INCIDENCE AND CLINICOPATHOLOGICAL FEATURES OF NEUROCUTANEOUS DISORDERS

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ABSTRACT

BACKGROUND

Neurocutaneous disorders are genetically determined disorders showing both cutaneous and neurologic involvement. The definition includes both hereditary and non-hereditary phenotypes, but excludes acquired disorders. Either they follow the established Mendelian modes of inheritance or they represent lethal mutations surviving by mosaicism or they belong to the group of chromosomal disorders.

MATERIALS AND METHODS

This study was conducted at the Department of Dermatology, Government KAPV Medical College, Trichy, for a period of 12 months from January 2016 to December 2016. Patients were selected among those attending the outpatient department with signs and symptoms pertaining to neurocutaneous syndromes. Preliminary information like age, sex, educational qualification, present and past illness, family history elicited. Dermatological examination consisted of thorough screening of patients to detect the cutaneous markers for neurocutaneous disorders. A detailed systemic examination was done, particularly central nervous system.

RESULTS

In this study, neurofibromatosis (68.8%) topped the list followed by tuberous sclerosis complex (18.3%) and other rarer disorders like xeroderma pigmentosum (2.7%), giant congenital melanocytic naevus (1.8%), Sturge-Weber syndrome (0.9%), Waardenburg syndrome (1.8%), epidermal naevus syndrome (1.8%), naevus comedonicus (0.9%), Elejalde syndrome (0.9%), oculocutaneous albinism (0.9%) and Adams-Oliver syndrome (0.9%).

CONCLUSION

In this study of 109 cases of neurocutaneous syndromes, neurofibromatosis topped the list followed by tuberous sclerosis complex. Classical features of xeroderma pigmentosum was observed in 1 patient. Sturge-Weber syndrome with unilateral port wine stain with seizures was reported in our study. Two cases of Waardenburg syndrome, epidermal nevus syndrome and giant congenital melanocytic nevus were reported in my study. One case of unilateral nevus comedonicus, Elejalde syndrome, oculocutaneous albinism and Adams-Oliver syndrome with Dandy-Walker malformation was reported in this study.

KEYWORDS

Neurocutaneous Disorders, Neurofibromatosis, Tuberous Sclerosis Complex, Xeroderma Pigmentosum, Melanocytic Naevus.

HOW TO CITE THIS ARTICLE: Money SK, Gnanadeepam RS. Incidence and clinicopathological features of neurocutaneous disorders. J. Evid. Based Med. Healthc. 2017; 4(64), 3849-3852. DOI: 10.18410/jebmh/2017/769

BACKGROUND

Neurocutaneous disorders are genetically determined disorders showing both cutaneous and neurologic involvement. Either they follow the established Mendelian modes of inheritance or they represent lethal mutations surviving by mosaicism or they belong to the group of chromosomal disorders. Genetic classification will confirm the well-established differences between autosomal dominant, autosomal recessive and X-linked gene expression.[1]

Financial or Other, Competing Interest: None.
Submission 31-07-2017, Peer Review 02-08-2017,
Acceptance 07-08-2017, Published 09-08-2017.
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DOI: 10.18410/jebmh/2017/769

The neurocutaneous disorders noted are Neurofibromatosis (NF), Tuberous Sclerosis Complex (TSC), Xeroderma Pigmentosum (XP), Waardenburg syndrome, Naevus comedonicus, epidermal naevus syndrome, giant congenital melanocytic naevus, Sturge-Weber syndrome, Elejalde syndrome, oculocutaneous albinism and Adams-Oliver syndrome.

The two main forms of NF are type-1 NF (85%) and type-2 NF (10%).[2] NF-1 (Von-Recklinghausen disease) is an inherited neuroectodermal disorder characterised by the presence of six or more Cafe-au-lait macules, freckling in axillary and inguinal regions, multiple neurofibromas and ocular abnormalities (Lisch nodules and optic gliomas). It is also associated with neurological manifestations,[3] skeletal abnormalities,[4] oral lesions, endocrine abnormalities, renal, pulmonary and gastrointestinal manifestations.

TSC is an autosomal dominant disease characterised by systemic haematomas involving mostly the skin, nervous system, heart, eyes and kidneys. The cutaneous features of

TSC include facial angiofibromas, ash-leaf macules,[5] Shagreen patch[6] and periungual fibromas (Koenen's tumour).

Xeroderma pigmentosum is a rare autosomal recessive disease characterised by photosensitivity, pigmentary changes, premature skin ageing, neoplasia and abnormal DNA repair. Waardenburg syndrome is an autosomal dominant neural crest disorder, phenotypically characterised by hearing impairment and disturbance in pigmentation. It has a variable penetrance of its constituent anomalies.[7]

Naevus comedonicus is an uncommon developmental defect of the pilosebaceous apparatus associated with various developmental abnormalities of the skeletal system, the CNS, skin and eye. The epidermal naevus syndrome is a disease complex of epidermal nevi and developmental abnormalities of different organ systems like skeletal, CNS, ocular, dental and cardiovascular system.

Giant congenital melanocytic naevus is a neurocutaneous melanosis defined by the presence of neurologic symptoms and increased number of melanocytes in CNS combined with the presence of large cutaneous naevus.

Sturge-Weber syndrome is a rare, sporadic, neurocutaneous disorder consisting of facial capillary vascular malformations or port wine stain in a trigeminal nerve distribution in association with ipsilateral neurologic and ocular abnormalities.

Elejalde syndrome is a neuroectodermal melanolysosomal disease[8] characterised by bronze skin, silvery hair, severe CNS dysfunction, mental retardation, severe hypotonia and seizures. Oculocutaneous albinism is an autosomal recessive disorder characterised by partial or complete failure to produce melanin in the skin and eyes.

The Adams-Oliver syndrome is an autosomal dominant disorder characterised by congenital midline scalp defects and asymmetrical distal limb reduction anomalies. The skin lesions include solitary or multiple bald scara near the vertex.

Objectives

1. To study the incidence of neurocutaneous disorders in the outpatients attending the Department of Dermatology in Government KAPV Medical College, Trichy, from January 2016 to December 2016.
2. To determine the age and sex wise distribution of neurocutaneous disorders.
3. To study the clinical morphology and distribution of lesions.
4. To evaluate the incidence of associated systemic abnormalities.

MATERIALS AND METHODS

This study was conducted at the Department of Dermatology, Government KAPV Medical College, Trichy, for a period of 12 months from January 2016 to December 2016. Patients were selected among those attending the outpatient department with signs and symptoms pertaining to neurocutaneous syndromes.

Preliminary information like age, sex, educational qualification, present and past illness, family history elicited. Dermatological examination consisted of thorough screening of patients to detect the cutaneous markers for neurocutaneous disorders. A detailed systemic examination was done, particularly central nervous system. Apart from routine investigations, all relevant investigations were carried out to find the systemic abnormalities.

Inclusion Criteria

1. Age - All ages.
2. Sex - Both males and females.
3. Patients with signs and syndromes pertaining to neurocutaneous syndromes.

Exclusion Criteria

1. Patients with HIV infection.
2. Drug-related cutaneous manifestations.
3. Moribund and noncompliant patients.

RESULTS

Out of the 75 cases of NF, 68 cases (90.6%) were of type-1, 4 cases (53.3%) were of type-V, 2 cases (2.6%) were type-VI and 1 case of type-II (1.3%). The age group of patients with neurofibroma ranged from 6 to 60 years with the mean age of 33 years.

Age	Number of Cases	Male	Female
0-10 yrs.	3	2	1
11-20 yrs.	23	14	12
21-30 yrs.	22	9	10
31-40 yrs.	14	9	5
41-50 yrs.	7	6	1
51-60 yrs.	6	2	4
Total	**75**	**42**	**33**

Table 1. The Age and Sex Distribution Among Patients with NF

There was history of consanguinity in 14 cases (18.6%).

Sl. No.	Systemic Manifestation	Number of Patients Percentage
1.	**Bony Abnormalities**	
	• Kyphoscoliosis	6 (8%)
	• Facial asymmetry	2 (2.6%)
	• Local gigantism	2 (2.6%)
2.	**CNS Manifestations**	
	• Delayed milestones	2 (2.6%)
	• Learning difficulty	3 (4%)
	• Mental retardation	2 (2.6%)
	• Seizures	4 (5.3%)
3.	**Ophthalmic Manifestations**	
	• Lisch nodules	61 (81.3%)

Table 2. Systemic Manifestations Observed in Patients with NF

Mollusca fibrosa was seen in 65 patients (86.6%). Plexiform NF was observed in 9 patients (12%). Cafe-au-lait macules occurred in 73 patients (97.3%) and freckling in 86.6% of cases.

Age	Number of Cases	Male	Female
0-10 years	3	1	2
11-20 years	8	3	5
21-30 years	5	3	2
31-40 years	2	1	1
41-50 years	2	-	2
Total	**20**	**8**	**12**

Table 3. The Age and Sex Distribution in TSC

The total number of cases diagnosed to have tuberous sclerosis was 20 (18.3%). The age of these patients ranged from 4 to 42 years. The mean age being 22 years. Seizures was noted in 14 cases (70%) and angiofibromas in 20 cases (100%). A positive family history was observed in 6 patients.

3 cases (2.7%) had XP, 1 patient (0.9%) had Sturge-Weber syndrome, 1 had (0.9%) naevus comedonicus, 2 patients (1.8%) had Waardenburg syndrome, 2 had (1.8%) epidermal naevus syndrome, 2 had (1.8%) giant congenital melanocytic naevus, 1 male child (10 months) had (0.9%) Elejalde syndrome, 1 had (0.9%) oculocutaneous albinism and 1 had (0.9%) Adams-Oliver syndrome.

DISCUSSION

Among the NF, NF1 was by far the most common and accounts for 96.6% in this study, which is consistent with the study reported by Husan SM et al,[9] which showed a 90% incidence. The frequent age group affected was 10-20 years, which is in par with the literature.[10] There is a male preponderance (56%) in this study as opposed to the studies of Jennifer R. Kam et al, which indicates equal sex incidence. The most common clinical sign being CALM (97.3%) followed by mollusca fibrosa (86.6%). Axillary freckling occurred in 72% of cases, which is consistent with 70% as studied by Crowe FW et al.[11] Lisch nodules is seen in 81.3% in contrast to 94-97% of patients in the literature by Flueler et al.[12]

TSC (18.3%) is the second most common neurocutaneous disorder in this study. The common age group was 10-20 years with a mean age of 16 years, which is consistent with literature.[13] Family history was positive in 30%, which is in par with the literature.[14] The commonest cutaneous manifestation is angiofibroma, which is consistent with the literature.[15] Shagreen patch was observed in 75% as opposed to 50% in one study.[16] Subependymal nodules were seen in 25% of cases as opposed to 50% incidence in one study.[17]

2.7% of patients had XP. Male preponderance was noted in contrast to equal sex incidence as per the study of Neel JV et al.[18] The multiple malignant presentation is in accordance with the study of Mohanty P et al.[19]

0.9% of patients were identified to have Sturge-Weber syndrome, naevus comedonicus, Elejalde syndrome, oculocutaneous albinism and Adams-Oliver syndrome. 1.8% of patients had Waardenburg syndrome, epidermal Naevus syndrome and giant congenital melanocytic naevus.

CONCLUSION

In this study of 109 cases of neurocutaneous syndromes, NF topped the list followed by TSC. NF 1 accounted for the maximum number of NF. The most common clinical sign in NF was CALM followed by mollusca fibrosa. TSC is the second most common neurocutaneous disorder. Angiofibroma was observed in 100% cases followed by ash-leaf macules (85%). Classical features of XP were observed in a patient who also had cutaneous malignancies. Sturge-Weber syndrome with unilateral port wine stain with seizures was reported in our study. One case of unilateral naevus comedonicus, Elejalde syndrome, oculocutaneous albinism and Adams-Oliver syndrome were noted. 2 cases of Waardenburg syndrome, epidermal naevus syndrome and giant congenital melanocytic naevus were reported.

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