Dermatological manifestations of epilepsy among adult Sudanese epileptic patients

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Epilepsy is a relatively common condition characterized by a tendency to have recurrent seizures, it is due to a disturbance of the spread of electrical discharge of the cortical neurons. The normal individual spread of electrical discharge between cortical neurons is very slow, however, in epilepsy there is a disturbance of this mechanism resulting in hyper synchronous discharge. Epilepsy is either idiopathic when there is no underlying cause, or secondary if there is an underlying cause.

Skin manifestations associated with epilepsy can be due to drug toxicity, or can be part of the manifestations of the diseases that can cause secondary epilepsy, for example, neurofibromatoma.

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Objectives: To study the pattern of dermatological changes associated with epilepsy among adult Sudanese epileptic patients.

Methods: This non-interventional descriptive study included 360 adult Sudanese epileptic patients and was conducted at the El Shaab Teaching Hospital, Khartoum, Sudan, from February 2004 to August 2007. All patients had full detailed history and clinical examination. A dermatologist assessed the dermatological changes. Investigations carried out included EEG, CT brain, and serial of drug serum levels.

Results: Out of 360 patients, 31 were found to have scars due to repeated attacks of convulsions, one patient was found to have neurofibromatoma, one had tuberous-sclerosis, one had Sturge-Weber syndrome, one had Kaposi sarcoma, one had systemic lupus erythematosus, one diabetic patient had skin atrophy, one patient taking phenobarbitone had skin eruption, one patient on carbamazepine had skin changes, while 5 patients on phenytoin had skin manifestations.

Conclusion: Skin changes can occur in epileptic patients as part of drug toxicity, or as part of the clinical manifestations of certain diseases that can cause secondary epilepsy, for example, neurofibroma.
Dermatological manifestations of epilepsy … Mohmad et al

neurofibromatosis (NF), tuberous sclerosis (TS), Sturge-Weber syndrome (SWS), systemic lupus erythematosus (SLE), and Kaposi sarcoma. In this study, we aimed to present the pattern of dermatological changes associated with epilepsy among adult Sudanese epileptic patients. These include the dermatological findings related to the toxicity of antiepileptic drugs (AEDs), neuroectodermal manifestation of some phacomatosis (NF and TS), skin scars due to repeated falls, and other rare causes.

**Methods.** This is a descriptive cross-sectional hospital-based study. It was conducted at El Shaab Teaching Hospital, Khartoum, Sudan, which is a 240-bedded hospital. There are 2 neurological units with 42 beds, and an intensive care unit. The study population included 360 epileptic patients referred to the hospital from February 2004 to August 2007. All were newly diagnosed and not on treatment. At first, 375 patients were included in the study, however, 15 patients were excluded due to difficulty of follow up. The remaining patients were followed until the end of the study period.

**Inclusion criteria.** All the patients were Sudanese, and aged 18 years or more.

**Exclusion criteria.** Non-Sudanese patients below 18 years of age.

All patients gave their verbal consent to participate, and the study was approved by the ethics committee. A full detailed history was taken from each patient, and a systemic and neurological examination was performed. The history included antecedent symptoms, for example, fever, trauma, skin rash, and family history of epilepsy. The presenting symptoms included history of convulsions, headache, and loss of consciousness. The physical signs were grouped into general, systemic, and neurological. A dermatologist confirmed the skin changes. The following investigations were carried out for each patient: random blood sugar, total blood count, liver function test, blood urea, serum sodium, serum calcium, serum magnesium, chest x-ray, and ECG. All patients had a CT of the brain and EEG. A neurophysiologist carried out the diagnosis of the EEG. Blood samples to determine plasma concentrations of antiepileptic drugs were obtained 6 weeks after starting the treatment, a second sample was taken after 6 months, and a third after one year. Stress was placed on the following at regular monthly follow up: 1. Whether the patients were taking medication regularly or not. 2. Whether they experienced an attack of convulsion. 3. History of symptoms of drugs intoxication, proper examination looking for signs of drugs toxicity.

**Data collection.** Data were collected by a self-administered questionnaire composed of personal data, full detailed history, and examination.

**Data analysis.** All collected data were finally entered into a computer using the Statistical Package for Social Sciences to analyze the data using simple descriptive statistics.

**Results.** Out of 360 patients, 195 were male (54.15%) and 165 patients were female (45.85%). The patient age distribution ranged between 18 and 80 years. In 242 patients (67%) no cause was identified. Fifteen patients (4%) had a history of trauma, also 15 patients (4%) had brain tumors, 21 patients (6%) had a history of infection, such as meningitis and encephalitis, 36 patients (10%) had cerebrovascular accident, 27 (7.5%) had infarction, and 9 (2.5%) patients had hemorrhage, 15 patients (4%) had a history of alcohol consumption, 9 patients (2.5%) had a degenerative disease of the brain, while 9 patients (2.5%) had mental retardation. Out of 360 epileptic patients, 72 patients (20%) had a family history of epilepsy. Generalized epilepsy was found in 309 (86%), while 51 patients (14%) had focal epilepsy. Out of 360 epileptic patients, 31 had scars due to repeated falls. Twenty patients had café au lait, while only one was found to have neurofibroma with axillary flickering and plexiform NF, and another patient had TS with Shagreen patches, hypopigmentation, sublingual hyperkeratosis, and adenoma sebaceous. Port wine spot was detected in one patient with SWS. Out of 3 diabetic patients, an area of skin hypertrophy and atrophy was detected in one patient. Kaposi sarcoma was observed in one patient with AIDS. An elderly man with carcinoma of the stomach was found to have migratory thrombophlebitis. Butterfly rash, vasculitic lesions, and lupus pernio were seen in one patient with SLE. Out of 20 patients that took phenobarbitone, only one had maculopapular rash. Out of 70 patients that took phenytoin, 3 had course facial appearance, one had butterfly rash, and one patient developed Steven Johnson syndrome. Out of 80 patients that received carbamazepine, only one patient had skin rash, while none of the 30 patients that had taken lamotrigine had skin rash. Skin changes were not observed among those that had taken sodium valproate (160 patients).

**Discussion.** Epilepsy is a clinical syndrome characterized by increased electrical excitability of cortical neurons with or without loss of consciousness. It may be idiopathic or secondary. The chance of finding abnormal signs is increased among patients with secondary epilepsy, this includes skin manifestations. Skin manifestations associated with epilepsy can be part of manifestations of certain diseases, or a side effect of AED’s. An example is NF, which has a strong relationship with brain meningioma, and which can present with convulsions. There are certain skin lesions from epilepsy.
that can be seen in patients with NF, such as axillary flickering, plexiform NF, and café au lait. Café au lait also can be seen in TS. Epilepsy is the most common neurologic feature in TS, occurring in 92% of patients. Seizures often begin in the first year of life and are frequently severe and intractable. In our studied group, we found that many patients had insignificant café au lait (number less than 5 and size less than one centimeter). Other skin manifestations seen in TS include: Shagreen patches, hypopigmentation, sublingual hyperkeratosis, and adenoma sebaceus. Sturge-Weber syndrome has a well known recognized association with epilepsy. The malformations of the meningeal vessels can be blamed as the underlying cause of seizures. Kaposis sarcoma is one of the skin manifestations associated AIDS. Epilepsy in patients with AIDS can be due to associated CNS lymphoma, toxoplasmosis, or brain abscess. Migratory thrombophlebitis can be seen in gastrointestinal carcinomas, and epilepsy can occur with secondary deposits in the brain. Areas of skin hypertrophy and atrophy can be seen in patients with insulin dependent diabetes mellitus. Convulsions can be part of the clinical manifestations of hypoglycemia. Systemic lupus erythematosus is a disease characterized by multiple autoimmune phenomena, and a broad clinical spectrum. Convulsions or epilepsy can be part of the clinical manifestations of SLE. Skin manifestations associated with SLE, such as butterfly rash, vasculitis, lupus pernio can be seen in small number of epileptic patients. Skin changes in the form of ecchymosis, and purpuric rash can be seen in bleeding disorders, either hereditary or acquired, for example, leukemia, which can cause intracerebral hemorrhage, resulting in secondary epilepsy.

As we have seen in our patients, scars on different parts of the body due to repeated attacks of falling down were seen in uncontrolled epileptic patients, most of the scars were observed in the head followed by the trunk then upper and lower limbs. In a small number of patients, the scars were due to burns. Although it is very rare and it was not observed in our study, neurocysticercosis is one of the parasitic infections of the nervous system, it can cause epileptic attacks in most of the affected patients. Cysticercoids can present with skin manifestation, for example, calcification. Also skin manifestations can be a side effect of drugs such as phenytoin, which can cause course facial appearance, SLE like syndrome, Steven Johnson syndrome, eruptive bullae, and very rarely ecchisosis. Skin reactions are reported in 1-3% of patients receiving phenobarbitone, and are most commonly maculopapular, morbilliform, or scarlatiniform rashes. Severe reactions such as exfoliative dermatitis, erythema multiforme, and toxic epidermal necrolysis are extremely rare. Carbamazepine can cause skin sensitivity reactions and rashes, erythematosus rashes, urticaria, and very rare exfoliative dermatitis, erythroderma, Stevens-Johnson syndrome, and SLE-like syndrome can be seen. Skin rash has also been reported as part of a hypersensitivity syndrome following lamotrigine therapy, it is associated with a variable pattern of systemic symptoms including fever, lymphadenopathy, and facial edema. Serious rashes like Stevens-Johnson can occur with the use of lamotrigine especially with the use of concomitant valproic acid. Sodium valproate can cause transient hair loss and rashes.

The fact that serum levels of AEDs can be affected by more than one factor is a limitation of this study, for example, the use of drugs that have an antagonistic or synergistic effect with AEDs, genetic and environmental factors.

Skin changes can occur in epileptic patients as part of drug toxicity, or as part of clinical manifestations of certain diseases that can cause secondary epilepsy, for example, neurofibroma. Skin manifestations among epileptic patients in relation to other factors, such as, environmental, genetic, and nutritional, need to be elucidated by further studies.

References

Dermatological manifestations of epilepsy … Mohmad et al


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