HISTOPATHOLOGIC CLASSIFICATION OF TUMOURS OF INFANCY AND CHILDHOOD

THESIS

Submitted in Partial Fulfilment
for the Degree of M.M.Sc.
(Pathology)

By

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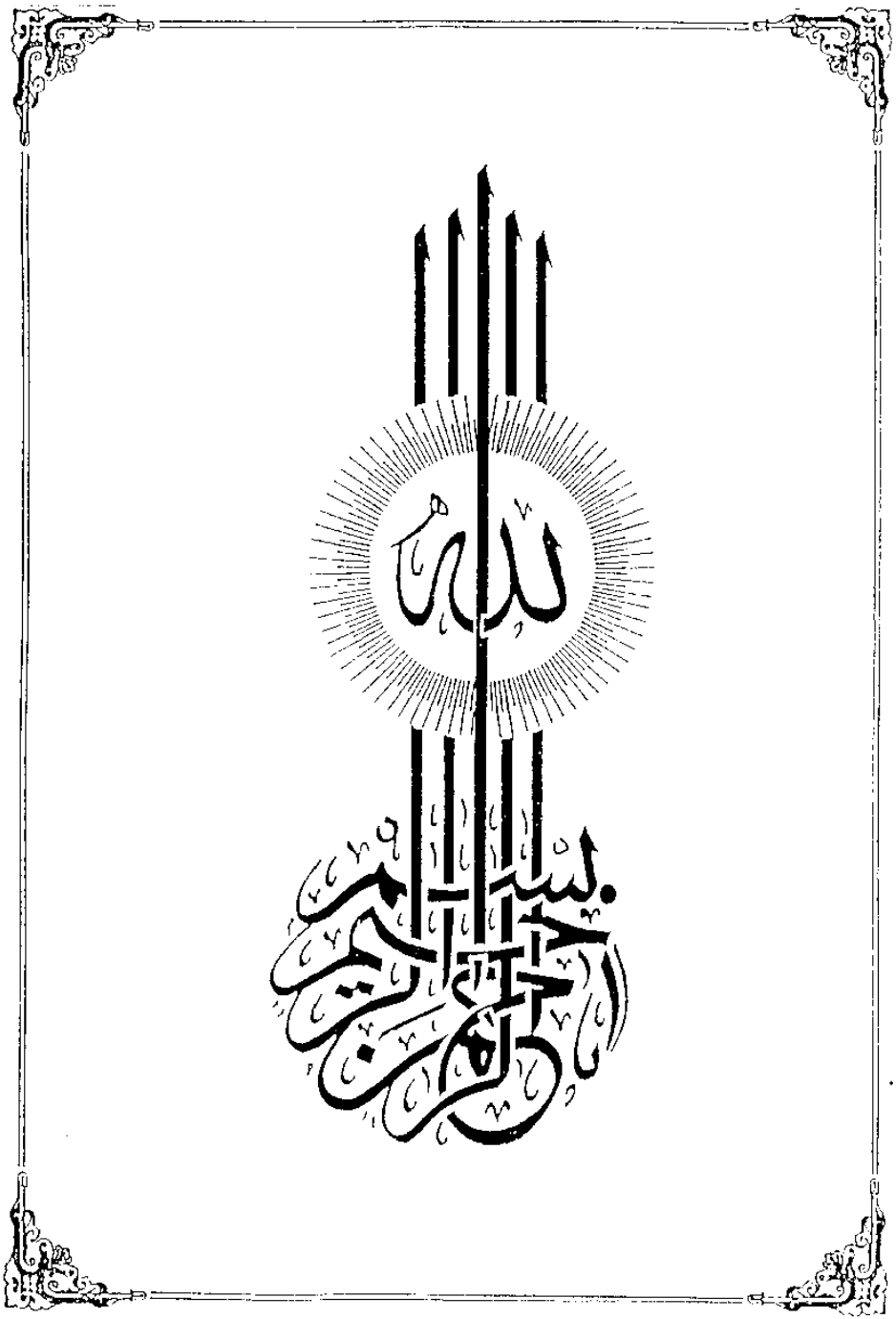
ACKNOWLEDGEMENT

I wish to express my feelings of deep gratitude to Professor M.A. Sherif, Professor of Pathology and Head of Pathology Department, Faculty of Medicine, Ain Shams University, for his supervision, sincere help and encouragement.

I would like to express my deepest gratitude to Dr. Laila El Shabrawy, Assistant Prof. of Pathology, Ain Shams University, who provided much of her time and offered me valuable assistance and sincere help. I thank her for her continuous support throughout the work.

My most sincere gratitude is also presented to Dr. Karima Sidhom, Lecturer of Pathology, Ain Shams University, to whom I am deeply indebted for her valuable advice and great help. She exhausted every possible effort helping me to accomplish this work.



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INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Certain peculiarities of neoplasms of early life distinguish them in mant respects from those occurring in adulthood.

Everson (1966) stated that many solid tumours of childhood are manifested in very early life, sometimes at birth and are characterized by cellular features indicating an origin in abnormal embryogenesis.

Bolande (1976) found that oncogenic viruses and chemical carcinogens more readily induce tumours in the newborn host than in mature ones.

Foulds (1969) stated that regression and cytodifferentiation occur most often in human tumours of early life. He added that many are manifested by an overgrowth of well differentiated cells and tissues; in either orderly or chaotic arrangements. The cells may be indigenous or alien to the site of involvement. Other tumours are composed of persistent embryonal or fetal tissues indicating a failure of proper maturation or cytodifferentiation in intrauterine or post natal life. Some tumours that are initially non-malignant become the seat of malignant transformation in later life. In other instances tumours may persist in a latent or cryptic form for long periods after birth, becoming manifest later in childhood or even in adult life.

Gerard-Marchant (1975) stated that all varieties of benign and malignant tumours have been described in children.

Meissner and Diamandopoulous (1977) found that there is less correlation between the histological characteristics of tumours in children and their biologic behaviour than in case with tumours of adults.

Robbins and Cotran (1979) reported that tumours are not common in childhood, only 2% of all malignant tumours occur in infancy and childhood. They added that benign tumours are even more common than cancers.

Birch et al. (1980) stated that in some developed countries with good environmental and personal health services, tumours represent the second most common cause of death (being surpassed by accidents) in children from one to fourteen years of age.

The aim of this work is to classify and describe pathologically tumours of infancy and childhood in the most simple way to avoid much confusion.

AETIOLOGY AND PATHOGENESIS

AETIOLOGY AND PATHOGENESIS

It is of utmost importance to study the aetiology and pathogenesis of tumours of infancy and childhood.

Bolande (1976) stated that it is well established that precarcinogenic agents in adults may induce cancer also in early life, but these agents may be more dangerous in infants and children because of the rapid growth of embryonic tissues.

Genetic factor :

Morris et al. (1979) stated that at the present time it seems unlikely that the majority of childhood tumours are due to genetic influences.

MacMahon and Levy (1964) stated that the higher concordence rate for leukaemia observed in monozygotic than in dizygotic twins may be an evidence of a genetic influence. Clarkson and Boyse (1971) suggested that it may be due to transplantation of leukaemic cells from one monozygotic twin to the other while sharing the placental circulation during intrauterine life.

Li and Fraumeni (1969), in a study of childhood rhabdomyosarcoma, showed that a tendency for the cancer to aggregate in sibling was associated with a high frequency of various cancers, especially of the female breast, in parents and other relatives.

Miller (1971) found that sarcomas were observed also in familial aggregation with adenocortical carcinoma and brain tumours.

Fraumeni (1973) stated that hereditary neoplasms may occur as the only manifestation of the gene defect (e.g. retinoblastoma) or as a part of a generalised disturbance with multiple neoplasms or developmental anomalies (e.g. nevoid basal cell carcinoma syndrome). They are characterized by familial patterns consistent with autosomal dominant inheritance and by a tendency to occur earlier in life and to arise from multiple foci within the affected organ.

Knudson (1975) found that embryonal cancers are all visualised as genetic diseases and their frequencies are limited by gene mutability. This mutability may be increased by such environmental agents as radiation, chemicals and virus.

Knudson (1974) found that Wilms' tumour and neuroblastoma probably have a similar mode of transmission. The hereditary forms of tumours are less frequent than non-hereditary sporadic forms. The hereditary variety of retinoblastoma, as an example, is related to the inheritance of a dominant gene. Knudson (1979) stated that this gene have a nearly 95% probability of developing a tumour in one eye or even bilateral neoplasms while those not having this mutation has a risk of approximately 1 in 30,000 of developing one tumour.

Fraumeni (1973) described different category of persons with hereditary preneoplastic syndromes, in which cancer arises as a complication of inherited precursor lesions which are clinically recognisable in a proportion of cases. These syndromes may be classified into four groups :-

I- Hamartomatous syndromes in which several organs show tumour-like malformations with faulty differentiation. These syndromes show an autosomal dominant inheritance and a tendency to develop some tumours. They include :-

- Multiple neurofibromatosis, in which sarcomatous change occur in 10% of cases with an increased risk of development of gliomas, meningiomas, accoustic neuromas and phaeochromocytoma.
- Tuberous sclerosis in which 1% of patients develop brain tumours especially giant cell astrocytoma.
- VonHippel-Lindau syndrome with an excessive frequency of hypernephroma, phaeochromocytoma and ependymoma.
- Multiple exostosis showing transformation to chondrosarcoma in 5 to 10% of cases.

II- Genodermatosis, which are genetic disorders involving the skin and are transmitted in an autosomal recessive manner. This group generally predispose to cancer of the skin. It includes :

- Xeroderma pigmentosum which predispose to basal cell carcinoma, squamous cell carcinoma and melanomas.
- Albinism which predispose to squamous cell carcinoma in sun-exposed areas.

- Werner's syndrome which predispose to soft tissue sarcomas.
- Naevoid basal cell which predispose to basal cell carcinoma.

III- Syndromes with increased chromosomal fragility in cell culture. These are inherited in an autosomal recessive fashion and are known to predispose to leukaemia (Miller, 1976). They include:

- Bloom's syndrome, which predispose to acute leukaemia, sigmoid carcinoma, squamous all carcinoma and reticulum cell sarcoma (German, 1974).
- Fanconi's aplastic anaemia, patients with this disease are predisposed to acute leukaemia (Dosik et al., 1970).
- Ataxia-Telangectasia; this is primarily an immune deficiency syndrome which sometimes show chromosome fragility on cell culture. It is associated with an increased occurrence of acute leukaemia, malignant lymphomas, medulloblastoma and gastric carcinoma (Harnden, 1974).

In addition to the chromosomal fragility syndromes, other specific chromosomal abnormalities may be associated with an increased incidence of neoplasms. Examples of these abnormalities include:-

- Down's syndrome; in which the incidence of acute leukaemia is increased 15 times (Miller, 1970).

- 13-q-syndrome; in which chromosome 13 may have deletions of the long arm of a D-group chromosome. In 20% of patients retinoblastoma develop later (Bolande, 1976).
- Gonadal dysgenesis; which are associated with increased risk of developing gonadoblastoma or dysgerminomas (Talerman, 1971).
- Klinefelter's syndrome; which is associated with an increased incidence of breast cancer (Lynch et al., 1977).

IV- Immunodeficiency syndrome; patients with these syndromes are particularly likely to develop lymphoreticular neoplasms. These include :-

- Ataxia-Telangiectasia.
- Wiskott-Aldrich syndrome.
- X-linked agammaglobulinaemia (Bruton type).

Kersey et al. (1974) stated that the incidence of malignancy in children with various immunodeficiency syndromes is approximately 100 times that seen in the general population. Penn (1974) added that it also increases in person receiving immunosuppressive therapy during transplant procedures. Cancer also occur in cases with fresh gene mutation or due to environmental influences as in:

The excessive occurrence of Wilms' tumour with congenital aniridia and with other genitourinary tract malformations (Bolande, 1976).

The association of Wilms' tumour, adrenocortical neoplasia and primary liver cancer with three other manifestations of excess growth; congenital hemihypertrophy, visceral cytomegaly (Beckwith Weidemann syndrome) and hamartomas including vascular or pigmented naevi (Miller, 1968).

Cryptochild testes were found to give rise to 3:11% of all testicular neoplasms (Kissane, 1975).

Enchondromatosis (Ollier's syndrome) or enchondromas and hemangiomas (Maffucci's syndrome) are associated with chondrosarcoma (Fraumeni, 1973).

Fraumeni (1973) found that the early diagnosis of cancer cases achieved by close surveillance of high-risk individuals may minimize added risks from specific environmental exposures or from genetic transmission.

Environmental factors :

Ionising radiation

A great deal has been written regarding the effect of irradiation during intrauterine life.

Jablon et al. (1971), after studying survivors of the atomic bomb explosions at Hiroshima and Negasaki, showed an increase incidence of leukaemia and other cancers among exposed children less than 10 years old. Mole (1974) showed that the incidence of malignant diseases occurring during

the first 25 years after exposure has been in the range of 100 cases per million person per rad exposure.

On the other hand, Jablon and Kato (1970) had not found a significant excess of mortality from leukaemia or other cancers among children exposed prenatally to atomic bombs in 1945.

Stewart and Kneale (1970) showed that there is increase incidence of childhood cancer in respect of in utero exposure to X-rays during obstetric investigations especially during the first trimester. Bithell and Stewart (1975) in the Oxford Survey revealed that the relative risk for all types of paediatric malignancies was increased about one and half times. The risk declined as the number and dose of X-ray diminished. They added that children irradiated for therapy of benign lesions are at high risk of developing cancer. Hempelman et al. (1975) found that there is a higher incidence of thyroid carcinoma in patients who have received therapeutic irradiation of the head or neck in early life. Modan et al. (1974) found that there was a significant increase in both malignant and benign head and neck tumours, especially those in the brain, the parotid and the thyroid glands following treating children with ring worm by radiotherapy.

Hutchison (1976) proved that sensitivity of foetal tissues is approximately ten times that reported for many adult tissues exposure.