relapse, (Miller, 1984).

* Ultrastructural characteristics of ALL :

The electron microscope is of limited use in the classification of ALL. Early studies with scanning electron microscopy suggested morphologic difference between the surfaces of T-cells, which are smooth, and B-cells, which have microvilli (Miller, 1984).

Glick et al. (1978) related the ultrastructural & immunologic findings in 29 patients. They concluded no relationship between lymphoblast morphology and immunologic cell surface characteristics.

II- Histochemistry :

Histochemistry is helpful in distinguishing lymphoid from non-lymphoid leukaemias. The most commonly used is the periodic-acid-Schiff (PAS) reaction, which is positive in 40% to 70% of the blasts in ALL (Raney et al., 1979).

The acid phosphatase reaction is much more useful in identifying subgroups of ALL. Positive reactions were found in 90% of 148 patients with T cell ALL, (Catovsky et al., 1978). Other tests such as B-Glucuronidase and acid α-naphthyl esterase are less helpful as they are difficult to perform and interpret (Bloomfield and Cajlpeczalska, 1980).

III- Immunology :

Immunologic studies using lymphocyte cell-surface markers have classified ALL into five major groups : common, T-cell, B-cell, pre-B cell and undifferentiated "nul" ALL, (Greaves, 1981).

- The common ALL group, representing approximately 70% of the patients, expresses the common acute lymphoblastic leukaemia antigen (CALLA).

- T-cell ALL accounts for approximately 15% of cases, can be identified by the presence of receptors for sheep red blood cells and reactivity with T-cell antisera and T-monoclonal antibodies, (Miller, 1984).

- Pre-B-cell ALL : Approximately 18% of patients have leukaemia blasts with pre-B features which are cells containing small amounts of intracytoplasmic IgM but lacking detectable surface immunoglobulins, (Seligmann et al., 1981).

- B-cell ALL : Blast cells in this small group have surface membrane immunoglobulin (IgM) and Fc receptors. Most blasts in B-cell ALL have L_3 morphology (Greaves, 1981).

- Nul cell ALL : True nul cell ALL represents approximately 15% of childhood ALL as identified by proper antisera (Miller, 1984). Some of the patients in this group may acquire CALLA at relapse (Greaves, 1981).