



Case Report

Tuberous sclerosis in a 16 years old female: A case report

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ABSTRACT

Introduction: Tuberous sclerosis complex (TSC) is an uncommon multisystem disorder that can affect the lungs, skin, kidneys, and brain. The study highlights the importance of genetic and clinical diagnostic criteria in identifying this rare condition and the role of surveillance in preventing complications.

Case presentation: Herein, we report a case of 16 years old female presenting with right flank pain, hematuria, hypopigmented macule over the back, ash leaf spots over the right upper and lower limb, and a palpable mass over the right lumbar region. Laboratory tests showed low hemoglobin with plenty of red blood cells in urine. She was admitted for symptomatic management of pain and blood transfusion was done to manage anemia. After a diagnostic workup for tuberous sclerosis, she was diagnosed with the condition and is under regular follow-up.

Clinical discussion: Tuberous sclerosis complex is one of the neurocutaneous syndromes, diagnosed based on the genetic or clinical diagnostic criteria as per the second International Tuberous Sclerosis Complex Consensus Conference 2012, which have been updated in 2021 with no changes in genetic diagnostic criteria and slight changes in clinical diagnostic criteria. After diagnosis, along with the management, surveillance is also crucial.

Conclusion: Tuberous sclerosis runs a progressive course and can lead to various complications. Thus, early diagnosis with the help of genetic and clinical diagnostic criteria is important along with regular surveillance of different body systems to prevent debilitating complications.

1. Introduction

Tuberous sclerosis is a multisystem disorder that can affect the lungs, skin, kidneys as well as brain with debilitating conditions like autism, epilepsy, and intellectual disability [1]. It is believed to be inherited in an autosomal dominant fashion, though the majority of cases do not demonstrate a clear family history and occur due to mutations spontaneously [2]. Hypomelanotic macules are the most frequently reported clinical signs in children below 14 years, followed by epilepsy, facial angiofibroma, and renal angiomyolipoma while cardiac rhabdomyoma is one of the most common findings in children aged less than two years [3]. As for renal angiomyolipoma, it can cause complications like mass effect or hemorrhage and thus can necessitate surgical procedures, highlighting the importance of periodic follow-up [2].

Herein, we report a case of 16 years old female who had intermittent episodes of hematuria for years and thus presented with significant anemia. She was diagnosed to have tuberous sclerosis with no significant

family history. Her acute condition was stabilized and is under the regular follow-up to screen for potential complications. This case report has been reported in line with the SCARE 2020 criteria [4].

2. Case presentation

History dates back around four and half years ago for a 16 years old Asian, non-smoker, non-alcoholic, normally menstruating female with no known co-morbidities, who presented with pain over the right upper quadrant. It was insidious in onset, non-progressive, non-radiating, and aggravated by physical exertion and decreased fluid intake. It was controlled by taking medication, mostly non-steroidal anti-inflammatory drugs (NSAIDs), and she rated pain severe in intensity. The pain had been on and off since then. There was no history of trauma.

She also had noticed blood during micturition for the first time around three years ago, which was present throughout the stream of flow, present intermittently throughout the period. There was

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occasional discomfort over the hypogastric region, burning sensation during micturition, and occasional blackish color of urine. Recently, the patient gets easily fatigued on physical exertion and has experienced dizziness sometimes.

There is no history of fever, significant weight loss, difficulty breathing, palpitations, abnormal body movements or seizure, and loss of consciousness. Her bowel habits are normal and she had her last menstrual period a couple of weeks ago. There was no family history of a similar illness, no past surgical history, and no significant psychosocial history.

She was averagely built, calm, cooperative, and well oriented to time, place, and person. Pallor was noticed over bilateral palpebral conjunctiva, however, there was no icterus, edema, or lymphadenopathy. Her pulse rate was 110 beats per minute with a regular rhythm, normal volume, and blood pressure of 100/70 mm of Hg, with normal temperature, respiratory rate, and oxygen saturation. There were patchy areas on her back, likely a Shagreen patch, and hypopigmented macules, likely ash-leaf spots, over the right upper and lower limb (Fig. 1). She had multiple dome-shaped papules on her face around the maxillary region and chin with no signs of excoriation marks or any sort of discharge. On abdominal examination, it was soft, non-distended with mild tenderness noted over the right lumbar region. There was a palpable mass over the right lumbar region measuring approximately 10*8 cm, with round edges and a smooth surface. The contralateral lumbar region was normal and the liver and spleen were not palpable. Her respiratory, cardiovascular, and nervous system examination findings were normal.

On laboratory investigations, hemoglobin level was 5.10 g/dl with hematocrit 15.32%. The rest of the cell counts were normal with a normal erythrocyte sedimentation rate and normal liver function tests. On urine routine microscopic examination, plenty of red blood cells (RBCs) was seen with no significant white blood cells (WBCs), casts, or crystals.

Ultrasonography of abdomen and pelvis revealed a 9.8*8.7 cm ill-defined mass in mid and lower regions of right renal sinus and parenchyma with no hepatic or suprarenal invasion. Likewise, computed



Fig. 1. Hypopigmented macule over the right upper arm.

tomography (CT) scan of the abdomen and pelvis demonstrated a 10.4*6.6 cm heterogeneous enhancing mass lesion in the right kidney with areas of contained hemorrhage and fat densities of 4.5*3.7cm (Fig. 2). There was a bilateral small sub-centimeter scattered multiple cystic areas in the renal cortex. Multiple sclerotic lesions were visualized in the dorsolumbar spine. Magnetic resonance imaging (MRI) of the brain showed multiple T2/FLAIR cortical and subcortical hyperintensities, white matter radial bands, and subependymal hamartomas (Fig. 3).

She was admitted to the ward for management of low hemoglobin level for which blood transfusion was done along with symptomatic management of pain with analgesics. She was also evaluated for diagnostic criteria of tuberous sclerosis as per the National Institute of Health (NIH) consensus conference criteria. She had hypo melanotic macule, more than three in number and facial angiofibroma, shagreen patch, subependymal nodule, the renal mass suspected to be angiomyolipoma with multiple renal cysts and bone cyst, thus fulfilling the clinical criteria for diagnosis of tuberous sclerosis complex as per second International Tuberous Sclerosis Complex Consensus Conference 2012.

As the disease runs a chronic and progressive course, the patient has been under regular follow-up since she was diagnosed with the disease complex.

3. Discussion

Tuberous sclerosis complex is one of the neurocutaneous syndromes that can present clinically with any seizures, facial angiofibroma, hypomelanotic macules, shagreen patch, retinal hamartomas, renal angiomyolipoma, subependymal nodules, or giant cell astrocytoma or

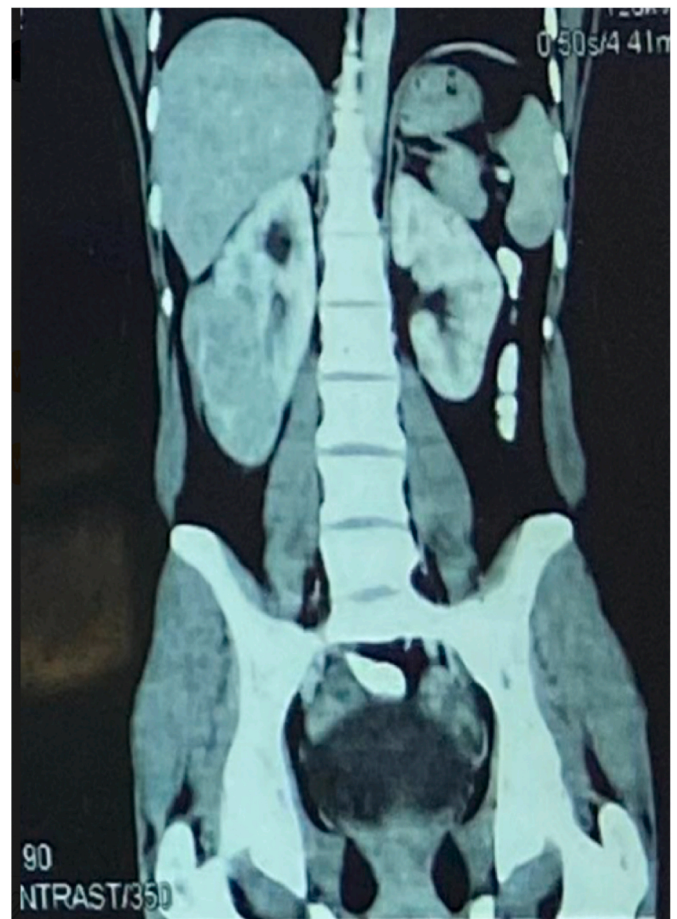


Fig. 2. CT scan of the abdomen showing heterogenous enhancing mass lesion in the right kidney and multiple renal cysts.

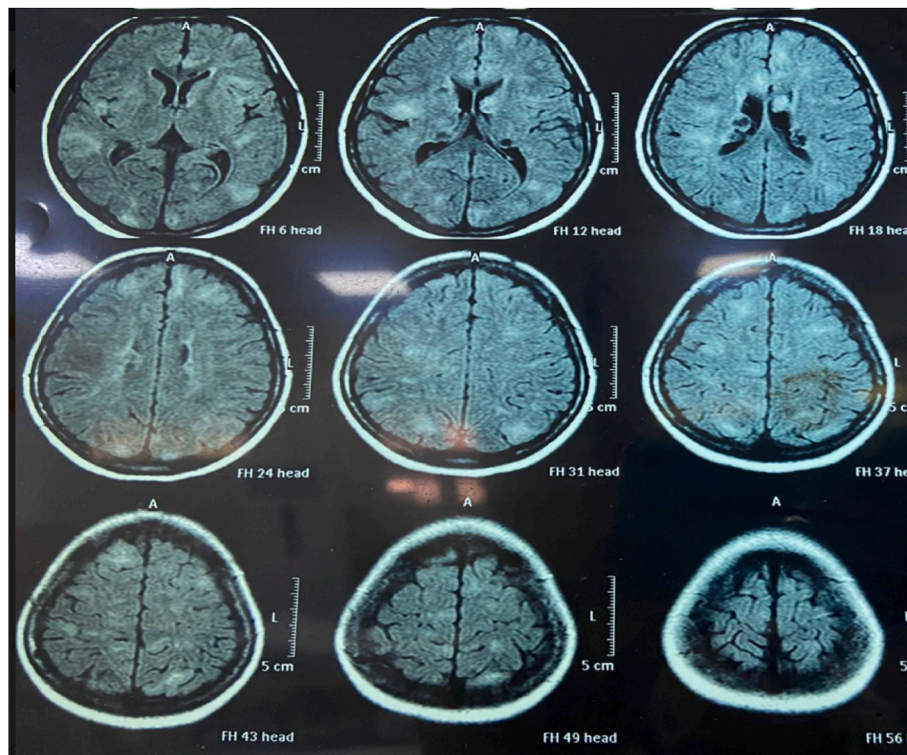


Fig. 3. MRI of the brain showing multiple T2/FLAIR cortical and subcortical hyperintensities, white matter radial bands, and subependymal hamartomas.

cardiac rhabdomyoma [5]. It is diagnosed based on genetic or clinical diagnostic criteria as per the second International Tuberous Sclerosis Complex Consensus Conference 2012 [6]. As per genetic criteria, the presence of inactivating mutation at either TSC1 or TSC2 gene of normal tissue is adequate for diagnosing of tuberous sclerosis complex. Clinical criteria include the following, requiring two from major features or one major along with two or more from minor features for making a definite diagnosis while either one from major or two or more from the minor category is classified as a possible diagnosis [6].

3.1. Major criteria

1. Hypo melanotic macules (three or more, at least five mm diameter)
2. Angiofibroma (three or more) or fibrous cephalic plaque
3. Ungual fibroma (two or more)
4. Shagreen patch
5. Multiple renal hamartomas
6. Cortical dysplasia
7. Subependymal nodules
8. Subependymal giant cell astrocytoma
9. Cardiac rhabdomyoma
10. Lymphangiomyomatosis (LAM)
11. Angiomyolipoma (two or more)

3.2. Minor criteria

1. Confetti skin lesion
2. Dental enamel pits (three or more)
3. Intraoral fibroma (two or more)
4. Retinal achromatic patch
5. Multiple renal cysts
6. Nonrenal hamartoma

The diagnostic criteria have been updated in 2021 with no changes in genetic diagnostic criteria however there have been two changes in

clinical diagnostic criteria [7]. First includes the change in “cortical dysplasia” from major criteria to “multiple cortical tubers and/or radial migration lines” as the former was found to be too vague and non-definite, creating confusion during clinical practice. The second change includes the addition of “sclerotic bone lesions” in minor criteria, which was removed previously in 2012 as per suggestion from the dermatology and dental working group [7].

Our patient had hypo melanotic macule, more than three in number and facial angiofibroma, shagreen patch, subependymal nodule, the renal mass that was suspected to be angiomyolipoma from major criteria along with multiple renal cysts and bone cyst from minor criteria thus making a definite diagnosis as per clinical criteria.

After the diagnosis has been confirmed, as per Krueger et al., regular surveillance is indicated along with early interventions if required [8]. As for renal angiomyolipoma, an MRI of the abdomen is required every one to three years for a lifetime to look for progression of the renal cystic disease as well as angiomyolipoma along with a yearly assessment of renal function. If a patient presents with acute hemorrhage, then embolization followed by corticosteroid is the preferred therapy avoiding nephrectomy. Similarly, for growing angiomyolipoma of diameter size greater than three cm without symptoms, mTOR inhibitors are recommended. Similarly, an annual dermatological examination is recommended and an MRI of the brain should be obtained every one to three years if a patient is asymptomatic with age less than 25 to look for the development of subependymal giant cell astrocytoma. Likewise, annual examination to look for TSC associated neuropsychiatric disorders (TAND) is required and routine electroencephalogram (EEG) is required for those with suspected or known to have a seizure disorder. Also, screenings are required for the eye, heart, teeth, and lungs [8].

4. Conclusion

Tuberous sclerosis is a neurocutaneous disorder with a progressive course and can lead to debilitating complications affecting multiple systems of the human body. Thus, early diagnosis is important along with the regular surveillance of different body systems, so that early

intervention can be done, whenever required to prevent complications.

Ethical approval

N/A.

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Authors contributions

Author 1: Led data collection, concept of the study, contributed to writing the case information, Author 2: Literature review, writing initial draft, revising, and editing the manuscript, Author 3: Literature review and writing the case information, Author 4: Literature review, revising, and editing the manuscript, Author 5: Revised and edited the rough draft into the final manuscript, All authors were involved in manuscript drafting and revising, and approved the final version.

Research registration

N/A.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

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Declaration of competing interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103331>.

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