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Case Report

Tuberous Sclerosis Complex (TSC) in 8-Year-Old Girl: A Case Report

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Abstract: Tuberous Sclerosis Complex (TSC) are clinically associated with the development of non-malignant tumors throughout the body. The clinical presentation of TSC is highly variable among individual in which make the diagnosis is challenging too. Based on the 2012 International TSC Consensus Group guidelines, diagnosis is made either by genetic diagnosis or clinical diagnosis. Managing Tuberous Sclerosis Complex (TSC) is as challenging as diagnosis. Multiple organs are affected, it requires multidisciplinary approach to deal with. An 8-year-old girl consulted from Dermato-venerology department with chronic facial angiofibroma with suspicion of TSC. The symptoms at the time of examination were face lump and decreased ability to concentrate at class subjectively reported by parents. Investigation were carried and revealed that patient had a history of seizure during infancy, had finished anti epilepsy medication and has been remaining symptoms free up to this case were investigated. Diagnosis were made by matching investigation result to clinical diagnosis of the 2012 International TSC Consensus Group guidelines. Several supporting examinations had been done, with result: subependymal nodule from head CT Scan; Rhabdomyoma from echocardiograph; multiple mass on kidney from USG; and EEG abnormality. Management were emphasized on treating the rose symptoms and prioritization of the most potential result that might possess significant burden. TSC possess potential challenge starts from case presentation to management. Thorough investigation and multidisciplinary approached are required to successfully manage the case and eventually reduce the burden of the disease.

Keywords: Tuberous Sclerosis Complex, Clinical Presentation, Management

1. Introduction

Tuberous Sclerosis Complex (TSC) are clinically associated with the development of non-malignant tumors throughout the body. The pathology is caused by mutations in the TSC1 and TSC2 genes, i.e. tumor-suppressor gene, which encode the proteins hamartin and tuberin [1, 2]. The genes mutations bring about the loss of inhibition of the mammalian target of rapamycin (mTOR) pathway, eventually leading to growth of hamartomas in various organs [1].

The clinical presentation of TSC is highly variable among individual in which make the diagnosis is challenging too. The Central Nervous System (CNS), dermatological, renal, and respiratory are the most commonly affected organs that is observed clinically [2]. The movement to alleviate the challenging diagnosis has been made. Based on the 2012 International TSC Consensus Group guidelines, diagnosis is made either by genetic diagnosis or clinical diagnosis. The clinical diagnosis consists of the fulfillment of 2 major features or 1 major feature plus 2 minor features [3]. In setting in where the ability to conduct genetic testing is lacking, the accepted consensus has come to aid with the criteria of clinical diagnosis provided.

Managing Tuberous Sclerosis Complex (TSC) is as challenging as diagnosis. Multiple organs are affected, it requires multidisciplinary approach to deal with [1, 3]. With limited diagnostic and medication resource available, we present here a case report of TSC in girl age 8 years old with emphasize of management priority among problems existed and suited to our available resources.

2. Case Illustration

An 8-year-old girl was consulted from the Dermatology Department of Sanglah Hospital, Bali with chronic facial angiofibroma and hypomelanotic maculae, suspicious of TSC (Figure 1). These small lumps had been reported for 6 years, and had been spreading ever since, subjectively she sometimes complained itchy, painless lump, and didn't bleed easily. Complained of numbness didn't report. Patient was consulted to the pediatric clinic as well because there were report from parents that patients had difficulty attending lessons at school. Based on hetero anamnesis (parents), it was said that patient often seem to daydream at school. The parents said that the patient has been having difficulty receiving information. The parents must repeat the subject matter at school to make the patient finally able to capture the information provided. The patient also had been having difficulty in conversation and was rather stuttering. This condition had made the patient hadn't have too many friends at school.

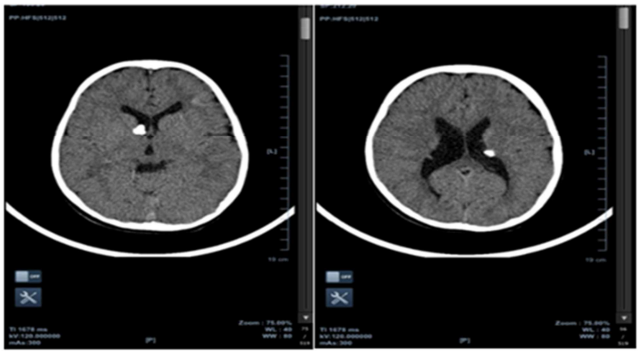
From a history of previous illness, it is said that the patient experienced seizures at the age of 2 years. Seizures was said to be the patient's right and left hands and legs stomping, occurring for approximately 1 minute. The seizure was lasted 1 time, stop on its own, afterward the patient was conscious. When seizures happened, the patient did not have any fever. After the seizure, the patient was brought to a Pediatrician and was diagnosed with epilepsy. The patient was then given an anti-epilepsy drug regimen until it was stopped 2 years ago. History of growth and development, especially motor had no disturbances or delays and fit to age. When the case was reported, the patient never failed the grade, test score was on average level.

The investigation of the patient was followed by an additional examination in the form of Computed Tomography with contrast (CT-Scan with contrast) of head; Electroencephalography (EEG); Urology ultrasonography (USG); and Echocardiography. CT scan with contrast of the head revealed multiple hypodense lesions without clear border in the subcortical area right and left frontal lobe accompanied by multiple calcifications in the subependymal area around left and right lateral and in the left and right frontal lobes (Figure 2a and 2b). EEG revealed multifocal epileptiform waves on left and right frontal area; left temporal area; and occipital area (Figure 3).

Echocardiography was shown hyperechoic mass on left ventricle without decrease in right and left ventricular function (Figure 4). USG urology found multiple calcifications in the bilateral renal cortex with no observed solid or cystic mass. Laboratory test for routine hematology and kidney function were done. No significant abnormalities were found from routine hematology and kidney function test. GFR for this patient was 149.05 ml/min/mmHg (within normal limit).

Pediatric Symptoms Checklist (PSC 17) revealed total score of 2 with impression of no behavioral impairment. IQ score was 110 with interpretation of above average. Physiological consultation was made, and patient was considered having slight decreased learning ability.

Figure 1. *Facial angiofibroma and hypomelanotic maculae.*



(a) ***(b)***

Figure 2. *Subependymal nodule with calcification from head CT Scan. Nodules were found on (a) right and (b) left subependymal area near lateral ventricle.*

3. Discussion

From this case report was found the commonest symptoms of a TSC, namely skin manifestations in the form of facial angiofibroma and hypomelanotic lesions; CNS manifestations in the form of abnormality of EEG waves, i.e.: epileptiform waves and subependymal nodules; and cardiac rhabdomyoma. From a cohort study in Germany, the 3 most frequent clinical manifestations of TSC are central nervous system (CNS) involvement, skin manifestations, and cardiac rhabdomyoma [3]. Manifestations of skin lesions develop with age onset, so there is a proposed general genetic timeline whenever certain lesions may appear on certain age, although it is not always clear in some cases [1, 3]. Among skin lesions associated with TSC, facial angiofibroma and hypomelanotic lesions are the most frequently present [1].

Other signs that were found in our patients, namely rhabdomyoma and kidney period had no clinical symptoms. It is already known that rhabdomyoma is a benign lesion and spontaneous resolution generally occurs with age and routine echocardiographic monitoring is recommended to monitor the development of its mass [4-6].

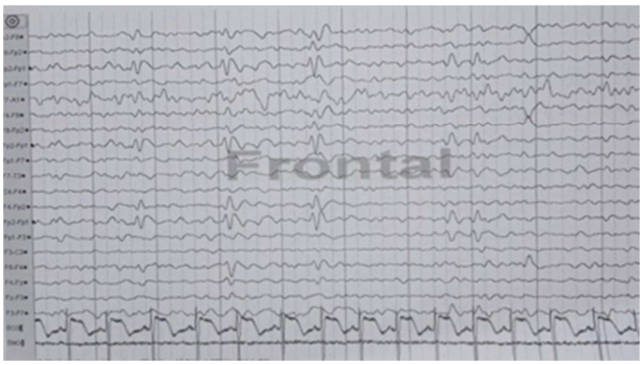


Figure 3. *EEG shows multifocal epileptiform wave over the right and left frontal region.*

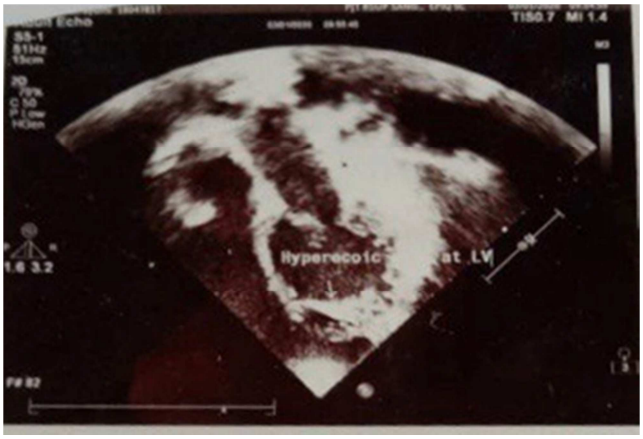


Figure 4. *Echocardiography showed hyperechoic mass in left ventricle.*

The diagnostic criteria follow the international consensus of the 2012 International Tuberous Sclerosis Complex Consensus Conference which states that diagnostic criteria include genetic diagnosis and clinical diagnosis [1]. The consensus also concluded that multiple facial angiofibroma's in children is a major feature on TSC [6, 7]. Criteria for clinical diagnosis are established from fulfilling 2 major criteria or 1 major and 2 minor criteria. In this patient multiple angiofibroma were found, multiple hypomelanotic macular lesions; and subependymal nodules. In this patient genetic testing was not carried out because it was still not available at the hospital where the patient was examined.

Of all the findings of the organ system, it is known that neuropsychiatric problems are those that have the greatest burden of disease on patients among others, because they are related to intellectual and mental status [8]. Management of our patient is focused on the management of neuropsychiatry. The plan of treatment is based on 2012 International consensus of TSC [6, 14, 15].

Starting preventive therapy when a diagnosis of subclinical epilepsy is discovered is still a debate [8-10]. Where there have been several reports from previous studies regarding a positive correlation between intellectual ability and seizure control at TSC. Although in this cohort there are still a small number of groups whose seizures are controlled but have intellectual disabilities [9]. In patients with epileptiform waves obtained after EEG and without clinical symptoms of epilepsy indicate subclinical epilepsy and also a history of seizures during this patient infancy have noted. In a multicenter cohort study from the TOSCA registry it was found that epilepsy is usually diagnosed before 2 years of age in> 70% of patients [9]. Provision of anti-epilepsy especially for cases of infantile spasm has been recommended. As for seizure type other than infantile spasm cases the evidence is still limited, so that the treatment protocol must follow standard treatment for each type of seizures [10]. Our patient has started carbamazepine after the EEG abnormality were found. Patients was given carbamazepine at a dose of 20 mg/kg body weight with a dose of 200 mg every 12 hours.

Most of time, seizure control in patient with TSC are well managed by AED and other non-pharmacological intervention [7, 10, 11]. However, one study epilepsy related with TSC were related with relapse of the disease after 24 months remission in half of respondent [12]. In those with confirmed epilepsy, the management is best when done by multidisciplinary approach: anti-epileptic drugs; vagal nerve stimulation as adjunctive; and ketogenic as a combined treatment [11]. Although not yet FDA and BPOM (Indonesia equivalence of FDA) approved for treating epilepsy in TSC, m-tor inhibitor shows promising option in treating epilepsy. One open label phase I/II clinical trial shows reduction of epilepsy in more than 50% respondent with refractory epilepsy [13]. In our patient, m-tor inhibitor wasn't given, close monitoring and AED were proposed for epilepsy management.

In neurological radiology study it is important to do MRI with contrast every 1-3 years until the age of 25 years to see the development of brain lesions and detect early SEGA. Nodules located on Monroe foramen with enhanced contrast of more than 5 mm in diameter possess a high risk of becoming SEGA [6, 10]. MRI becomes a challenge in handling patients in Sanglah Hospital, in which MRI facilities are not yet available so contrast CT scan is an alternative.

To summarize treatment plan for this patient, that EEG will be re-done after at least 2 years from the start of carbamazepine. USG and echocardiography will be done after the 6 months of the first diagnosis of to monitor progression of the mass of kidney and heart. Behavioral and neurological symptoms are also closely followed in order to measure quality of life by checklist such as TAND or regular phycological session.

4. Summary

An 8-year-old girl consulted from Dermato-venerology department with chronic facial angiofibroma with suspicion of TSC. The symptoms at the time of examination were face lump and decreased ability to concentrate at class subjectively reported by parents. Investigation were carried and revealed that patient had a history of seizure during infancy, had finished anti epilepsy medication and has been remaining symptoms free up to this case were investigated. Physical examination revealed multiple facial angiofibroma. Several supporting examinations had been done, with result:

subependymal nodule from head CT Scan; Rhabdomyoma from echocardiograph; multiple mass on kidney from USG; and multifocal epileptiform waves from EEG.

Patients symptoms and signs fulfilled the clinical diagnosis of 2012 International Consensus of TSC with at least 2 major features had been found. Treatment for subclinical epilepsy has been started with administration of daily carbamazepine, 200 mg every 12 hours. Routine follow and multidisciplinary approach were done in conjunction with dermatologic department and phycology department.

this level of image detail, all three basic varieties of configural information (hanged of spatial quantization between 11 pixels/face and 6 pixels/face levels altogether indicate that this ERP- component is especially sensitive to the first order configural cues. Some other works have supported both of these ideas [6, 16].

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References

[1] Cardis, M. A. and DeKlotz, C. M. C (2017). Cutaneous manifestations of tuberous sclerosis complex and the paediatrician's role. Arch Dis Child. 2102 (9), 858–863.

[2] Kingswood, C., Bolton, P., Crawford, P., Harland, C., Johnson, S. R., Sampson, J. R., et al. (2016). The clinical profile of tuberous sclerosis complex (TSC) in the United Kingdom: A restrospective cohort study in the Clinical Practice Research Datalink (CPRD). Eur J of Paed Neur. 20 (2), 296-308.

[3] Ebrahimi-Fakhari, D., et al. (2018). Incidence of tuberous sclerosis and age at first diagnosis: new data and emerging trends from a national, prospective surveillance study. Orphanet J Rare Dis. 13 (1), 117.

[4] Günther, T., Schreiber, C., Noebauer, C., Eicken, A., Lange, R. (2018). Treatment strategies for pediatric patients with primary cardiac and pericardial tumors: a 30-year review. Pediatr Cardiol. 29 (6), 1071-1076.

[5] Sciacca, P., Giacchi, V., Mattia, C., et al. (2014). Rhabdomyomas and tuberous sclerosis complex: our experience in 33 cases. BMC Cardiovasc Disord. 14, 66.

[6] Northrup, H., Krueger, D. A. (2013). International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 Iinternational Tuberous Sclerosis Complex Consensus Conference. Pediatr Neurol. 49 (4), 243-254.

[7] Henske, E. P., Jóźwiak, S., Kingswood, J. C., Sampson, J. R., Thiele, E. A. (2016). Tuberous sclerosis complex. Nat Rev Dis Primers. 2, 16035.

[8] Zöllner, J. P., Franz, D. N., Hertzberg, C., Nabbout, R., Rosenow, F., Sauter, M., et al. (2020). A systematic review on the burden of illness in individuals with tuberous sclerosis complex (TSC). Orphanet J Rare Dis. 15, 23.

[9] Nabbout, R., Belousova, E., Benedik, M. P., et al. (2018). Epilepsy in tuberous sclerosis complex: Findings from the TOSCA Study. Epilepsia Open. 4 (1), 73-84.

[10] Curatolo, P., Moavero, R., de Vrie, s P. J. (2015). Neurological and neuropsychiatric aspects of tuberous sclerosis complex. Lancet Neurol. 14 (7), 733-745.

[11] Saxena, A. and Sampson, J. R. (2015). Epilepsy in Tuberous Sclerosis: Phenotypes, Mechanisms, and Treatments. Semin Neurol. 35 (3), 269-276.

[12] Overwater, I. E., Bindels-de Heus, K., Rietman, A. B., et al. (2015). Epilepsy in children with tuberous sclerosis complex: Chance of remission and response to antiepileptic drugs. Epilepsia. 56 (8), 1239-1245.

[13] Krueger, D. A., Wilfong, A. A., Holland-Bouley, K., et al. (2013). Everolimus treatment of refractory epilepsy in tuberous sclerosis complex. Ann Neurol. 74 (5), 679-687.

[14] Roach, S. E. Applying the lessons of tuberous sclerosis: the 2015 Hower Award Lecture. (2016). Pediatr Neurol. 63, 6-22.

[15] Leclezio, L., Jansen, A., Whittermore, V. H., Vries, P. J. Pilot Validation of the Tuberous Sclerosis-Associated Neuropsychiatric Disorders (TAND) Check. (2015). Pediatr Neurol. 52, 16-24.

[16] Thomas, N. and Darling, A. J. Tuberous sclerosis complex. In: Goldsmith L, A., Katz, S. I., Gilchrest, Paller, A. S., Leffell, D. J., Woff, K., editors. Fitzpatrick's Dermatology in General Medicine (8th ed.). New York: McGraw Hill, 2012; p. 1671-1679.