Neurocutaneous Syndromes In Infancy and Childhood

Thesis

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By

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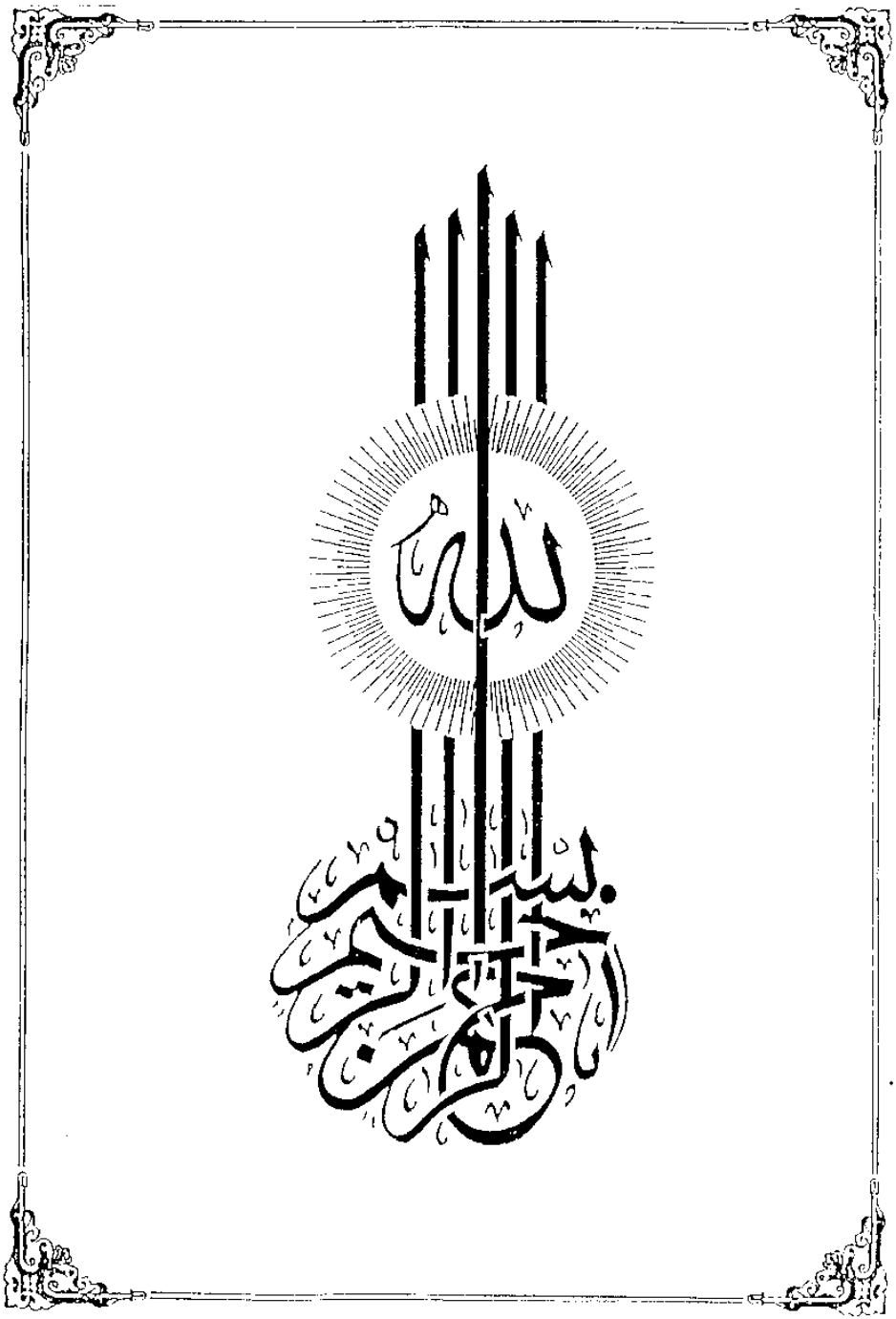

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Introduction

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Neurocutaneous Syndromes are a group of diseases in which there is association of lesions of the central nervous system with lesions of the skin.

The primary members of this disease group are neurofibromatosis, Tuberous selerosis, sturge-weber syndrome and Von-Hippel Lindeau disease. They are notable for their dysplatic nature and tendency to develop tumours of the central nervous system, skin, or viscera.

Each of these cendition except for sturge-weber syndrome has a genetic basis but sporadic cases do occur.

Since both skin and nervous tissue have a common ectodermal origin, additional syndromes characterized by skin lesions as well as abnormality of the Central Nervous System have been subsequently added to this group of disorders. (Bergo, 1982). In addition to the disorders of the neuroectodermal derivatives, alterations of the structures of mesodermal origin may occur. Varying from patient to patient, there may be single or multiple dysplastic, hyperplastic, or neoplastic processes. (Elizabeth 1982)

Ataxia telangiectasia was added later according to the suggestion of Louis-Bar (1941). (coated by Berg 1982).

Other Neurocutaneous syndromes are Bloch Sulzberger's syndrome, linear sebaceous nervus syndrome, Sjogren-Larson syndrome, Chediak-Higashi syndrome and xeroderma pigmentosum (Abraham Julien 1982).

Also, Klippel Trenaunay syndrome, Parry-Romberg syndrome, and neurocutaneous melanosis are added to these diseases (Edward M.B. 1983).

Aim of the work.

Is to study all possible neurocutaneous syndromes in infancy and childhood as regard their inheretance, clinical presentations, management and possible ways of prophylaxis.

Neurofibromatosis

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"Von Recklinghausen Disease"

Neurofibromatosis is a disease of great importance, not only to the thousands of affected patients, but also to researchers concerned with genetics, melanine synthesis, neural-crest embryology, cell-cell interaction, cancer, and other disciplines. However, only recently has neurofibromatosis been the subject of widespread, systematic studies of its nature and pathogenesis (Riccardi VM, Mulvihill JJ, 1981).

An unusually severe case was the subject of Pomerance's play "The Elephant Man" the story of disfigured man who was exhibited in fairs and was rescued from this life by a surgeon who described his condition.

The diagnosis of neurofibromatosis in this man was made later by weber (weber 1909).

Although significant disfigurement is common, many patient carrying the gene have only minimal evidence of the disease and must be examined very carefully. (Samuel L, Harry 1985).

Historical View:

Worster-Drought et al. 1937 recognized the following:

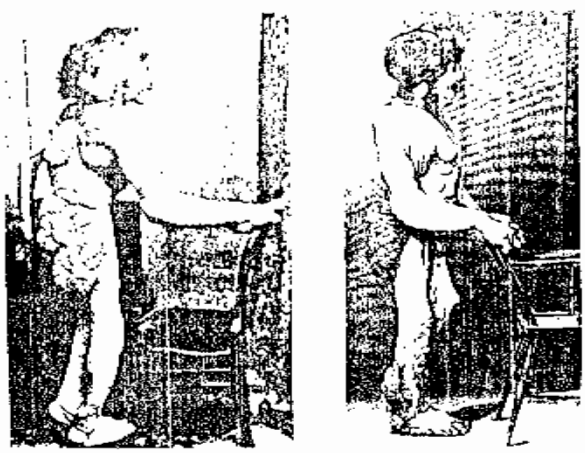

Fig. (1): The Elephant Man
from: Neurology 31:661, 1981.

I. Peripheral type of neurofibromatosis:
first described by Tilesios in 1793.

II. Central type of neurofibromatosis:
which is of 3 types also:

(a) Meningeal and perineurial
(syndrome of Wishart 1822) rare.

(b) Perineurial only:
(syndrome of Knoblauch 1843) commenest.

(c) Meningeal only:
(syndrome of Schultz 1880) the rarest.
(Walton 1977).

But Von Recklinghausen (1882) first carefully reported the clinical and pathological features of this disease. (Berg 1982).

Genetics:

Autosomal dominant transmission is the only type established; this is supported by a 1:1 ratio of affected to unaffected siblings, equal male and female incidence, and male to male transmission. Neurofibromatosis with C.N.S. lesions may be accompanied by relatively few cafe-au-lait spots, but predominance of central or peripheral lesions was not observed to be a hereditary characteristic in a

large group of patients studied by Crowe (Crowe et al 1956).

Since tumours of the optic and auditory nerves are the commenest C.N.S. tumours in neurofibromatosis, it has been proposed that patient with hereditary acoustic neuromas have "central" neurofibromatosis. There is evidence that pedigrees with hereditary acoustic neuromas also have family members with neurofibromas,(Young et al. 1970), but these patient, have few cafe-au-lait spots, and most do not have cutaneous tumours.

Expression is variable in successive generations as with many dominant disorders. Some patients are born with neurofibromas, but in others, cafe-au-lait spots are the only manifestation until adult life.

Penetrance is virtually 100 per cent.

Incidence:

Crowe et al (1956), from a careful statistical study, concluded that any person with more than six cafe-au-lait spots exceeding 1.5 cm. in broadest diameter should be presumed to have Neurofibromatosis.

Whitehouse (1966) considered five or more spots necessary for the diagnosis. Crowe et al (1956) estimated the frequency

to be between 1 in 2500 and 1 in 3000 births. Males and females both are equally affected.

Etiology and Pathogenesis:

Increased nerve growth-stimulating activity (measured by bilogic assay using nerve ganglia in vitro) has been described in sera of patients with neurofibromatosis (Schenkein et al., 1974).

A second careful study subsequently failed to show a difference between sera of patients and control and found that substantial increase in nerve growth-stimulating activity could be produced by technical modifications in the assay, casting doubt on the original findings (Tischler, 1974).

Later, increased concentrations of nerve growth-stimulating activity cross-reacting with nerve growth factor were described in several patients' sera assayed by radioreceptor assay (which measures material capable of displacing labeled nerve growth factor from receptors on nerve cells) and radioimmuno assay (Fabricant et al. 1979).

Pathology:

The neurofibromas are tumours usually situated upon peripheral nerves and composed of bundles of long spindle

cells. There has been much controversy as to the nature of the cells of which neurofibromas are composed.

Russel and Rubinstein (1959) distinguished on histological grounds Schwannomas, derived from cells of the neurilemma (Sheath of Schwann), and neurofibromas, which they believe to be also of Schwannian origin and not derived from fibroblasts.

Both may be found on the peripheral nerves and also upon the cranial nerves, most frequently upon the vestibulocochlear nerve, but also upon the others, especially the vagus, trigeminal, and hypoglossal, and they may occur upon spinal nerve roots, usually the dorsal, or upon the cauda equina. Schwannomas particularly may be solitary.

The cutaneous fibromas or mollusca fibrosa are formed from the connective tissue elements of the cutaneous nerves. Nerve elements are absent, but there are characteristic whorls of spindle cells.

The bone changes associated with neurofibromatosis may consist either of hyperostosis or rarefaction, with or without cyst formation.

According to Thannhauser (1944) the bone lesions in neurofibromatosis and in osteitio fibrosa cystica of Von Recklinghausen are similar. The cause of the "scalloping"

of vertebral bodies seen in some cases is unknown.

Neurofibromas may become sarcomatous. Abnormalities may be present in parts of the nervous system other than the peripheral nerves.

Patches of gliosis, neuronal heteropathios and vascular malformations (Pearce, 1967) and ependymal overgrowth may occur in the brain and spinal cord; syringomyelia, and even malignant tumours-gliomas and ependymoma-may develop.

Glioma of the optic chiasma may be associated with neurofibromatosis, and meningiomas are sometimes present. Pearce (1967), in a study of nine autopsied cases, found a high incidence of intracranial gliomas which were often clinically latent.

Neurofibromatosis is occasionally associated with other congenital abnormalities, such as spina bifida, cerebral meningocele, buphthalmus, syndactyly and haemangiectatic naevi. (Walton 1977).

Manifestations:

The manifestations of neurofibromatosis are very complex.

In a general way the disease can be described as dysgenetic blastomatous condition. Multiple neoplasm may be encountered