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Williams-Beuren's Syndrome: A Case Report in Prince Sultan Military City, Riyadh, Saudi Arabia 2022

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ABSTRACT

A rare familial multisystem neurodevelopmental disease known as Williams-Beuren's syndrome affects people of all racial and ethnic backgrounds and both sexes equally. A thirteen-year-old man presented to Prince Sultan Military Medical City to the psychiatric department with common mental health comorbidities and suffered from psychosis. It is a known case of WB Syndrome. It was recommended for a follow-up referral to pediatric cardiology consultation to follow up on the case and also to assess the safety of starting him on stimulants vs. Strattera for ADHD. Neurology impression is needed to figure out if there is any other medical cause of hallucination and to neurology to discover any other organic causes of such hallucinations. The condition was explained to both mothers and determined if there is any other medical cause of hallucination and the child; they are in agreement with the plan. The present study is the first Williams-Beuren syndrome in our hospital. Our results indicate that specific psychotic episodes are part of Williams-Beuren's syndrome.

Keywords: *Williams-Beuren's Syndrome, Adolescents, Psychotic episode, Hallucinations*

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INTRODUCTION

Williams-Beuren's syndrome (WBS) is a rare familial multisystem disease that impacts both sexes and all ethnic groups equally. It affects 1 in 20,000 live births. It is a neurodevelopmental disorder with the ability to affect all organ systems that is brought on by a gene deletion on chromosome 7q11.23 (Meyer-Lindenberg *et al*., 2006; Pober *et al*., 2010). This indicates that the majority of individuals who have Williams syndrome did not inherit it from a parent. Williams syndrome sufferers have a 50% chance of passing the disease on to their offspring. Clinical suspicion is necessary because genetic studies—which are not carried out by regular chromosomal analysis—are used to establish the diagnosis (Huang *et al*., 2002).

WBS is marked by elfin features, abnormalities of the eyes, teeth, heart, kidneys, and skeleton, mental underdevelopment, excessive friendliness, and rarely infantile hypercalcemia (Jones & Smith, 1975). In addition to somatic symptoms, WS is linked to neurocognitive abnormalities like cognitive development delays and deficits in number and visuospatial reasoning (Stinton *et al*., 2012). In addition, a lot of people with WS have a complex behavioral construct that mixes a lot of empathy and hypersociality with emotional problems and anxiety (Stinton *et al*., 2012). The most prevalent psychiatric comorbidity in people with WS appears to be anxiety, both trait and state anxiety, followed by sadness and attention-deficit/hyperactivity disorder (Fisher & Morin, 2017). Inappropriate social behaviors, obsessions, preoccupations, impulsivity, and distractibility were also listed as prevalent emotional and behavioral issues in WBS patients (Udwin *et al*., 1987; Einfeld *et al*., 2001). Researchers have recently looked into these issues in terms of diagnosable psychiatric illnesses (Dykens, 2003; Cherniske *et al*., 2004; Janet *et al*., 2006; Leyfer *et al*., 2006). According to the findings of these studies, people with WS have a variety of anxiety disorders, including specific phobias (35 to 54%), agoraphobia (24%), generalized anxiety disorder (12 to 16%), obsessive-compulsive disorder (2 to 12%), separation anxiety (4 to 7%), posttraumatic stress disorder (0.8 to 5%), social phobia (1.7%), and panic disorder with/without agoraphobia (0.8 to 5%).

Although there have been reports of a few cases in the same family, presumably due to autosomal dominant inheritance, the occurrence is typically sporadic in most families (White *et al*., 1977; Cortada *et al*., 1980). Due to the lack of obvious symptoms at an early age, the syndrome may go undiagnosed; however, a few years after delivery, infants frequently appear with failure to thrive, short stature, and supravascular aortic stenosis (Morris, 1999). Children may also have peripheral pulmonary stenosis, hypertension, and other elastin arteriopathies as a result of the elastin deficiency (Morris, 1999). Despite being younger in age, they may exhibit a variety of other endocrine and physical anomalies. The patient may also have generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), intellectual impairment (ID), and attention-deficit hyperactivity disorder (ADHD). (GAD) (Leyfer *et al*., 2006). Physical characteristics can frequently be used to identify the condition.

Fluorescent in situ hybridization, a test, can be used to corroborate the diagnosis. (FISH). In this experiment, DNA sequences are marked with a substance that glows under UV light.

Rarely do these patients exhibit psychotic symptoms, and there are very few accounts of such comorbidity in the literature. We describe a patient with WS who experienced a psychotic episode in this instance.

Case presentation

A thirteen-year-old man presented to Prince Sultan Military Medical City (PSMMC) with his mother to the psychiatric department for reassessment due to concerns from a geneticist as he had common mental health comorbidities and suffered from psychosis. It is a known case of WB Syndrome, which is a rare genetic syndrome. The main complaint was that he heard voices frequently. The mother stated that the main reason for this assessment is sudden changes in behavior in the form of reporting that he hears voices talking to him and harassing him, and when asked, he described them as 3 to 4 voices of men and women of different ages, hearing. Sometimes it is very clear, and other times it is muffled. The voices tell him to do non-serious things like to make tea, walk, etc. And sometimes, the voices speak negatively of him and say that others don't like him. He also reported seeing things, and sometimes humans passing by, that no one else could see, and that terrified him. It is not clear whether he suffers from paranoid delusions or not because some of the examples he gave have occurred commonly in schools. He knows the sounds aren't real, and she can't control them; they bother and distract him. The whole abnormal experience two months ago suddenly started without apparent stress. The current illness history was taken from the mother and son at the same time, and the file was reviewed for additional information as he was following up with psychiatry from 2015-2018.

The patient's IQ was tested in 2018 and reported as normal (81 in SB). Has a history of developmental delay with learning disabilities; learning remains a major concern. In addition, he has a history of coronary heart disease - pulmonary artery branch stenosis in balloon dilatation of the right pulmonary artery in December 2009. Status after fixation of the right orchid in 2010. Status after right inguinal hernia repair in 2008.

After examination, there was no other type of anxiety suggestive of mood or anxiety disorders. Regarding his ADHD, he remains talkative and restless due to poor academic performance. The mother owes this to his IQ or a genetic syndrome, but his IQ is within normal limits, and his cognitive function is generally good.

Clinical examinations and investigations

Vitality and mental and physical status measurements were reported and were mostly normal, T: 36 °C, (oral) HR: 101, (peripheral) RR: 16, BP: 139/69, WT: 42 kg and overall was pleasant and male Polite adolescent, no deformity traits with long stature, bio-stable, flaring, alert, x3 oriented, intact CN, normal tone, strength 5/5, DTR +2, -ve Babinski, normal gait. There are no hallucinatory gestures, but he does mention that he felt voices on two occasions in clinics (trumpets, calling his name). No imminent safety concerns. The vascular system was examined, blood pressure was 129/81, and heart rate was 93 bpm. The respiration rate was 20/min. The saturation od O2 was 99% in R.A. CVS: S1 + S2 + SM Grade II-III over LSB, no chest pain, palpitations, or syncope. The chest was examined, and a good A/E bill was. No additive sounds were found, and no shortness of breath or coughing. The abdomen was soft, flabby, and not muscular, with no nausea, vomiting, or diarrhea. The eyes, ears, and nose were all normal. In general, no fever, chills, sweating, or convulsions were recorded.

Chromosomal analysis on his peripheral blood specimen revealed 46, XY, a normal male karyotype with no numerical or structural aberrations. Cytogenetic analysis was carried out on G-banded chromosomal preparations. A total of 4 metaphase cells were fully analyzed up to the 550 band level. Further, 6 metaphase cells were counted to establish the modal number. In addition, FISH for 7q11.23 deletion using a probe for the Williams Syndrom critical region (ELN) at 7q11.23 and a control locus (D7S486) at 7q31 (Abbott, USA) was carried out. * Interpretation: Abnormal signal pattern detected. Only one copy of the ELN region hybridized to one chromosome 7q11.23 was observed. A total of 10 metaphase cells and 50 interphase nuclei were scored; all showed the deletion of one copy of the William critical region. This is consistent with Williams Syndrome microdeletion. After investigations, the EEG reported that the background rhythm was well-developed and well-regulated. The development of activity is 8-9 Hz, bilateral synchronous, and symmetric. The hyperventilation was done well and did not result in anything significant. The photocatalysis produced a good leader without any significant variance. Drowsiness and sleep not achieved. There is no clear and precise evidence seen in the waking record for any focal or diffuse abnormality, and also no epileptiform discharge.

Final diagnosis

William syndrome with; pulmonary artery branch stenosis, status post right pulmonary artery balloon dilatation on December 2009, status post right orchidopexy in 2010, in addition to status post right inguinal hernia repair in 2008.

Follow-up and recommendations

Hallucinosis secondary to stress in the presence of borderline IQ and developmental syndrome. Regarding the learning piece, he was diagnosed with LD and ADHD before, however, his mother is still not convinced about hallucinosis and the medications, and is worried about side effects. The patient should be observed for any recurrent abnormal behaviors or perceptions and seek the emergency room if needed. Follow up a referral to pediatric cardiology consultation was ordered to follow up on the case and also to assess the safety of starting him on stimulants vs. Strattera for ADHD. Neurology impression is needed to figure out if there are any other medical causes of hallucination. The case was also referred to neurology to discover any other organic causes of such change. The mother will observe more until the next visit as she refused to start medications at this visit. The condition was explained to both mother and child; they are in agreement with the plan.

RESULTS AND DISCUSSION

In the instance at hand, auditory and verbal hallucinations, as well as a sudden shift in prior interpersonal functioning, point to a psychotic diagnosis. Psychosis is a rare comorbidity among WS patients, according to earlier research. Therefore, a

thorough medical examination was needed to rule out what at first seemed like more likely organic causes of psychosis. Despite having obvious morphological and clinical signs of WS and psychosis in this research, the patient had maintained a generally good state of health. Furthermore, thorough investigations in the medical, laboratory, and neuroimaging fields turned up no conditions frequently associated with the organic etiology of psychosis. Although it is a rare comorbidity, psychosis has been observed in a grown man with Williams syndrome who was getting medical care. His symptoms included worsening speech stuttering and poorly organized megalomaniacal delusions [duration of treatment to onset of reaction not mentioned] (Kim *et al*., 2016). Nineteen of the 20 participants in a different study (Cherniske *et al*., 2004) had clinically significant issues with anxiety and/or depression, according to their caregiver. Thirteen subjects had moderate to extreme anxiety, according to the psychiatrist's diagnosis, and three more had mild or subclinical anxiety. Specific fear was the most typical anxiety subtype, and generalized anxiety disorder was the second most typical. (e.g., anticipatory and performance anxiety). The patient showed no symptoms of anxiety, contrary to our reports, but he did exhibit some signs of restlessness.

Around three-quarters of patients have cardiovascular anomalies. Although septal defects and other intracardiac anomalies have been documented, they are uncommon. The two defining anomalies are peripheral pulmonary artery stenosis (PPAS) and supravalvular aortic stenosis (SVAS), with other muscular arteries being less frequently affected. The patient in our research had a history of coronary heart disease (CHD) and right pulmonary artery balloon dilatation in December 2009 due to pulmonary artery branch stenosis. In a different study conducted by Cherniske (2004) in the past, three of the 20 adult patients who had cardiovascular abnormalities had pulmonary artery stenosis. In addition to VSD, mitral regurgitation, bicuspid aortic valve, mitral valve collapse, and other cardiovascular conditions were discovered (N = 1). Ten of the twelve individuals who had hypertension were being treated with medication. Additionally, ten subjects received abdominal Doppler ultrasound examinations of their mesenteric, renal, and descending aortas (Cherniske *et al*., 2004).

It was reported in previous studies that there was a significant relationship between cognitive characters and WS. In the current study, although the patient was talkative and cognitive functioning generally is good, he had an IQ measurement test in 2018 and reported to be within lower normal (81 on SB), and also he has a history of developmental delay with learning difficulties, the learning is still a major concern. A full-scale IQ was measured for each participant in a previous research, and the group's average full-scale IQ was 68 (Cherniske *et al*., 2004). In another study done by Kim *et al*. (2016), two cases of WS were recorded. The first one was an old woman aged 82 years, and she had endocrine affection associated with WS as well as atrial fibrillation. A 30-year-old man in the second instance did not have any significant cardiovascular disease. He does walk awkwardly and has minor hamstring contractures.

CONCLUSION

The present study is the first Williams-Beuren syndrome in our Hospital. Our results indicate that specific psychotic episodes are part of Williams-Beuren's syndrome.

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