A VARIED PRESENTATION OF TUBEROSES SCLEROSIS

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Abstract

Tuberous Sclerosis should always be considered in the differential diagnosis of children presenting with behavioral problems and academic difficulty. Though seizures, mental retardation and adenoma sebaceum are considered as the triad for the diagnosis, they may not be present on initial evaluation. In such instances, the revised diagnostic criteria are often helpful for making a diagnosis. We report a case of a thirteen-year old girl who presented in psychiatry outpatient clinic with behavioral problems since early childhood and academic difficulty and was subsequently diagnosed with tuberous sclerosis based on clinical grounds and neuroimaging.

Keywords: *behavioral problems; mental retardation; tuberous sclerosis*

Introduction

Tuberous sclerosis is a neurocutaneous syndrome with a prevalence of 1 per 6000-9000 in general population.[1] It is inherited as an autosomal dominant trait with variable penetrance. Two genes responsible for tuberous sclerosis includeTSC1 (located at chromosome 9q34) and TSC2 (located at chromosome 16p13.3). TSC1 gene is responsible for familial cases of tuberous sclerosis. The disorder is characterized by a triad of mental retardation, seizures and facial angiofibromas. However, the diagnosis of tuberous sclerosis is established by following the revised criteria for tuberous sclerosis complex (TSC). [1]

Definite tuberous sclerosis complex, as defined by the 1998 consensus conference sponsored by the Tuberous Sclerosis Alliance and the National Institutes of Health (NIH), is diagnosed when at least two major or one major plus two minor features are present. Probable tuberous sclerosis complex includes one major and one minor feature. Possible tuberous sclerosis complex includes one major or two or more minor features. Major features include skin manifestations (facial angiofibromas, ungual fibroma, more than three hypomelanotic macules, and shagreen patch), brain and eye lesions (cortical tuber, subependymal nodules, subependymal giant cell astrocytomas, multiple retinal nodular hamartomas), and tumors in other organs (cardiac rhabdomyoma, lymphangioleio myomatosis, renal angiomyolipoma). Minor features include multiple randomly distributed pits in dental enamel, rectal polyps, bone cysts, cerebral white-matter migration abnormalities on brain imaging, gingival fibromas, nonrenal hamartomas, retinal achromic patches, confetti skin lesions, and multiple renal cysts.[2]

There is a high frequency of both seizures and mental retardation among individuals with tuberous sclerosis, which are present approximately 80% and 50% of the time respectively. In addition to physical and cognitive impairments, behavioral disorders such as autism are often present.[3] Behavioral

and psychiatric disorders, including autism, attention deficit hyperactivity disorder, aggression, and anxiety, are often co-morbid with TSC and intellectual deterioration may be complicated by marked emotional instability or behavioral disorders.[4,5]

In view of the problem, we here report a case of tuberous sclerosis that was initially diagnosed as a case of mental retardation with behavioral problems and attention deficit hyperactive disorder (ADHD) traits.

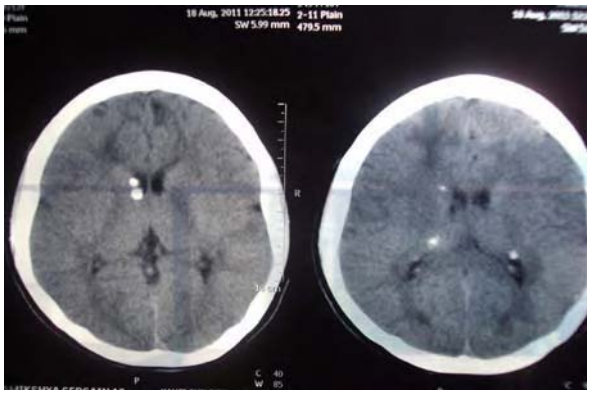
Case Report

A thirteen year old girl was brought to our department by her mother with complaints of behavioral problems and hyperactivity for eight years along with poor academic performance. Her behavioral problems consisted of not obeying commands, abusing family members verbally and physically, being inattentive and showing hyperactive behavior, easy irritability and restlessness with frequent mood swings since early years. Her birth history was complicated by post-term delivery and developmental history revealed delayed milestones, both motor and psychosocial. She started speaking at six years of age and was sent to school one year later, where her poor academic performance and delayed adaptive functioning became obvious. She grew up to be stubborn and abusive. However, her sleep and appetite was good. Her past history was significant for history of seizures at the age of one year which was treated with antiepileptic for one year. Family history was not contributory.

Her physical examination revealed hyper pigmented patchy eruptions over face, including forehead and above the nasal bridge. An initial mental state examination revealed restless and inattentive child with low intelligence and poor judgment. Psychological testing revealed IQ of 68 (< 70%) (Mallin's Intelligence Scale for Intelligence Quotient Testing) and ADHD score of 26 (>15) (Conner's Abbreviated Rating Scale for ADHD) suggestive of hyperactivity. Routine hematology and biochemical profiles were within normal limits.

She was then diagnosed with mild mental retardation with ADHD traits and was discharged on request with antidepressants. During her first follow-up visit one week later, her mother complained of new- onset seizures, typical of generalized tonic- clonic type. A detailed physical examination was done which revealed multiple shagreen patches over her trunk. Ophthalmological evaluation did not reveal any significant findings. CT scan head was advised which showed multiple bilateral subependymal calcifications and multiple cortical tubers on right frontal lobe. Her chest X- ray, abdominal ultrasonogram, Electrocardiogram and Echocardiography were normal.

With aforementioned constellation of clinical and neuroimaging features, her diagnosis was changed to tuberous sclerosis as she fulfilled the requisite criteria for the entity. She was treated with antiepileptics for seizure and atomoxetine for behavioral problems and ADHD. She has responded to these medicines and has been doing well in subsequent follow ups.



CT Scan (noncontrast) of Head Showing Multiple Subependymal Nodules

Discussion

Most children with tuberous sclerosis have epilepsy and about half of them have intellectual disability. Autism spectrum disorders and ADHD are common.[6] Neuropsychologic studies (N = 5) suggest additional deficits in executive functioning and attention in children with tuberous sclerosis complex. In addition, children with tuberous sclerosis complex are at risk of symptoms of autism (◘ 40% of patients) and exhibit an increased risk of disruptive behavior disorders (impulsivity and aggression) and social problems (poor judgment and social awkwardness).[6] Early onset of seizures (< 3 years of age; infantile spasm) and/or intractable seizures appear to be associated with an increased risk of neurodevelopmental and cognitive problems. [2] In addition to autism and mental retardation, hyperactivity, aggressive behavior and sleep disturbances have been described. Hyperactivity can occur in as much as 86% of patients and aggressive behavior occurs in 13% of patients with TSC.[7] Several studies of behavior problems in children with TSC have documented a history of infantile spasms and autism, and in one of these studies 69% of these children by the age of 5 years had behavior problems that were disruptive to family life.[7]

The present case illustrates the example of tuberosis sclerosis presenting with solely behavioral problems leading to diagnosis of Mild Mental Retardation with ADHD traits on initial presentation. In addition, this case emphasizes the importance of detailed physical examination in a child with behavioral problems and past history of seizures and delayed developmental milestones. In a developing country like ours where ordering an expensive test like neuroimaging by physicians is limited by low socioeconomic status of the patients and diagnosis is made on clinical grounds, it is important that we be aware of the varied presentation of tuberous sclerosis. Neuropsychiatrists therefore need be cautious that mere presentation of behavioral problems with academic difficulty merits detailed physical examination and neuroimaging when necessary, not to miss the diagnosis.

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