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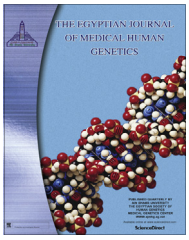

ORIGINAL ARTICLE

Multidisciplinary approach for evaluation of neurocutaneous disorders in children in Sohag University Hospital, Upper Egypt

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Abstract *Background:* Neurocutaneous syndromes (NCS) are a broad term for a group of neurologic disorders that involve the nervous system and the skin. The most common examples are neurofibromatosis type 1 (NF-1) and type 2 (NF-2), tuberous sclerosis (TS), Sturge–Weber syndrome (SWS), ataxia telangiectasia (AT), and Von Hippel Lindau disease (VHL). These disorders are characterized clinically by neurological manifestations such as convulsions, mental retardation and learning disabilities in addition to cutaneous manifestations, and lastly tubers (benign growths found in different organs of the body).

Aim of the study: This study aimed to identify clinical, imaging, and neurophysiological profiles of neurocutaneous disorders. Children presented to the Pediatric neurology and Dermatology clinics, Sohag University Hospital who fulfilled the criteria for diagnosis of specific neurocutaneous syndromes were eligible for this study.

Patients and methods: All studied patients were subjected to thorough clinical history, full clinical examination, developmental assessment, and dermatological examination. Computed tomography of the brain (CT) and electroencephalography (EEG), ophthalmic, and phoniatric evaluation were also done for all children. Echocardiography was done for only twenty children.

Results: During the period of the study we diagnosed 27 cases with neurocutaneous disorders, tuberous sclerosis represented the majority of cases as it was detected in 12 cases (44.45%). The main complaint was convulsions in 19 cases (70.37%), whereas skin pigmentation was detected in 18 cases (66.66%). Developmental assessment showed that global developmental delay was found in 20 cases (74%). CT of the brain showed that 15 cases (55.55%) had intracranial calcifications and abnormal EEG findings were detected in 23 cases (85.2%). 85% of the studied children had various degrees of mental retardation. Echocardiography showed that three cases (15%) had ventricular wall tumor mostly rhabdomyoma.

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Conclusion: Neurocutaneous disorders had multiple clinical presentations and required a team work approach including various specialties in their evaluation and management.

1. Introduction

Neurocutaneous syndromes are a broad term for a group of neurologic disorders that involve the nervous system and the skin. These syndromes are due to defects in differentiation of the primitive ectoderm and usually life-long conditions that can predispose to malignancies. The most common examples are neurofibromatosis type 1 (NF-1) and neurofibromatosis type 2 (NF-2), tuberous sclerosis (TS), Sturge–Weber syndrome (SWS), ataxia telangiectasia (AT), and Von Hippel Lindau disease (VHL) [1]. Neurocutaneous disorders are relatively common and could be seen in different societies with different incidences for example, NF-1 affects one in every 4000 births while NF-2 affects one in every 60,000 births in the United Kingdom [2] while in other countries NF-1 has a birth incidence of 1 in 2500 to 1 in 3000 [3,4]. Tuberous sclerosis affects one every 6000–9000 births and nearly one million people worldwide are known to have tuberous sclerosis [5]. Sturge–Weber syndrome, ataxia telangiectasia and the Von Hippel Lindau disease are rare disorders.

These disorders are characterized clinically by neurological manifestations as convulsions, mental retardation and learning disabilities [6], in addition to cutaneous manifestations including café au lait patches, port-wine stain (facial birth mark covering one upper eyelid and forehead), telangiectasia (tiny red spider-like blood vessels), and tubers (benign growths found on different organs as brain, eyes, heart, skin, kidneys and lungs) [6,7]. These manifestations are present in various combinations according to the type of syndrome allowing clinical diagnosis in most of the cases.

Clinical features required for diagnosis of NF-1 are; (1) one to six or more café-au-lait spots over 5 mm in greatest diameter in pre-pubertal individuals and over 15 mm in greatest diameter in post-pubertal individuals, (2) two or more neurofibromas of any type or one plexiform neurofibroma, (3) Freckling in the axillary or inguinal regions, (4) optic glioma, (5) two or more lisch nodules (iris hamartomas), (6) osseous lesions such as sphenoid dysplasia or thinning of the long bone cortex with or without pseudoarthrosis, (7) first degree relative affection (-parent, sibling, or offspring) with NF-1 by the above criteria with discovered mutations of the NF-1 gene, which is located at chromosome 17q11.2. Two of these seven "cardinal clinical features" are required for positive diagnosis [8].

Clinical diagnostic criteria for TS include 11 major features and six minor features. Major features include: hypomelanotic macules ($\geqslant 3$, at least five-mm diameter), angiofibromas ($\geqslant 3$), ungual fibromas ($\geqslant 2$), shagreen patch, multiple retinal hamartomas, cortical dysplasias (includes tubers and cerebral white matter radial migration lines), subependymal nodules, subependymal giant cell astrocytoma, cardiac rhabdomyoma, lymphangioleiomyomatosis (LAM), and angiomyolipomas ($\geqslant 2$). Minor features include; "confetti" skin lesions, dental enamel pits (> 3), intraoral fibromas ($\geqslant 2$), retinal achromic patch, multiple renal cysts, and nonrenal hamartomas. Definite diagnosis should include two major features or one major feature with $\geqslant$ two minor features and possible diagnosis: either one major feature or $\geqslant$ two minor features [9].

Sturge–Weber syndrome (SWS) is a congenital non inherited neurocutaneous disorder. It is characterized by cutaneous manifestations, neurological abnormalities, and eye affection [10]. Xeroderma pigmentosum (XP) is a rare, autosomal recessive disorder. There is an impairment of skin ability to repair damage from ultraviolet light, leading to early skin changes, and eye damage [11].

Early diagnosis of these disorders is very important as it allows early treatment, proper follow up and genetic counseling. This requires the integrated work of pediatricians, dermatologists, ophthalmologists and other specialties to make appropriate diagnosis and management strategy. To the best of our knowledge a few studies were done in Upper Egypt to clarify this topic so our aim was to identify clinical, imaging, and neurophysiological profiles of neurocutaneous disorders in Sohag, Upper Egypt.

2. Patients and methods

2.1. Study design

This is an observational hospital based study, done in the Pediatric neurology and Dermatology clinics at the Sohag University Hospital, Upper Egypt, during the period from December 2012 through November 2013. All children from birth up to 15 years old who fulfilled the criteria for diagnosis of specific neurocutaneous syndromes were eligible for this study. Informed consent of the parents of the children was taken to conduct this research in addition to the approval of the Faculty of Medicine, Sohag University Ethics committee. The work has been carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) for experiments on humans.

2.2. 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 a 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), developmental assessment, and dermatological examination were done. Computed tomography of the brain (CT) and electroencephalography (EEG) were done for all patients. Echocardiography was done for only 20 children. All patients were referred to the Phoniatric Unit and were subjected to language evaluation as well as assessment of passive and active vocabulary. Also evaluation of the autistic