CONGENITAL MALIGNANT TUMORS

Essay

Submitted for the Partial Fulfilment
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By

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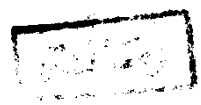

Faculty of Medicine
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1987

بسم الله الرحمن الرحيم

وعلمك ما لم تكن تعلم

وكان فضل الله عليك عظيماً

.. صدق الله العظيم ..

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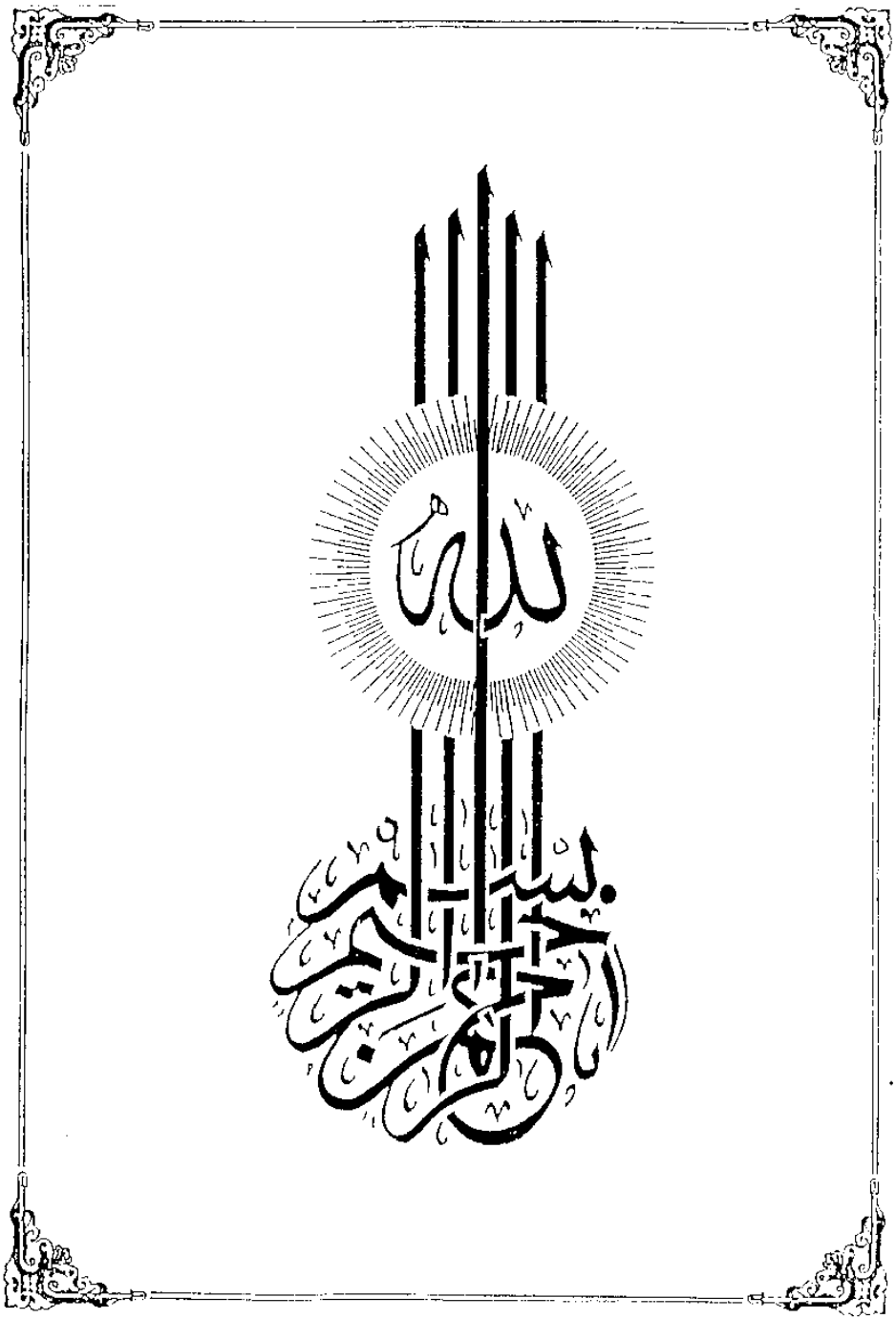

ACKNOWLEDGEMENT

Thanks First to God

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CONTENTS

ABBREVIATIONS

DES	:	Diethylstilbesterol.
FHS	:	Fetal hydantoin syndrome.
RES	:	Reticuloendothelial system.
LSD	:	Letterer-siwe disease.
BWS	:	Beckwith wiedmann syndrome.
NCT	:	Neural crest tumor.
HVA	:	Homovanillic acid.
VMA	:	Vanilmandelic acid.
VG	:	Vanilglycol.
VLA	:	Vanillactic acid.
BAIB	:	Beta-amino isobutyric acid.
CTH	:	Cysta thionine.
NMN	:	Normetanephrine.
3MT	:	3 methoxytyrosine.
LDH	:	Lactic dehydrogenase.
CEA	:	Carcinoembryonic antigen.
NWTS	:	National Wilms' tumor study.
CN	:	Cystic nephroma.
HAS	:	Hepatic angiosarcoma.
PHC	:	Primary hepatocellular carcinoma.
AFP	:	Alpha feto protein.
EG	:	Esinophilic granuloma.
HSD	:	Hand Schuller-christian disease.
CID	:	Commbined immune deficiency.
DIC	:	Disseminated intravascular coagulation.
FHR	:	Familial Hemophagocyctic reticulosis.

DHIA	:	Dehydroepiandrosterone.
CFU-GM	:	Colony forming unit-granulocyte monocyte.
CSF	:	Colony stimulating factor.
CMV	:	Cytomegalovirus.
VIP	:	Vasoactive intestinal peptide.
WDHA	:	Watery diarrhea hypokalemia achlorhydria.
E.M.	:	Electron microscope.
TEM	:	Triethylenemelamine.
AGR	:	Aniridia, ambiguous genitalia, mental retardation.

INTRODUCTION & AIM OF THE ESSAY

INTRODUCTION

The overall number of congenital malignant tumors that appear within the neonatal period is small. Congenital malignant tumors are one of the leading causes of death in an infant. The pediatricians, therefore, must be alert to the possible diagnosis of a rare but important disease. They must be aware of the clinical features, location of tumors and metastasis if any.

Staging must be known for each type of tumor depending on thorough clinical examination and radiological studies at the time of diagnosis.

Grading of tumors also will depend on pathological examination of biopsy taken from the site of origin of a tumor. This will be described with tumors that are commonly seen among the neonatel period such as Neuroblastoma, Leukemia, teratomas, Renal tumors and CNS tumors.

Leukemia appear to be the most common cancer causing mortality among infants under one year of age, where as, Neuroblastoma is the most common tumor as regard the incidence.

Prognosis of congenital malignant tumors is markedly affected by prompt treatment (through good program of surgery, radio therapy and or Chemotherapy) as well as early diagnosis.

The Aim of the Essay

The aim of this essay is to present a review of the more common malignant tumors that may occur in the neonate including an exhaustive list of case reports of every congenital tumor recorded in the literature.

INCIDENCE AND MORTALITY

CONGENITAL MALIGNANT TUMORS

Incidence and Mortality

Fraumeni and Miller (1969) did a study of death certificates during the 5 year period ranging from 1960-1964. They revealed that the death rate from malignant diseases in infants under 28 days of age was 6.24 per million live births. Over one half of cancer deaths in the neonatal period occurred in the first week of life, and over one third occurred on the first day.

Basing their report on the third National Caner Survey (1969-1971), *Badder and Miller (1979)* found the incidence of malignant neoplasms in the United States to be 183.4 per one million live births in infants younger than 1 year, and 36.5 per one million live births in new borns younger than 29 days. The cancer incidence in those under 1 year was almost 3.5 times greater than mortality determined from death certificates from 1960 to 1969. When mortality of infants under age 1 year is used as an indicator of frequency, leukemia appears to be the most common cancer followed by neuroblastoma, CNS tumors, and renal tumors. When ranked by incidence, neuroblastoma is most common, followed by leukemia, renal tumors, sarcomas, retinoblastomas, and CNS tumors. Because retinoblastoma is so often cured, the incidence is 159 times greater than the mortality. Among newborns, the incidence of neuroblastoma is more than ten times greater than the mortality for this tumor, whereas the incidence of leukemia is less than two times greater than its mortality. Thus, a study of mortality differs markedly from one of incidence, since certain malignancies are rapidly fatal, others lead to death beyond the neonatal period, and a large number are curable or undergo spontaneous regression. A summary of incidence, mortality, and types of malignancies seen in the neonates and infants is shown in table (1) by *Badder and Miller (1979).*

Table 1: Incidence and mortality of malignant tumors in United States neonates and infants

Tumor Type	Incidence				Mortality				
	< 29 Days		< 12 Mos.		< 29 Days		12 Mos.		
	No.	Rate*	No.	Rate*(A)	No.	Rate*	No.	Rate*(B)	Ratio (A/B)
Leukemia	5	4.7	34	31.8	101	2.6	807	20.8	1.5
Neuroblastoma	21	19.7	67	62.7	70	1.8	302	7.8	8.0
CNS	1	0.9	15	14.0	12	0.3	257	6.6	2.1
Kidney	5	4.7	21	19.7	21	0.5	141	3.6	5.4
Reticuloendotheliosis	0	0.0	3	2.8	7	0.2	131	3.4	-
Sarcoma	4	3.7	19	17.8	29	0.7	129	3.3	5.4
Liver	0	0.0	8	7.5	15	0.4	99	2.6	2.9
Lymphoma	1	0.9	2	1.9	2	< 0.1	60	1.5	1.3
Teratoma	0	0.0	3	2.8	11	0.3	28	0.7	4.0
carcinoma	1	0.9	6	5.6	6	0.2	18	0.5	11.2
Germ cell, excluding teratoma	0	0.0	0	0.0	0	0.0	6	0.2	0.0
Retinoblastoma	0	0.0	17	15.9	1	< 0.1	4	0.1	159.0
Other	1	0.9	1	0.9	20	0.5	62	1.6	0.0
Total	39	36.4	196	183.4	295	7.6	2044	52.7	3.5

* Per one million livebirths per year

(From Bader, J.I., and Miller, R.W.: Am. J. dis. Child., 133: 157, 1979. Copyright 1979, American Medical Association)

PREDISPOSING FACTORS

There are certain factors known to increase the risk for cancer development, these are:

I. Environmental factors: as
   1. X-ray irradiation.
   2. Drugs.
      a. Alcohol.
      b. Hydantoins and other anticonvulsants.
      c. Betamethasone.
      d. Vaginal spermicide.
      e. Diethylstilbesterol.

II. Host factors.

III. Congenital defects.

I. Environmental Factors

1. X-ray Irradiation

It was reported by many authors that abdominal radiation of the mother during pregnancy increased the risk of the child in utero to subsequently developing leukemia *(Diamond et al., 1973)*, whereas, others do not substantiate the existence of a relationship between prenatal X-ray exposure and childhood cancer *(Totter and Mac-Pherson, 1981)*.

Diamond and coworkers *(1973)* found that 3 general variables may have an influence on mortality:

1. Type of pregnancy i.e. ideal or non-ideal as those with congenital malformations.
2. Time of X-ray exposure i.e. in the first two trimester.

3. Type of X-ray exposure i.e. pelvimetry or others that intrauterine radiation was responsible for the excess mortality among white exposed children which was not observed in black children. Two possible explanations were put:
   1. There may be genetically determined differences in susceptibility to radiation between whites and blacks.
   2. Total mortality experience of the black group is exceedingly high because of other factors e.g. low socioeconomic status.

Jablon and Kato (1970) did a study on children exposed prenatally to the atomic bombs in Hiroshima and Nagasaki, they found no significant excess of mortality from leukemia or other cancers.

Ionizing radiation and several antineoplastic drugs can induce gonadal failure and can cause fetal malformations and death when exposure occurs during pregnancy *(Stillman et al., 1981 and Byrne et al., 1986).*

Li and his colleagues *(1987)* found among 114 pregnancies in women who had received abdominal radiotherapy for Wilms' tumor (W.T.), an adverse outcome occurred in 30%. There were 17 perinatal deaths. In contrast, an adverse outcome was found in 3% of 77 pregnancies in non-irradiated female patients with W.T. and wives of male patients. The high risk of adverse pregnancy outcome should be considered in the counselling and prenatal care of women who have received abdominal radiotherapy for W.T.

2. Drugs

a. Alcohol

In 1973, the fetal alcohol syndrome was defined as a syndrome of developmental delay, growth deficiency and multiple minor anomalies. Since

then, the syndrome has been increasingly recognized in infants of mothers with excessive alcohol intake *(Jones et al., 1973).*

The maternal alcohol consumption during pregnancy and the development of a malignant tumor in the child many years later could be fortuitous *(Hornstein et al., 1977).*

Specific malformations and developmental abnormalities now known as the fetal alcohol syndromes have been reported in infants born to mothers who drank substantial amounts of alcohol during pregnancy *(Clarren and Smith, 1978).* A variety of liver abnormalities *(Habbick et al., 1979)* and two forms of adrenal cancer have been described in patients with this syndrome *(Hornstein et al., 1977 and Seeler et al., 1979).*

Khan and coworkers *(1979)* reported a case of black male infant with multiple features of fetal alcohol syndrome as characteristic dysmorphic facies, psychomotor retardation, dysplastic kidney, cancer liver, and abnormalities of the palmar creases. His mother had used both alcohol and illegal drugs heavily throughout pregnancy. Transplacental exposure to alcohol could have promoted to liver cancer in this infant.

With recognition of fetal alcohol syndrome, alcohol has been established as a teratogen *(Kronick et al., 1976 and Clarren and Smith, 1978).*

Adrenal carcinoma has been reported in a child with fetal alcohol syndrome *(Hornstein et al., 1977)* and ganglionueroblastoma, in a child with fetal hydantoin-alcohol syndromes *(Seeler et al., 1979).*

These two cases, in addition to *Kinney* case *(1980)* suggest a possible relation between maternal gestational alcohol abuse and neoplasia. In the