EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 7
368-374
Year: 2019

RARE CASE OF INTRACTABLE SEIZURE WITH POLYPHARMACY DUE TO TUBEROUS SCLEROSIS

***Dr. Motwakil Imam Awadelkareim Imam**

Consultant Physician Assesstant Professor of Medicine Shendi University Sudan Elmek Nimer University Hospital.

***Corresponding Author: Dr. Motwakil Imam Awadelkareim Imam**
Consultant Physician Assesstant Professor of Medicine Shendi University Sudan Elmek Nimer University Hospital.

Article Received on 22/05/2019 **Article Revised on 12/06/2019** **Article Accepted on 02/07/2019**

ABSTRACT
Tuberous Sclerosis exhibits an autosomal dominant inheritance pattern, with a high spontaneous mutation rate. The *TSC2* gene was named tuberin. The highest levels of tuberin are found in adult human brain, heart, and kidney; tuberin also has been localized to arterioles of kidney, skin, and heart, as well as to pyramidal neurons and cerebellar Purkinje cells. Complications of neurological involvement are the most common causes of mortality and morbidity. These are due chiefly to intractable epilepsy, status epilepticus, and subependymal giant cell astrocytoma (SEGA) with associated hydrocephalus. We report a case a 33 years old sudanese female with intractable seizure in spite of polypharmacy with skin, renal, and cerebral manifestations of tuberous sclerosis.

KEYWORDS: Intractable seizure, polypharmacy and Tuberous Sclerosis.

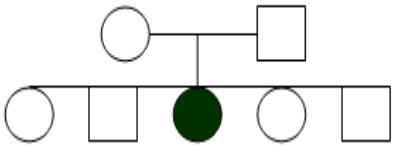
INTRODUCTION
In 1880, Bourneville first described the cerebral manifestations of this disorder, applying the term "sclerose tubereuse" to indicate the superficial resemblance of the lesions to a potato. In 1908 Vogt set forth the triad of intractable epilepsy, mental retardation, and adenoma sebaceum. Tuberous Sclerosis [TSC] exhibits an autosomal dominant inheritance pattern, with a high spontaneous mutation rate. Spontaneous mutations are also much more likely to reflect TSC2 disease. Suggestions that TSC1 disease is more likely familial than sporadic appear to be incorrect. TSC affects all races without a clear-cut predominance. TSC affects both sexes equally.[1,2]

TSC can present at any age. History, diagnostic criteria according to Committee of the National Tuberous Sclerosis Association (USA), major features:, these include facial angiofibromas or forehead plaque, non traumatic ungual or periungual fibroma, hypomelanotic macules, shagreen patch, multiple retinal nodular hamartoma, cortical tuber, subependymal nodule, subependymal giant cell astrocytoma, cardiac rhabdomyoma, single or multiple, Lymphangioleiomyomatosis and renal AML Minor features, these include pits in dental enamel, hamartomatous rectal polyps, bone cysts cerebral white matter radial migration lines, gingival fibromas, nonrenal hamartoma, retinal achromic patch, and multiple renal cysts. Diagnostic criteria: definite TSC, either two major features or one major feature plus two minor features. Probable TSC, one major plus one minor feature. Possible TSC, either one major feature or two or more minor features. Rapamycin is a commercially available immunosuppressant, which forms an inhibitory complex with the immunophilin FKBP12, which binds to and inhibits the ability of mTOR to phosphorylate downstream substrates, such as the S6Ks and 4EBPs. It inhibits T-cell proliferation, and has been approved for use in this therapeutic setting in the United States since 2001. Vigabatrin_is the drug of first choice for children with TSC and infantile spasms Topiramate, lamotrigine, valproate, and adrenocorticotropic hormone (ACTH)/steroids are also useful.[3,4,5]

CASE REPOTR
A 33 years old, Female, presented to us with intractable seizure and poly pharmacy. This lady was diagnosed as epilepsy at early child hood following sudden, repeated generalized seizures which started at age of 3 months .She is an outcome of a normal vaginal delivery, full term, without any complications. She showed normal development as her peers until 3 months of age, when she suddenly developed seizures which became worse in frequency and duration with age. This made her to be delayed in her mile stones. The increase in frequency, duration and severity of seizures prevented her from normal schooling in spite of a good performance in the 2nd year of the primary school Apart from a relatively preserved memory, her mental functions decreased at the age of 8 year. At the age of 9 years she developed spontaneous massive macroscopic haematuria, diagnosed as Rt renal tumor, ended with Rt nephrectomy. No PMH

of D.M or HTN No FH of similar condition, + FH of D.M and HTN first degree relative.

2nd Degree [family tree]



Her recent medication include Phenytoin tab 300mg o.d, Lorazepam tab 5mg o.d, Topiramate tab 50mg B.D, Phenytoin tab 300mg o.d, Lorazepam tab 5mg o.d, Topiramate tab 50mg B.D. Her current medication include Phenytoin tab 200mg o.d, Topiramate tab 50mg B.D, Lamotrigine tab 50 o.d. O/E Pt looks unwell, frail, depressed, withdrawn, and disinterested to her surrounding PR: 80/min regular good volume BP: 120/80 RR: 20/min, C.V.S, Chest, Abd : Unremarkable CNS: Unremarkable in spite of mild dystonia in upper limbs, Skin manifestations showed Flat fibrous plagues (fore head) figure,[1] Facial angio fibroma figure,[2] Pitting of dental enemal figure,[3] Unpigmented white hair figure,[4] Gum hyperatrophy figure,[5] Periungual fibroma of fingers nails + ungular sulcus figure,[6] Periungual fibroma of toes nails figure,[7] Lateral kyphoscliosis figure,[8] Shagreen Patchs figure,[9] Rt paramedial longitudinal scar figure.[10]

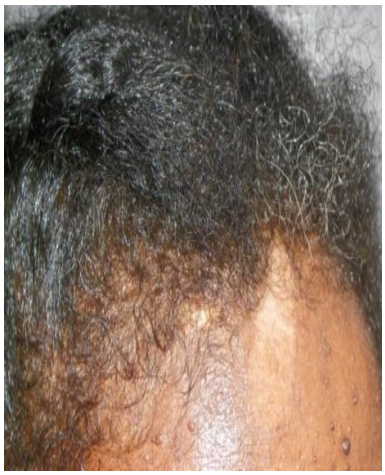


Figure [1]: Flat fibrous plagues (fore head).

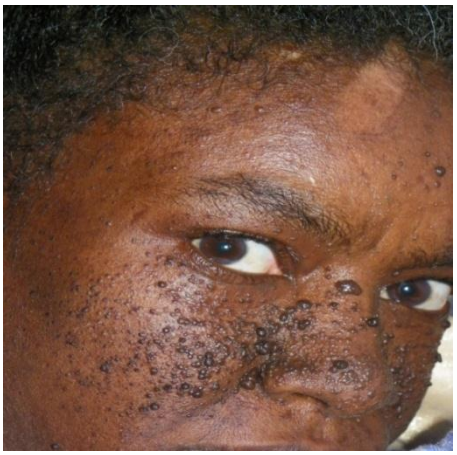


Figure [2]: Facial angio fibroma.

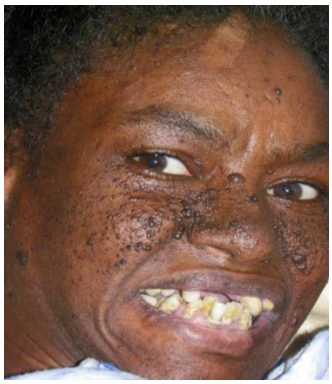


Figure [3]: Pitting of dental enemal.

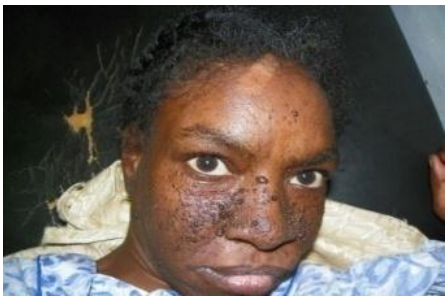


Figure [4]: Unpigmented white hair.

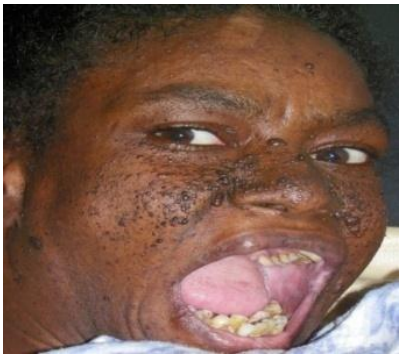


Figure [5]: Gum hyperatrophy.

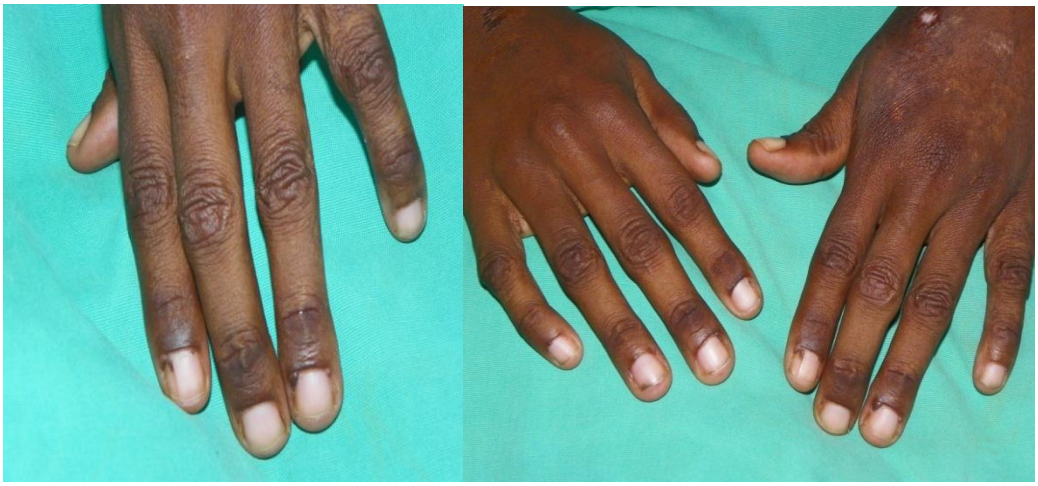


Figure [6]: Periungual fibroma of fingers nail and ungular sulcus.

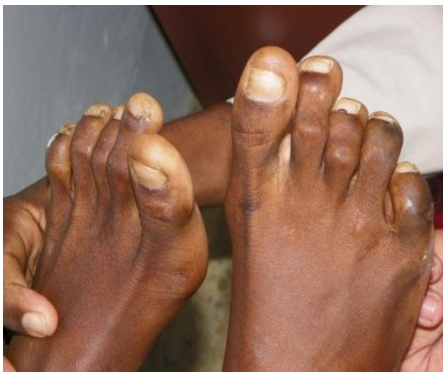


Figure [7] Periungual fibroma of toes nails

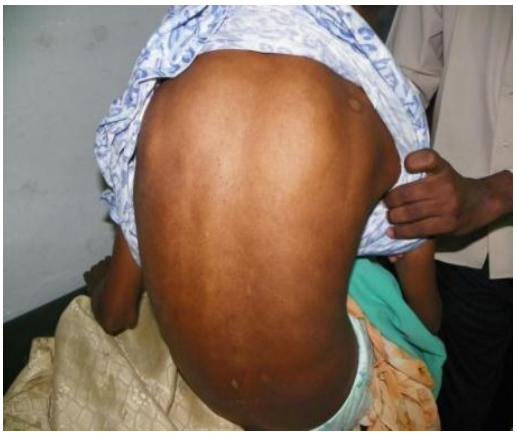


Figure [8]: Lateral kyphoscliosis.

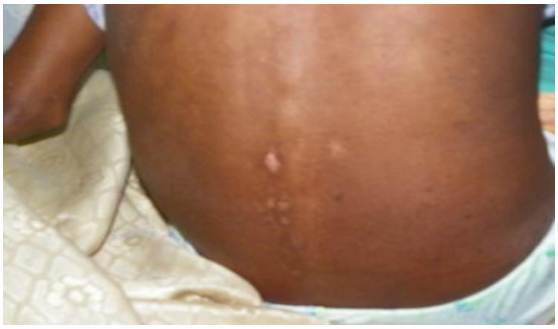


Figure [9]: Shagreen Patchs.

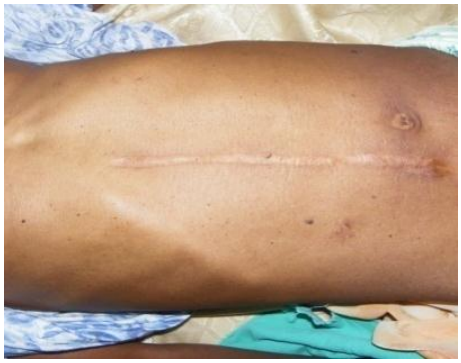


Figure [10]: Rt paramedial longitudinal scar.

Investigations: CBC, RFT, LFT, UA, RBG normal, CXR showed lateral kyphoscliosis figure,[11] CT – head showed tuberous calcification figure,[12] MRI – head (T2 and FLAIR) showed sub-ependymal calcification figure,[13] MRI – head (T1 sagittal) showed sub-ependymal calcification figure,[14] MRI – head (T2 Coronal) showed sub-ependymal calcification figure,[15] ultra sound abdomen showed multiple Lt renal angiomyolipomas figure,[16] normal echo cardiograph figure,[17] normal fundal examination figure,[18] normal ECG figure.[19]

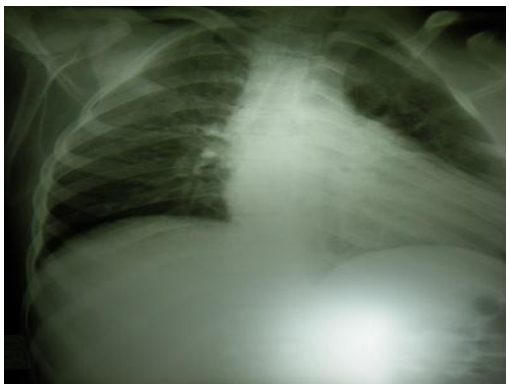


Figure [11]: Chest X ray (Lateral kyphoscliosis).

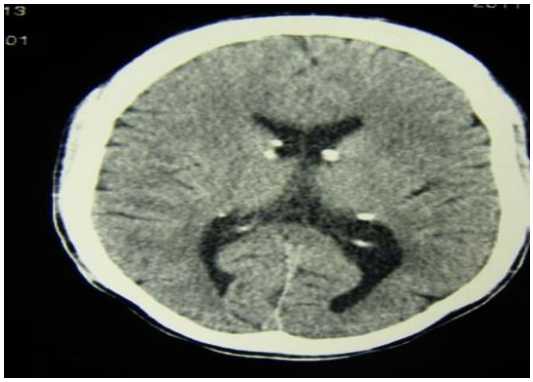


Figure [12]:CT – head (tuberous calcification).

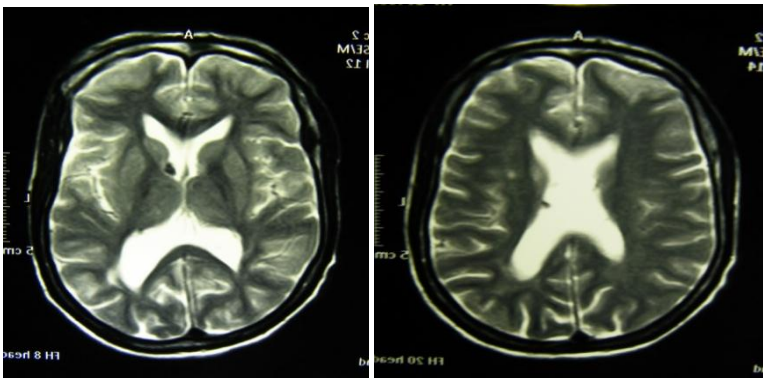


Figure [13]: MRI – head (T2 and FLAIR) Sub-ependymal calcification.

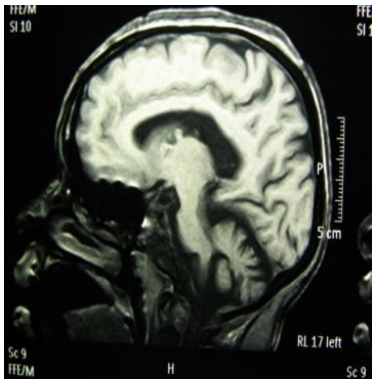


Figure [14]: Sub-ependymal calcification T2 Coronal.

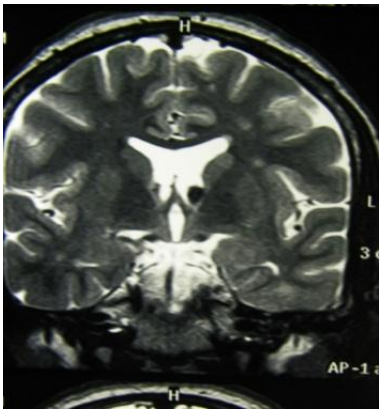


Figure [15]:MRI – head (T1 sagittal).

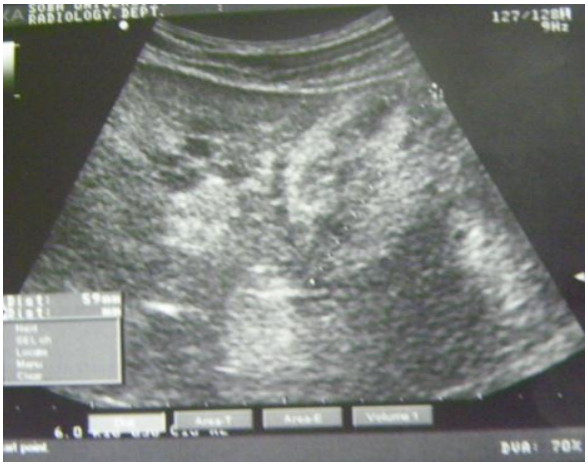
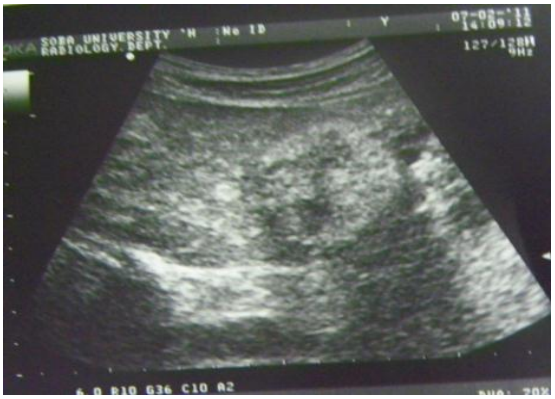


Figure [16] Sub-ependymal calcification



Multiple Renal angiomyolipomas

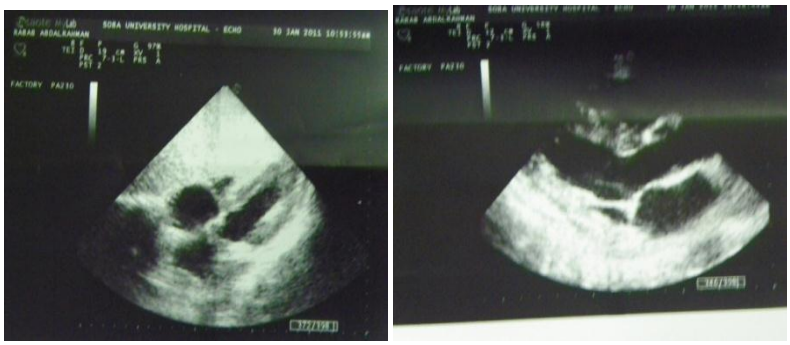


Figure [17]: Normal Echo Cardiograph.

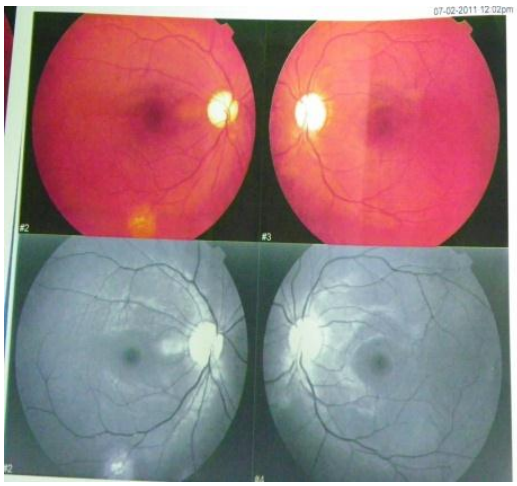


Figure [18]

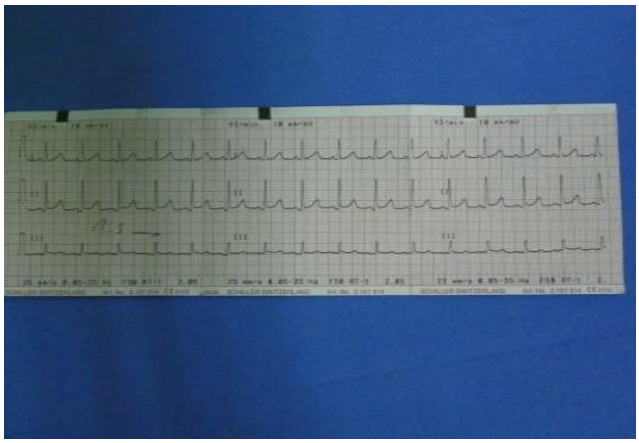


Figure [19]

DISCUSSION

Tuberous Sclerosis [TSC] exhibits an autosomal dominant inheritance pattern, with a high spontaneous mutation rate. Two distinct genetic loci: one on chromosome band 9q34 and another on chromosome band 16p13. The TSC2 gene was named tuberin. The highest levels of tuberin are found in adult human brain, heart, and kidney; tuberin also has been localized to arterioles of kidney, skin, and heart, as well as to pyramidal neurons and cerebellar Purkinje cells. Hamartin, the TSC1. Hamartin and tuberin together form a tumor suppressor. When mTOR is constitutively activated through mutations in either hamartin or tuberin this results in the hamartomatous lesions.[1,2]

Complications of neurological involvement are the most common causes of mortality and morbidity. These are due chiefly to intractable epilepsy, status epilepticus, and subependymal giant cell astrocytoma (SEGA) with associated hydrocephalus. Renal complications are the next most frequent cause of morbidity and death. Less common are cardiac arrhythmias, CHF, and end-stage lung disease.[4,6]

Differential Diagnosis: clinical diagnosis of tuberous sclerosis is challenging because of the increase tuberous sclerosis features of other neurological diseases Differential Diagnosis could include Rt paramedial longitudinal scar complex partial seizures, epilepsy in children, adults with mental retardation, glioblastoma multiforme, hydrocephalus, sturge weber syndrome (encephalofacial angiomatosis), and Von–Hippel Lindau Syndrome (retino Cerebellar angiomatosis). So imaging lilke CT- head, MRI –head, CXR, CT –chest, Echocardiography, Abdominal Ultrasound, and genetic analysis have been undertaken widely as a method to distinguish between Tuberous Sclerosis and other similar- featured disorders.

CONCLUSION

Tuberous Sclerosis is an inheritable neurological disorder and is rare as compared to acquired neurological disorders. We report a case of Sudanese young female with early childhood onset epilepsy with mental retardation also with major and minor clinical and radiological features of Tuberous Sclerosis with intractable seizure in spite of multiple drugs taken. This case illustrate that Tuberous Sclerosis caused uncontrolled convulsion with drug resistant. Antiepileptic drugs like Carbamazepine, oxcarbazepine, and phenytoin may cause exacerbation of seizures, particularly in younger children and infants. Long-term use of agents with prominent sedating properties, such as benzodiazepines or barbiturates, generally should be avoided. These drugs often aggravate underlying behavioral or cognitive problems.

REFERENCES

1. Lewis JC, Thomas HV, Murphy KC, Sampson JR. Genotype and psychological phenotype in tuberous sclerosis. J Med Genet, 2004 Mar; 41(3): 203-7.
2. Schwartz RA, Fernandez G, Kotulska K G, Jozwiak S. Tuberous sclerosis complex: advances in diagnosis, genetics and management. J Am Acad Dermatol, 2007 Aug; 57(2): 189-202.
3. Maria BL, Deidrick KM, Roach ES, GutmannDH. Tuberous sclerosis complex: pathogenesis, diagnosis, strategies, therapies, and future research directions, J Child Neurol, 2004 sep; 19(9): 632-42.
4. Crino PB, Nathanson KL, Henske EP, The tuberous sclerosis complex. N Engl J Med, 2006 sep 28; 355(13): 1345-56.
5. Curatolo P, Bombardieri R, JozwiakS. Tuberous sclerosis. Lancet, 2008 Aug 23; 372(9639): 657-68. doi: 10.1016/S0140-6736(08)61279-9.
6. Franz DN, BIssler JJ McCormac FXk, Tuberous sclerosis complex: neurological, renal and pulmonary manifestations. Neuropediatrics, 2010 Oct; 41(5): 199-2008. Doi 1055/s-0030-1269906. Epub 2011Jan 5.
7. Hyman MH. Whittemore VH. National Institutes of Health consensus conference: tuberous sclerosis complex. Arch Neurol, 2000 May; 57(5): 662.5.

.