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ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2018, 7(5): 128-135

Clinical Presentations and Pattern of Neurocutaneous Syndromes Among Sudanese Children Attending Outpatient Clinic of Soba University Hospital, 2015

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ABSTRACT

Background: *The neurocutaneous syndromes are a group of diseases where characteristic skin lesions are seen in association with abnormalities of the central nervous system, and by consequence are at risk of developing epilepsy and other comorbidities.* ***Objectives:*** *The objective of this study is to study clinical presentations and diagnoses among Sudanese children with neurocutaneous syndrome, attending outpatient clinic of Soba University Hospital, 2015.* ***Patients and Methods:*** *This is a cross-sectional hospital-based study. Fifty children with neurocutaneous syndrome were included in the study aged between 6 months to 15 years attending the hospital from April 2014 to April 2015. The data was collected by designed data collection sheet and detailed skin examination was done and reviewed by dermatologist.* ***Results:*** *The mean age of the whole study group was 4.45 ± 1.96 years. Most of study group were in the age group between 1-5 years constituting 36% of total population of the study. Thirty-seven patients (74%) were males and 13 (26%) patients were females. About 24% of patients presented complained of skin lesions from total patients, the most common skin lesion is ash leaves.* ***Conclusion:*** *Neurocutaneous syndromes had multiple clinical presentations. Most of the patients with neurocutaneous disorders had convulsions, which was commonest presentation for those children; generalized convulsion was the commonest among the studied group. Tuberous sclerosis was the most frequent type of the neurocutaneous disorders in our patient clinic. Dermatological examination is important, for early detection of neurocutaneous disorders.*

Keywords: Neurocutaneous syndromes, Sudanese, Skin lesion, Tuberous sclerosis, Subependymal tubers

INTRODUCTION

The neurocutaneous syndromes are a group of diseases where characteristic skin lesions are seen in association with abnormalities of the central nervous system, and eventually are at risk of developing epilepsy. Although the features of some disorders have included abnormalities of the cerebrum within diagnostic criteria, advances in imaging and genetics have further delineated some of the rarer forms and outlined associations with malformations of cerebral development. This has major implications for management as it is apparent that many, if drug resistant epilepsy is a feature, may be suitable for surgery [1,2].

The most common skin lesions are: Hypopigmented maculae, also known as ash-leaf spots, which are usually elliptic in shape most common found in tuberous sclerosis, angiofibromas (sometimes called fibro adenomas; previously called adenoma sebaceous) which typically involve the malar regions of the face, Shagreen patches, seen most commonly over the lower trunk, distinctive brown fibrous plaque on the forehead, which may be the first and most

readily recognized feature of TSC to be appreciated on physical examination of affected neonates and infants, café au lait spots which are depigmented skin lesions found in neurofibromatosis and tuberous sclerosis and whorls and streaks also present in hypomelanosis of Ito [3,4].

The characteristic cardiac feature of TSC (tuberous sclerosis complex) is a rhabdomyomas, a benign tumor that often presents as multiple lesions; cardiac rhabdomyomas are one of the most common pediatric cardiac tumors [5].

Most infants and children who have cardiac rhabdomyomas also have TSC. However, rhabdomyomas are not a universal finding in children with TSC found in 31% of children with tuberous sclerosis [5].

The neurocutaneous syndromes associated with considerable mortality and morbidity includes uncontrolled epilepsy, cerebrovascular event, learning and behavioral difficulties, brain malformations with greater impact on family and clinician.

No specific treatment is defined for neurocutaneous syndrome. Management includes genetics counseling and early identification of treatable conditions or complications, electrophysiological test, and brain imaging of no values in asymptomatic patients. Many studies recommend such investigations in all symptomatic patients such as visual loss or disturbance, proptosis, symptoms, and signs of increased intracranial pressure [6-9].

Sudan is a country with high consanguinity rate which may increase the incidence of such syndromes among the population.

The objective of this study is to demonstrate clinical presentation and pattern of neurocutaneous syndromes among Sudanese children with neurocutaneous syndrome, attending outpatient clinic of Soba University Hospital, 2015.

PATIENTS AND METHODS

Study Design

Descriptive cross-sectional, observational hospital-based study.

Study Area

This study was conducted at Pediatric Neurology Outpatient Clinic, Soba University Hospital. The number of patients seen per clinic was around about 50-60 patients. Soba University Hospital is a reference hospital for all pediatric neurological cases from entire country.

Study Period

The study was conducted from April 2014 to April 2015.

Study Population

This study included 50 patients whose age ranged between 6 months to 15 years attending the Pediatric Neurology Outpatient Clinic at Soba University Hospital and diagnosed with neurocutaneous syndrome.

Inclusion Criteria

All children from 6 months to 15 years old who fulfilled the criteria for diagnosis of specific neurocutaneous syndromes were eligible for this study. The subjects whose guardians agreed to participate in the study were included in the study.

Exclusion Criteria

- Age more than 15 years.
- Parents/caregiver refused to participate in this study.

Data Collection Tools

Check sheet prepared beforehand for this study was used for data collection which included personal information, Sociodemographic data, details presenting complains, detailed skin examination including Wood lamp examination, electroencephalography (EEG) features, magnetic resonance imaging (MRI) findings were recorded.

Sample Size

Total 50 patients were included.

Methods

All studied patients were subjected to thorough clinical history including detailed history of the presenting symptoms like seizures and developmental history. Autistic symptoms, hyperactivity symptoms, and family history of similar conditions such as presence of epilepsy, mental retardation or global developmental delay were also clarified. Full clinical examination (general, systematic, and detailed neurological examinations), dermatological examination was done. MRI and/or computed tomography of the brain were reviewed by radiologists. EEG was done for the patients with convulsions.

Ethical Considerations

Informed consent was obtained from all parents or caregivers included in this study. Written approval was obtained from hospital administration. Ethical clearance was obtained from research committee in Sudan Medical Specialization Board (SMSB).

Data Management and Statistical Analysis

The collected data was analyzed using the Statistical Package for Social Science (SPSS) version 16. The data for numerical values was expressed in (Mean ± SD). A value of $P \leq 0.05$ was considered statistically significant.

RESULTS

Descriptive Data of the Studied Patients

Age and Sex

The mean age of the study group was 4.45 ± 1.96 years. The age ranged between 6 months and 15 years. The majority of study group were in the age group between 1-5 years constituting 36% of total population of the study. The least age range were between 10-15 years with 8 patients constituting 16% of the total. Thirty-seven patients (74%) were males and 13 (26%) patients were females. Male to female ratio 3:1 (Table 1 and Figure 1).

Table 1 Age distribution among study population

Age group in years	No. of patients	Percentage
6 month - 1 year	13	26
1-5 years	18	36
6-10 years	11	22
11-15 years	8	16
Total	50	100

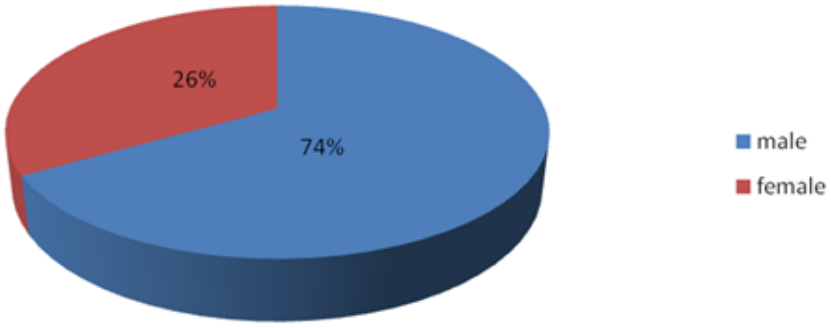

Figure 1 Sex distribution among study group

Presenting Complains among Study Group

The main presenting complain was convulsions which was detected in 26 children (52%). Skin lesions was the presenting complain in 12 cases (24%), abnormal conjunctivae were detected in 5 children (10%) and delayed development and abnormal head size were presenting complaint in 8%, and 4% respectively. One patient with tuberous sclerosis presented with headache at age 12 years (2%) (Figure 2).

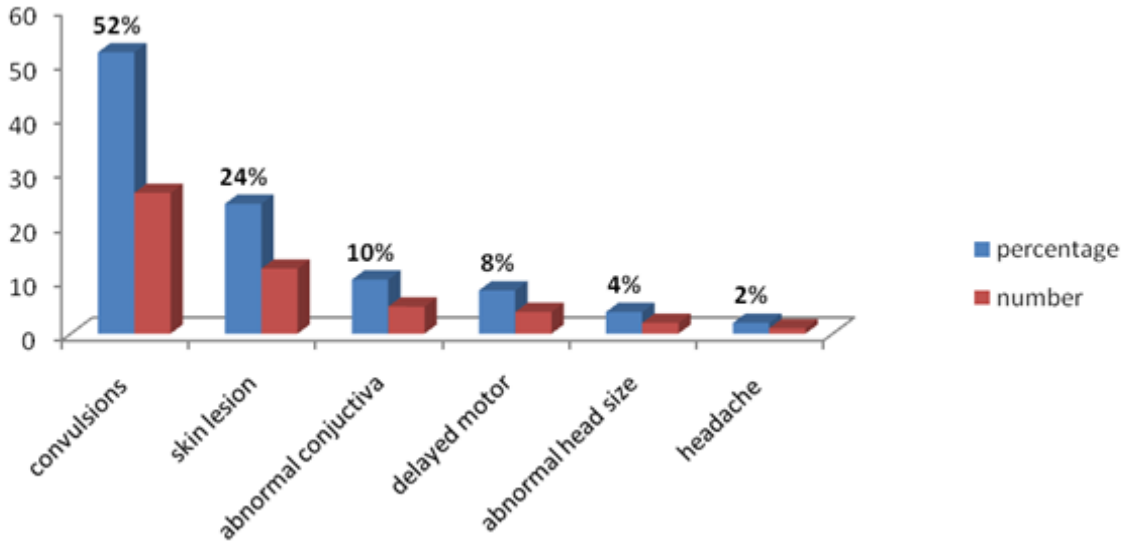

Figure 2 Frequency of the presenting complains among study population (n=50)

Convulsions

Convulsions were the presenting complains in 21 (80%) with children tuberous sclerosis. No convulsions were reported in ataxia telangiectasia cases and neurofibromatosis. Around 44% children with convulsions experienced their first episode at age ranging from 6 months to 1 year. Generalized convulsions were the most common type reported in two third of patients (65.4%). Focal convulsions were found in (23.1%) and focal with a secondary generalization was the seizure type in 3 patients (11.5%). Among the generalized seizures, myoclonic seizures namely infantile spasm was the commonest type and it was reported in 17 (65%) patients. All of them were children with tuberous sclerosis. Focal convulsions were diagnosed in all patients with Sturge-Weber syndrome and four patients with focal convulsion were diagnosed with tuberous sclerosis and two patients with hypomelanosis of Ito (Table 2, Figures 3 and 4).

Table 2 Percentage of Convulsions among Specific Neurocutaneous

Syndromes	Convulsions among study group		
	Yes	No	Total
Neurofibromatosis	0	10	10
Tuberous Sclerosis	21	1	22
Sturge -Weber Syndrome	3	0	3
Hypomelanosis of Ito	2	4	6
Ataxia telangiectasia	0	9	9
Total	26	24	50

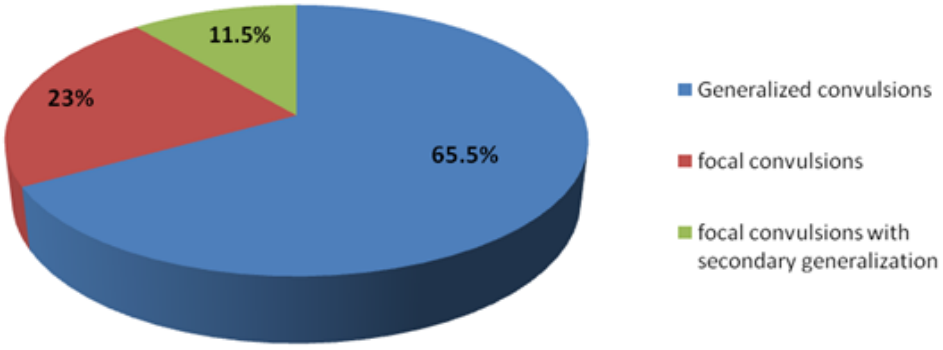

Figure 3 Percentage of the convulsions among study group

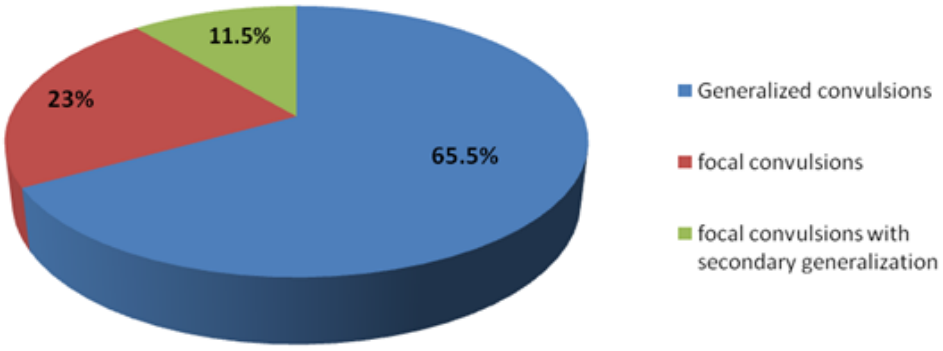

Figure 4 Distribution of the types of convulsion among study group

Skin Manifestations among Studied Group

About 24% of patients presented complained of skin lesions from total patients, ash leaf-shaped white macules were found in 15 patients. Seven children had café au lait spots, 5 patients with neurofibromatosis and two patients with tuberous sclerosis. Shagreen patches were found in 9 patients, facial angiomatosis in 7 patients, whorls, and streak in 6 patients, port wine stain ophthalmic in three patients, plexiform neuroma in one patient with neurofibromatosis type 1. The main of the skin lesions in tuberous sclerosis was ash leaf-shaped white macules found in 15 patients constituting 30%, Shagreen patch in 9 patients, and facial angiomatosis in 7 patients (Table 3).

Table 3 Skin lesions findings of fifty patients of the studied group (n=50)

Skin lesions	Number	Percentages
Hypo pigmented patches, ash leaf-shaped white macules	15	30
shagreen patches	9	18
Adenoma sebaceous	7	14
café au alit patches	7	14
Whorls and streaks	6	12
Birth mark-port wine stain	3	6
Neurofibroma	3	6
Total	50	100

Syndromic Diagnosis

Tuberous sclerosis was the diagnosis in 22 patients (44%) of study group. The next common was neurofibromatosis type 1 which was diagnosed in 10 patients, representing (20%) of the study population. Ataxia telangiectasia and hypomelanosis of Ito was found in 18% and 12% respectively, Sturge-Weber syndrome percentage was the least and it represented 6%. Regarding the distribution of the different diagnoses according to sex, there was clear male predominance in all syndromes, but this correlation was not statistically insignificant (Table 4 and Figure 5).

Table 4 shows sex distribution among different study population (n=50)

Syndromes	Sex		
	Male	Female	Total
Neurofibromatosis	7	3	10
Tuberous sclerosis	16	6	22
Sturge Weber syndrome	2	1	3
Hypomelanosis of Ito	5	1	6
Ataxia telangiectasia	7	2	9
Total	37	13	50
P=0.08 insignificant			

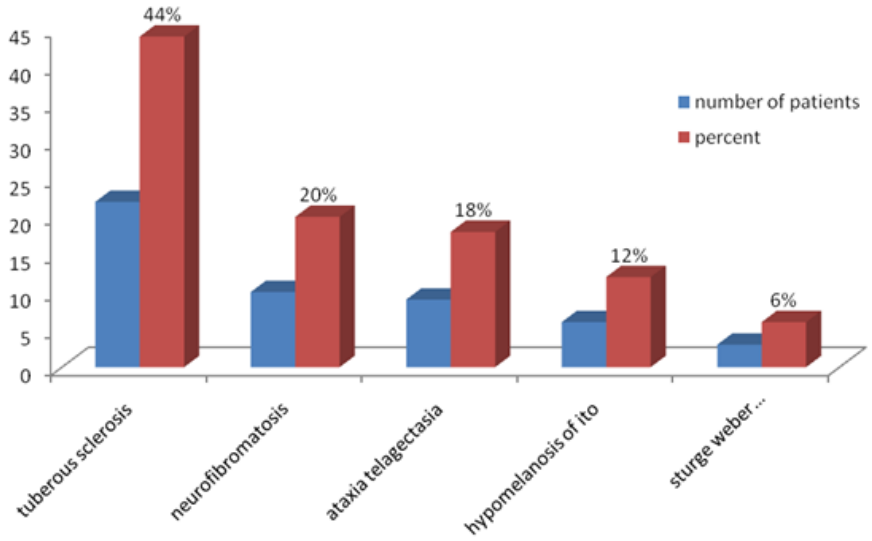

Figure 5 Distribution of the neurocutaneous syndrome among study group

DISCUSSION

Neurocutaneous syndromes include a heterogeneous group of disorders characterized by abnormalities of both the skin and central nervous system. While some can be diagnosed at birth, others do not produce symptoms until later in life. Although neurocutaneous syndromes cannot be cured, treatment can help to manage symptoms and health problems that occur [3,4,7,10-13].

The mean age was 4.45 ± 1.96 years which was nearly similar to other studies [14-16]. The mean age was lower than results of Smirniotopoulos study, where mean age was 10 ± 1.45 years as their study included a wide range of age group [17].

In the present study, the most common presenting complain was convulsions in 52% of the studied children. This result was in agreement with the results obtained by other researchers who found convulsions in 56% in their studies [14,15]. In study done by Kalinina, she found skin manifestations e.g. ash leaf-shaped white macules and café au lait spots were the commonest presentation in 45% [18-22]. These variations between studies with regard to initial presentations could be related to severity of clinical presentations as we proposed patients with skin manifestation seek medical advice later than neurological symptoms. In this study, we found no convulsions in neurofibromatosis and this was similar to study done by Dahan [23]. The age of onset of the first convulsions was from 6 months to 12 years and this was similar to the other study [24].

According to our study, convulsions, in most cases of neurocutaneous syndrome were generalized seizures (65%) and the results were similar to the other studies with regard to the types of convulsions [25] with variation in percentage among different studies, this variation may be due number of study population in the study.

The result disagrees with other studies, where the commonest type of convulsions was complex partial types [24]. The difference in types of seizures may be attributed to severity of brain involvement or other factors which act independent, and to the age group of the study which was younger ages.

In tuberous sclerosis, all children were complaining of convulsions which were generalized in 66.7% and focal 33.4% in majority of cases of tuberous sclerosis, convulsions started in early years of life and this agrees with the other studies [26-29].

In our results, we observed that the majority of patients with melanosis of Ito developed generalized convulsions which is in agreement with results obtained by Smirniotopoulos [17]. Nearly all three cases of Sturge-Weber syndrome in our study had convulsions difficult to control. In majority of patients, there was hemiplegia which was similar to the reports of Abdelrahman, et al. who reported convulsions in lower rate in 60%, and difference may be attributed to sample size [15].

Authors have observed that no convulsions among patients with neurofibromatosis type 1 in studied group; similar finding was obtained by other [14,15].

CONCLUSION

Neurocutaneous syndromes had multiple clinical presentations, the majority of the patients with neurocutaneous disorders had convulsions, which was commonest presentations for those children; generalized convulsions were the commonest among the studied group. Tuberous sclerosis was the most frequent type of the neurocutaneous disorders in our patient clinic. Dermatological examination is important, for early detection of neurocutaneous disorders. Skin manifestations, hypopigmented skin patches (ash leaf-shaped white macules) was the commonest lesion and help in early diagnosis.

Recommendations

Skin examination is important for early detection and diagnosis of various neurocutaneous syndromes. Skin examination of other family members is essential part of evaluation of child with neurocutaneous syndromes.

DECLARATIONS

Conflict of Interest

Authors have disclosed no potential conflicts of interest, financial or otherwise.

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