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Tuberous Sclerosis Complex Co-Existing with Bilateral Cryptorchidism: A Case Report and Review of Literature.

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ABSTRACT:

Background: Tuberous sclerosis is a rare multisystemic, genetic neurocutaneous syndrome that causes benign tumours to grow in the brain and vital organs. It demonstrates high clinical and radiological manifestations.

AIM: To report a case of tuberous sclerosis complex co-existing with bilateral cryptorchidism in the University of Port-Harcourt Teaching hospital, Port Harcourt.

CASE REPORT: A case of 11year old male, a primary three pupil, who developed seizure disorder at the age of 7 months and subsequently developed facial angiofibroma and periungual fibroma at the age of 9years. Neuroimaging revealed multiple calcified subependymal harmatomas on the walls of the lateral ventricles and multiple subcortical and cortical tubers. The patient is currently on anticonvulsant and his seizures are controlled. He has moderate degree of mental retardation. The angiofibroma are not receding.

CONCLUSION: Tuberous sclerosis complex is an uncommon disease entity. Treatment is symptomatic. Prognosis varies in accordance with the severity of the specific symptoms. A regular imaging follow up is advised for patients with this condition to avoid development of obstructive hydrocephalus from the tumours.

INTRODUCTION

Tuberous sclerosis (TSC) is a rare multisystemic genetic disorder that causes benign tumours to grow in the brain and other vital organs such as the kidneys, heart, eyes, lungs, and skin. The name tuberous sclerosis comes from the characteristic tuber or potato- like nodules in the brain, which calcify with age and become hard and sclerotic.[1] The disorder was once known as epiloia or Bourneville's disease after the French physician Bourneville who first described it in 1880 at post-mortem in patients with epilepsy and mental retardation.[2] In 1908, Vogt reported the classical triad of tuberous sclerosis consisting of mental retardation, seizures and a facial skin eruption.[3] In 1920, Van der Hoever described the small retinal tumour which he called retinal phakomas and he noted that similar lesions do occur in the intestine, thyroid and bone.[4] Gunther and Penrose described the autosomal dominant pattern of inheritance of TSC in 1935.[5] The gene loci on chromosome 9 and 16 were discovered in 1987 and 1992 respectively.[6]

The true incidence of tuberous sclerosis is difficult because of the varying manifestation. Dawson (1954) estimated an incidence of 1 in 300,000 for England.[7] However, since testing method that permit the identification of less severe manifestations of TSC have been developed, estimates of the frequency of this disorder have risen sharply. In 1998 O'Callaghan et al in a population based studies indicated a prevalence of 8-9 per 100,000 individuals.[6]The tuberous sclerosis Alliance estimates that 50,000 Americans and 1 million individuals worldwide have TSC and that its incidence is approximately 1 in 6,000 live births.[8]

The first reported case in African child was published in 1967 by Agbessv and Vovor[9]. In Nigeria there has been very few publications, no such report has been published in University of Port Harcourt Teaching Hospital. We present a case of TS which was managed by the Paediatric neurology and

radiology units.

CASE REPORT:

A.D, an 11 year old male primary three pupil presented at the Paediatric unit, University of Port Harcourt, Nigeria on account of recurrent convulsion since age of 7months and a 4 year history of facial growth. Episodes of convulsions were generalised tonic, clonic in nature lasting for about 10minutes each time, associated with impairment of consciousness, involuntary micturation and usually followed by post ictal sleep. The frequency of convulsion was about 2-5 times per month. It was unprovoked and not related to febrile illness. Facial growth started when the child was 7years old as dark rashes on the face. Subsequently, the rashes grow bigger and concentrated on the nose and malar region of the face. The growth later spread to the neck and back of the trunk. A progressive enlargement of the distal aspect of the right index finger was also noticed.

Pregnancy, birth and neonatal periods were uneventful. His developmental milestones were attended within the recognized normal limits with exception of speech which was delayed until 4 years of age. His academic performance was poor. He is the older of two siblings; the younger one is 5months old. There is no family history of similar illness.

On examination at presentation, he was healthy looking, conscious, afebrile and anicteric. He had a firm, discrete, dark, papules on the nose and cheek, having a butterfly distribution; and also on the neck and upper trunk. He was inattentive and hyperactive. There was no significant lymphoadenopathy. There was also fusiform enlargement of the distal aspect of the right index finger which was firm, non tender and normotensive. The scrotum was small and devoid of testes. A clinical diagnosis of tuberous sclerosis with undescended testis (cryptorchidism) was made.

Ophthalmic examination revealed no significant finding. Laboratory data revealed a packed cell volume of 36%, total white cell count of $7.6x10^9/L$, Neutrophil of 56%, Lymphocytes 44% and erythrocyte sedimentation rate of 37 westergren. Urea, creatinine and electrolytes were all within normal limits.

Radiological features

Computed Tomography scan of the brain revealed multiple hyperdense nodules on the wall of both lateral ventricles. A larger hyper dense nodule was seen in the left parietal region of the cerebrum. There were also multiple non-enhancing hypodense areas of varying sizes with poorly defined margin in the right frontal and both parietal regions. The cerebellum and brain stem were normal. There was no hydrocephalus. A diagnosis of brain tuberous sclerosis was made. Abdominal ultrasound scan revealed normal intra- abdominal structures. There was no renal cyst or mass seen. Scrotal scan revealed empty scrotal sac, search for the testes was unfruitful. Chest X-r ay was normal. X-ray of the hands revealed a fusiform soft tissue mass around the distal interphalangeal joint of the right index finger. No bone abnormality was detected. Electroencephalogram (EEG) was not done because it is not available in our center.

Patient is being managed with anticonvulsant (carbamezepine) on outpatient, he is drug compliant and has good seizure control. He keeps his appointments and on regular follow up.

DISCUSSION

Tuberous sclerosis complex is a genetic disorder associated with mutation in two different genes.TSC1 on chromosome 9 and TSC2 on chromosome 19 cause benign tumor called hamartomas. Tuberous sclerosis may be inherited as autosomal dominant disorder. However most (about 60%) are sporadic and are due to new spontaneous mutations. The patient in this case has no family member with similar illness hence he belongs to the sporadic cases.

The classical features, epilepsy ,mental retardation and facial angiofibroma are found in most patients with tuberous sclerosis while retinal tumours (phakomas), visceral tumours, skeletal lesions and other cutaneous manifestations are noted less frequently.[5,10] In most cases, the first clue to recognizing TSC is the presence of seizure and delayed development, in others the first sign may be hypomelanotic macules.[1] Convulsion often begins in infancy in childhood and may take the form of infantile spasms. There is high prevalence of seizure in patients with tuberous sclerosis complex. Menor et al[11] and Jozwaik et al[12] recorded a frequency of 96% and 98% respectively in their studies. Our patient started having generalized seizures at the age of 7 months, he had delayed speech development and mental retardation.

Neuroimaging with CT scan in our patient revealed presence of calcified subepenymal hamartoma along the walls of the lateral ventricles which is one of its most common sites[13]. Multiple

subcortical and cortical tubers were also seen. There was no astrocytoma, however MRI is the investigation of choice for demonstrating these lesions when available. In that case they are seen as hyperdense lesions on T2 weighted sequence and are more easily visualized on fluid attenuation inversion recovery sequence (FLAIR).[13,14]

The cutaneous features were also evident on our patient who developed facial angiofibroma, periungual fibroma, moluscum fibrosum pendulum and shagreen patches at the age of nine years. Other cutaneous manifestations which were not present in this patient are hypomelanotic macules, ungula and gingival fibromas.

Angiomyolipoma is the commonest renal tumor found in patients with TSC. It has been estimated to occur in 40% -80% of the patients.[3] It is commoner in females. Renal cyst may also occur, but cysts in TSC are usually small and rarely exceed 3cm in size. These renal changes were not found in this patient rather the patient was found to have bilateral crytorchidism. Cryptorchidism is of multifactorial aetiology with hereditary, chromosomal, hormonal and environmental factors, as well as maternal health, birth weight and ethnicity being implicated.[15] Bilateral cryptorchidism is relatively rare in our environment, a study by Okeke et al[16] in South-Eastern Nigeria revealed no case of bilateral cryptorchidism. In Osun State South Western Nigeria a similar study revealed an incidence of 12.5% of patients with bilateral cryptorchidism.[17]

Cardiac rhabdomyoma is found in at least 50% of patients with TSC.[3] These usually appear as intracardiac tumours, either protruding into the chamber or contained in the myocardium. [3] The patients with this condition are often diagnosed inutero with obstetric ultrasound Scan, however some are diagnosed early in postnatal life . Rhabdomyomas regress in the first several years of life.[18,19]

Pulmonary involvement in TSC consists of cystic lesions and nodules in lungs. These occur independently of each other. Cysts are almost exclusively found in women but nodules are found in both men and women.[18] This was not found in our patient.

Phakomas are sometimes found in the eyes as white patches in the retina. They do not cause visual loss, but aid in making a diagnosis.1 None was found in our patient.

Gomez[20] established a diagnostic criteria for TSC that consist of major features such as cortical tubers, cardiac rhabdomyoma, facial angiofibromas, retinal harmatoma and renal angiomyolipoma; and minor features such as gingival fibroma, hamartoma, rectal polyp and renal or bone cyst. A diagnosis of TSC is definite when two major features or one major and two minor features exist. Our patient has two major features and one minor feature.

There is no cure for TSC, treatment is symptomatic and may include anticonvulsant therapy for seizures, drug treatment and psychotherapy for neurobehavioural problems, treatment of high blood pressure caused by kidney dysfunction and surgery to remove growing tumours.[1] The prognosis for individuals afflicted with TSC varies in accordance with the severity of the specific symptoms.

A regular imaging follow up is advised for patients with tuberous sclerosis at risk of developing intracranial tumours to avoid obstructive hydocephalous.[10]

Conclusion: Tuberous sclerosis (TSC) is a rare genetic disease that causes benign tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin. Common symptoms include seizures, mental retardation, behavior problems, and skin abnormalities which are usually very worrisome to parents and caregivers. Regular and close monitoring of the patients with this condition is mandatory to delay neurological sequelae and increase life expectancy.

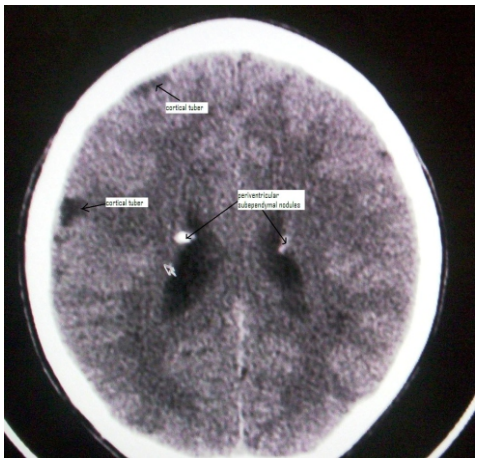

Fig 1. Showing CT Scan of the brain with cortical tubers and peri-ventricular subependymal nodules.

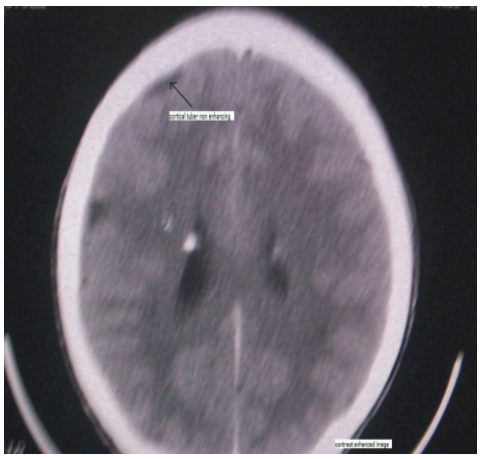

Fig 2. Showing CT scan of the brain with non enhancing cortical tubers

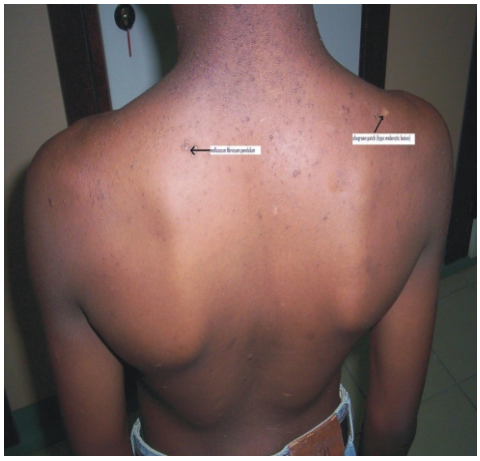

Fig. 3. Shows Moluscum Fibrosum Pendulum and the hypomelanotic lesions (shargreen patches)

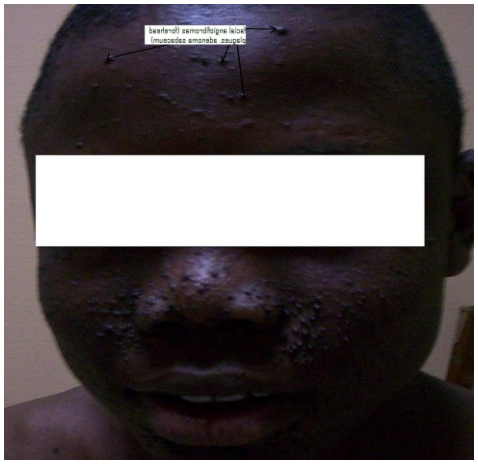

Fig. 4. Shows multiple facial angiofibromas

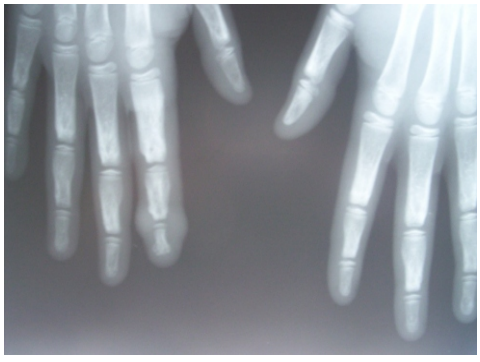

Fig. 5. Showing right Index Finger that is Sclerotic and expanded with Cysts in the Distal Phalanges (Periungual Fibroma)

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