SMALL CELL TUMORS IN CHILDHOOD

Thesis Submitted for the Partial Fulfillment of the Master Degree in Pathology

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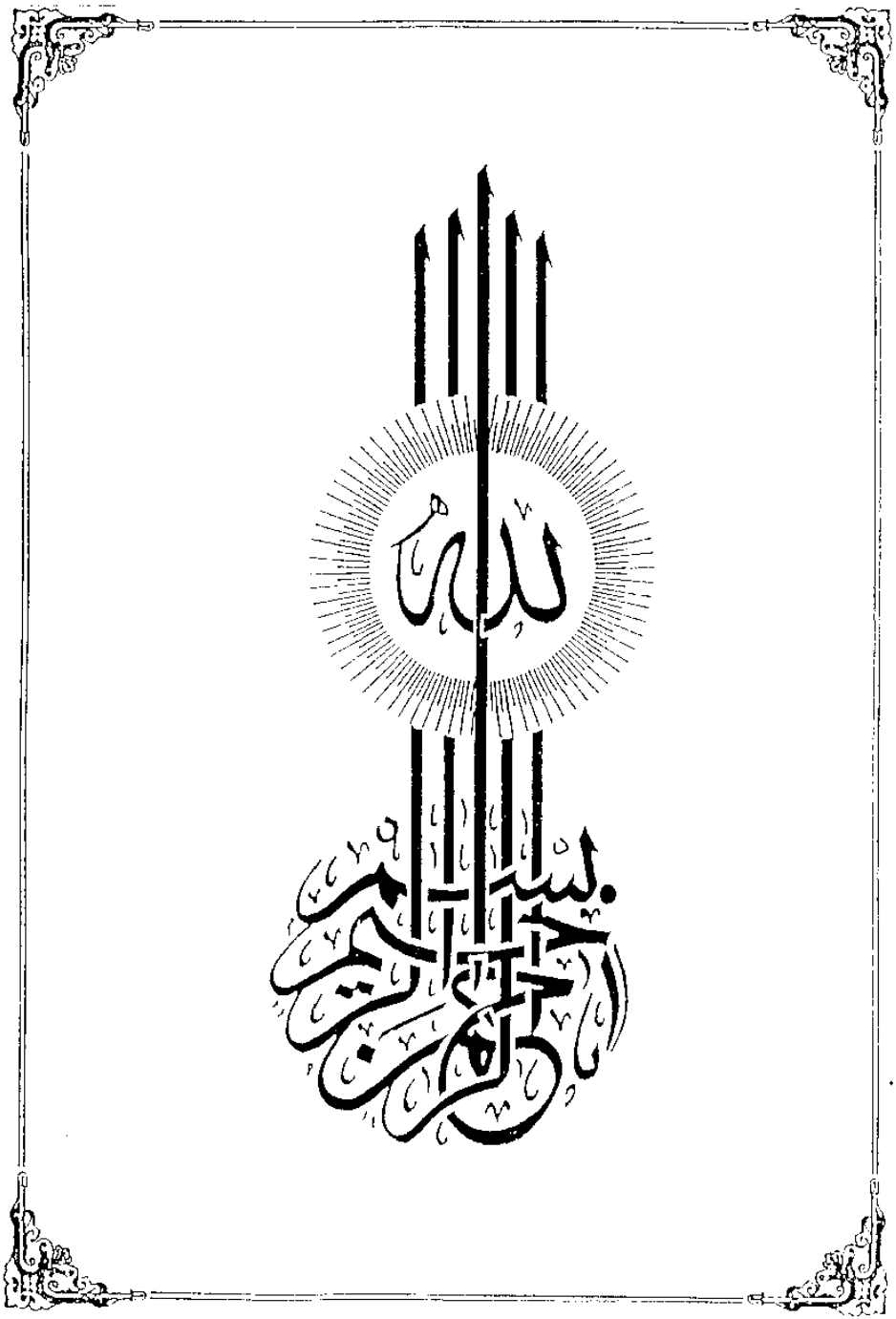
بسم الله الرحمن الرحيم

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

صدق الله العظيم

سورة البقرة-الآية: ٣٢



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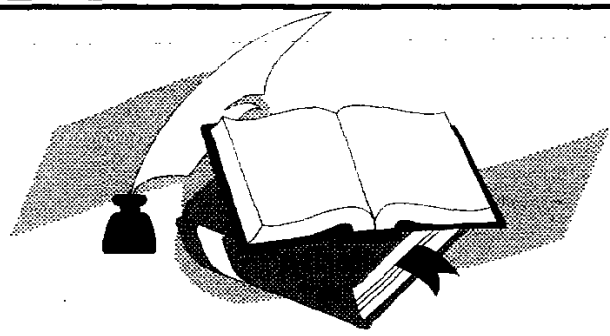

Introduction and Aim of the Work

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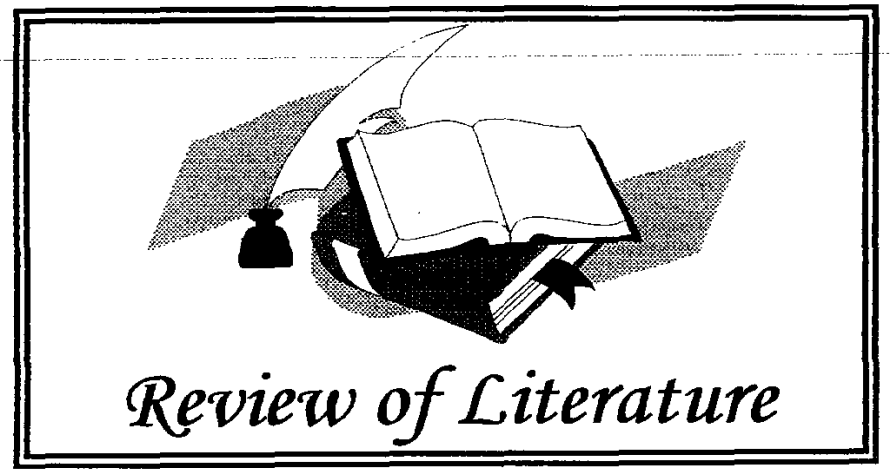
A lot of children under the age of 15 years develop cancer each year. Approximately a third of these have leukaemia, a third, brain tumors and the remainder have a wide range of solid tumors. Of these, the commonest are lymphomas, neuroblatoma, soft tissue sarcomas and Ewing's sarcoma. These tumors make up the "small-round-cell tumors" of children, so called because in many cases, there undifferentiated appearance makes them almost indistibguishable with conventional light microscopy (***Variend, 1995***).

Ross Pinkerton (1994) stated that in a few other tumor types, e.g. small cell osteosarcoma, metastatic retinoblastoma, undifferentiated hepatoblastoma and granulocytic sarcoma, the cells may also be small round and non-specific in appearance. He also added that in the days when treatment of childhood tumors was simply a matter of resecting as much of the tumor as possible, followed by radiotherapy to the primary site, the precise histological diagnosis was of little importance. With advances in the three main forms of treatment chemotherapy, radiotherapy, and surgery, correct classification of these lesions has become of paramount importance.

Aidan McManus (1994) also recorded that the availability of specifically tailored treatment protocols in small-round-cell tumors renders accurate pathological diagnosis of extreme importance.

AIM OF THE WORK:

The aim of this work is to study the morphological features and behavioral characteristics of different types of small cell tumors that occurs in infancy and childhood with a trial to reach a correct diagnostic entity of these lesions.



Review of Literature

NEUROBLASTOMA

Garrett et al., (1988) stated that neuroblastoma, a tumor of autonomic nervous system, is one of the most common tumors of childhood. It occurs in nine per million per year in children less than 15 years of age with slight male predominance.

Peter Anthony et al., (1997) added that amongst congenital tumors in infancy 30-50% are neuroblastoma. ***Sebestiano Cavalloro et al., (1993)*** reported that neuroblastoma may occur at any site of the body where neural crest tissues are present. They added that 25% to 35% of neuroblastoma arise in the adrenal medulla but in 20% of cases it develops from the paraspinal ganglia of the posterior mediastinum.

Sebastiano Cavalloro et al., (1993) also recorded a case of ectopic neuroblastoma in the thorasic wall arising at the anterior mamillary line from the inner surface of the second and third right rib in a 17 month-old male child.

Robbins et al., (1994) reported that 35 percent of this tumor appears during the first year of life and 20% during the second year. Alltogether, 85% to 90% are found in children younger than five years of age.

According to the last authors, macroscopically neuroblastoma range in size from minute nodules to large masses more than 1 kg in weight and added that some neuroblastomas are sharply demarcated and may appear encapsulated, but others are far more infiltrative and invade surrounding structures. On transection, neuroblastoma is composed of soft, gray, "brain-like" tissue which have areas of necrosis, cystic, softening, haemorrhage and calcification.

Juan Rosai (1996) classified neuroblastoma microscopically into 3 types: classic, desmoplastic, and transitional.

The classic neuroblastoma is composed of small, mitotically active cells possessed of densely hyperchromatic nuclei and disposed in highly populous sheets variably punctated by a delicate, fibrillary matrix material representing their tangled cytoplasmic processes. He added that this variant is most likely to contain diagnostic Homer Wright rosettes and large, differentiated neuron (ganglion cells).

The "desmoblastic" neuroblastoma is defined by a fibrous stroma, most developed in regions where tumor contacts the leptomeninges, that imposes a lobular, trabecular, or Indian File arrangement. Its constituents cells

are larger than the classic neuroblasts and are characterized by vesicular nuclei and often prominent nucleoli.

Transitional neuroblastoma, as its name implies, combine features of both the classic and desmoplastic variants.

Shimada et al., (1984) classified neuroblastoma microscopically into stroma-poor and stroma-rich groups according to the degree of stroma development.

1. **Stroma-poor:** is characterized by a diffuse growth of neuroblastic cells irregularly separated by thin septa of fibrovascular tissue, this group roughly corresponds to classical neuroblastoma and diffuse ganglioneuroblastoma.
2. **Stroma-rich:** is characterized by an extensive growth of Schwanian and other supporting elements. Tumors of this group might all be called "ganglioneuroblastoma".

Shimada et al., (1984) also divided the stroma poor neuroblastoma according to the grade of differentiation into:

[a] Undifferentiated histology: composed of immature neuroblasts with less than 5% of differentiating population.

[b] Differentiating histology: composed of a mixture of neuroblastic cells of various degree of maturity with at least 5% or more of differentiating population.

The authors subdivided the tumors of stroma rich group into the following 3 subgroups according to the gross and/or microscopic distribution of the immature neuroblastic elements.

[a] Well-differentiated: composed of a dominating mature ganglioneuromatous tissue with only a few randomly distributed immature neuroblastic cell. These cells aggregate but do not make distinct nests interrupting the stroma.

[b] Intermixed: composed of ganglioneuromatous tissue studdied with scattered, variably differentiated neuroblastic cell nest. These neuroblastic cell-foci are sharply defined in the stroma, so they are easily distinguished microscopically.

[c] Nodular: characterized by the presence of one (or a few) grossly discrete mass(es) of stroma poor neuroblastoma tissue trapped in mature matrix. The nodule is usually appreciable grossly as a haemorrhagic focus.

Garrett et al., (1988) reported that diagnosis of neuroblastoma is established if (1) an unequivocal