NEUROBLASTOMA IN INFANCY AND CHILDHOOD

An Essay Submitted For The Partial fulfilment of

Master Degree in General Surgery.

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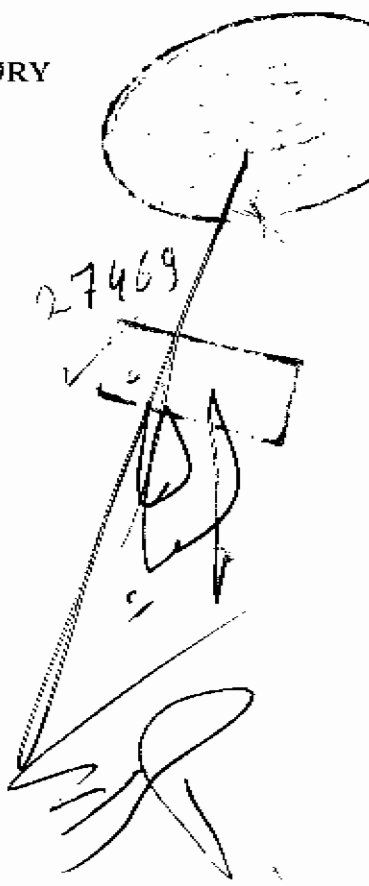

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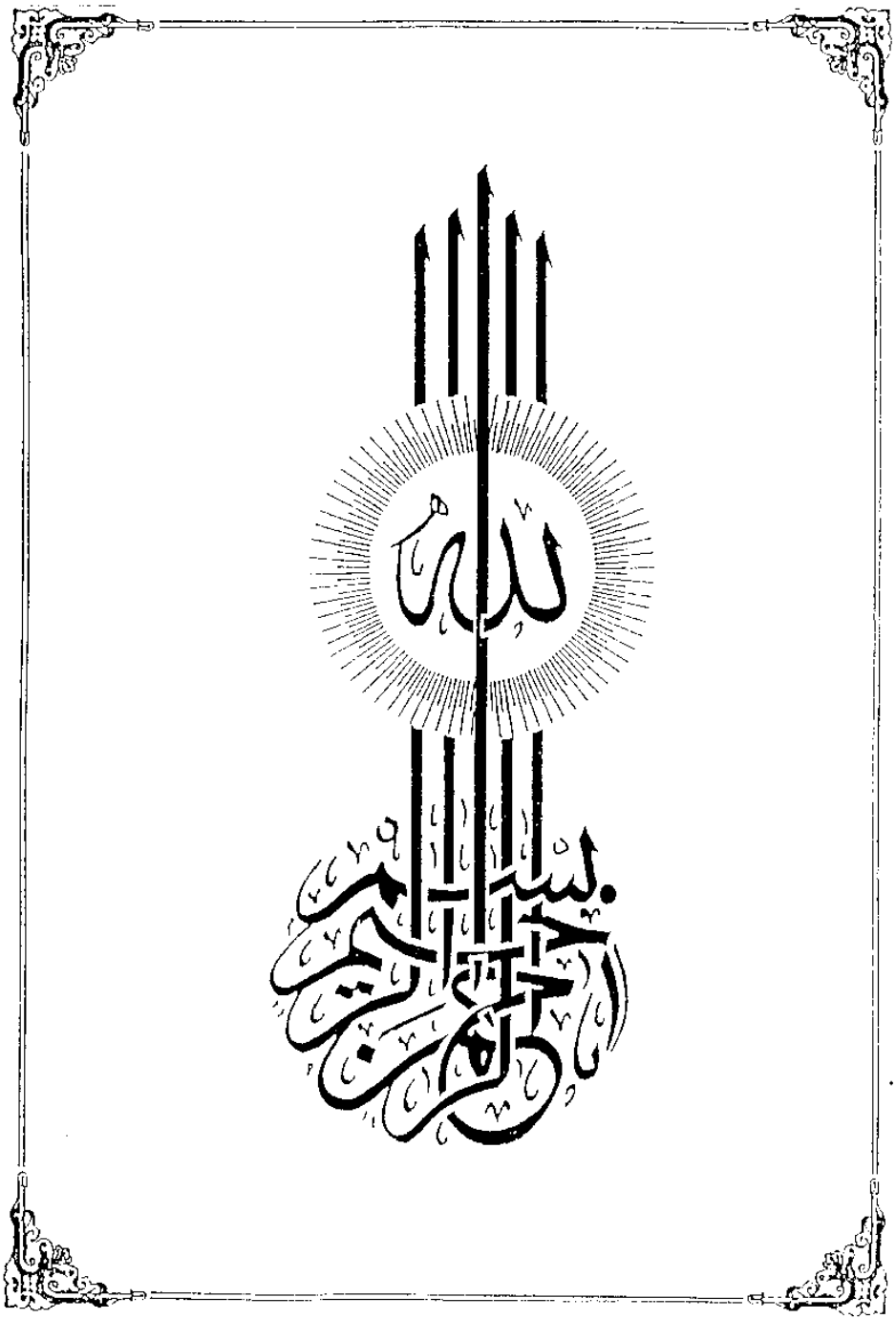

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HISTORY

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Neuroblastoma, along with ganglioneuroma and ganglioneuroblastoma, may arise initially from any site along the craniospinal axis. This is because the origin of the tumor is from the neural crest.

In 1864 Virchow was the first to characterize neuroblastoma, which he labeled a glioma.

Marchand in 1891 commented on the histologic similarities between neuroblastoma and developing sympathetic ganglia.

Herxheimer (1914) , using a specific neural silver stain, showed that fibrils in neuroblastoma shared staining characteristics with nervous tissue. This contributed to establishing the tissue of origin of this tumor. The biochemical aspects of neuroblastoma began to be understood as Mason et al., (1957) reported the presence of pressor amines in the urine of a child with neuroblastoma.

Subsequently , we have come to recognize elevated levels of norepinephrine and its precursors and metabolites in the urine of patients with this tumor.

Another Landmark in our understanding of neuroblastoma came in 1927 when Cushing and Wolbach reported for the first time a transformation of neuroblastoma into benign ganglioneuroma.

Everson and Cole (1966), noted that this generally occured in infants under the age of 6 months. That spontaneous regression of neuroblastoma may be more common than is clinically evident was suggested by Beckwith and Perrin 1963, who noted microscopic clusters of neuroblastoma cells in the adrenal glands of a number of infants under 3 months of age who had died of other causes. These foci of tumor cells they called neuroblastoma in situ. They estimated neuroblastoma in situ to occur about 40 times more frequently than the number of cases of neuroblastoma clinically diagnosed.

Under normal circumstances, recession appeared usually to be complete after 3 months of age.

ETIOLOGY

ETIOLOGY

Although the cause of neuroblastoma , as for most other carcinomas, is unknown, it arises from cells of the neural crest that form the sympathetic ganglia and adrenal medulla.

Bolande (1979) has termed this tumor a type of neurocristopathy. Other neurocristopathy include pheochromocytoma, paraganglioma , medullary carcinoma of the thyroid, carcinoid, melanoma, neurocutaneous melanosis, neurofibromatosis, and multiple endocrine neoplasia.

Sympathetic nervous system tumors can apparently differentiate along two lines, the pheochromocytoma line and the sympathoblastoma line. It is this latter line that forms neuroblastoma, ganglioneuroblastoma and ganglioneuroma.

* In normal fetal development, nodular collections of neuroblast cells are found in the adrenal glands in the seven - week fetus life. At 14-18 weeks of gestation, aggregates of neuroblastic nodules closely resembling neuroblastoma can be found. The nodules sub-sequently split into smaller nodules with differentiation into chromaffin cells .(Iked et al., 1981).

* A persistence of this developmental stage into neonatal life could explain the presence of neuroblastoma in situ.

Measurements of nuclear size suggest that the nucleus of a neuroblastoma cell is significantly larger than that of a neuroblastic nodule in situ and may be an indicator of malignant potential

There appears to be a genetic influence in this tumor. Knudson and Strong (1972) have suggested that approximately 20 percent of cases arise in children predisposed to the tumor by a dominant transmittable mutation . Knudson and Meadows (1976) have suggested that familial cases result from a prezygotic mutation and the non-familial ones from a post-zygotic somatic mutation, rare families having more than one member affected with this tumor have been discribed. (Chatten and Vorhees, 1967, Arenson et al., 1976).

INCIDENCE

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Neuroblastoma is the most common malignant tumor of infancy and, after brain tumors, the most common malignant solid tumor of childhood. Neuroblastoma accounts for 6 to 8 percent of all childhood malignancies (Young and Miller, 1975).

Neuroblastoma in situ is seen in the adrenal gland in one of every 100 infants who die whithin the first three months of life from other causes.

Yet, in the clinical setting this tumor occurs in approximately one in 10,000 chilren (Grosfeld et al., 1980 , Koop et al., 1980).

Ninety percent of cases of neuroblastoma occur within the first eight years of life, with 50 percent of the patients being under two years of age at diagnosis.

Fifty percent of the cases occur in children under the age of 2 years, and over 75 percent of cases have been encountered by the fourth year of life. (Peterson et al., 1969 , Fortner et al., 1968). This is a younger age of distribution than that of Wilms' tumor.

This tumor is slightly more common in boys than in girls, this male predominance is in the ratio of 1.1:1 (Miller et al., 1968).

This neoplasm has been described in twins , and familial occurrences in both mother and children and father and sons has been reported. (Arenson , et al., 1976 , Chatten et al., 1967 , Gerson, et al., 1974, Pegelow, 1975 and Prasad et al., 1973).

Neuroblastoma has been noted in infants suffering from the Beckwith-Wiedemann syndrome and Hirschsprung's disease,(Allen, et al., 1980, Emery et al., 1983 , Kinney et al., 1980 and Seeler , et al., 1979).

Unlike Wilms' tumor, neuroblastoma has a low incidence of associated congenital anomalies . One exception is an increased incidence of brain and skull defects, approaching 2 percent in children with neuroblastoma (Miller et al.,1968).

PATHOLOGY

PATHOLOGY

On gross examination, small tumors usually are well encapsulated and firm.

On cut surface, the tumor is fairly soft and lobulated, with greyish-to-pink color.

The tumor has a tendency to break through it's pseudocapsule and infiltrate surrounding tissues. When it does, it generally is found to be friable and very soft, with haemorrhage and necrosis. Cystic areas may be present.

On microscopic examination, neuroblastoma is one of the small round cell tumors of childhood (Reynolds et al;,1981).

There is a similarity by light microscopy between neuroblasts, lymphocytes, and the cells of lymphomas, embryonal myosarcomas and Ewing's sarcomas. When the tumor cells can be seen to form themselves into rosettes and neurofibrils are evident, the degree of differentiation is quite good and the tumor is recognizable as a neuroblastoma.

Unfortunately these signs are often absent. Ewing's sarcoma and rhabdomyosarcoma usually contain glycogen which can be