

WILLIAMS SYNDROME: A CASE REPORT

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Abstract- William's syndrome (WS) is a neuro-developmental, multi-system genetic disorder characterized by distinctive personality traits. It is characterized by congenital heart defects (CHD), Skeletal and renal anomalies, cognitive disorder, social personality disorder, endocrine abnormalities, dental abnormalities, dysmorphic facies and growth retardation. FISH test is the confirmatory diagnostic test for Williams Syndrome which demonstrates the deletion of chromosomes 7q11.23.

Keywords: Williams Syndrome (WS), Dysmorphism, Mental retardation, elf-like face, FISH test, Gene mapping.

INTRODUCTION

Williams syndrome (WS) is a neurodevelopmental disorder which is caused by the deletion of genes 26-28 in the long arm of chromosome 7 in 7q11.23 with a potential impact on virtually all organ systems. It is also known as Williams-Beuren Syndrome (SWB). It was first described in 1961 by a cardiologist named John Williams and colleagues^[1].

Williams syndrome is a rare autosomal dominant multisystem genetic disorder, that occurs equally in all ethnic groups and both sexes. Clinical findings mainly includes distinct facies (elf-like face), cardiovascular abnormalities, growth retardation, connective tissue abnormalities, dental abnormalities and endocrine abnormalities. Individuals with WS often have a personality and behavior pattern that includes distractibility, restlessness, social disinhibition, excessive talking, mood swings and anxiety. WS phenotype is usually associated with a distinctive pattern of cognitive abilities but it is highly variable. Prevalence of Williams syndrome is approximately 1 in every 25,000 live births. This syndrome could account for 6% of all cases of mental retardation of genetic origin. Studies have reported that the IQ of these patients range between 40 and 90^[2].

Endocrine disorders, such as diabetes mellitus and subclinical hypothyroidism, mainly occur in adults, while hypercalcemia, which occurs with varying frequency and severity, is more common in infants. Most children with hypercalcemia are asymptomatic at the time of diagnosis, while a few develop symptoms, such as vomiting with secondary weight loss, feeding difficulties, irritability, polyuria, and convulsions^[4].

Clinical suspicion is essential because the diagnosis is set through genetic studies, which are not performed by routine chromosomal analysis. The vast majority of WS cases were detected by FISH (fluorescent in situ hybridization). Gene mapping has been capable of detecting various elastin mutations that have been attributed to cardiovascular manifestations of WS as isolated supra-aortic stenosis^[3].

CASE REPORT

A 9 years old male child second born to a NCM couple was brought with known delayed developmental milestone since 1 year age presented with complaints of not gaining weight, reduced appetite, difficulty in eating and difficulty in writing. On examination, Child is able to understand simple commands, can name family members, no abnormal movements, no repetitive behavior, can't write numbers, can't copy shapes. Child have a weight of 9.7kg and height of 88.3cm. The heart rate was 90 BPM, respiratory rate was 26 cpm. On systemic examination CVS, RS and P/A were normal.



On physical examination, the child was severely thin, have pallor, large ears, high arched palate, wide spaced nipples, webbed neck, short limbs, and avoidance of eye contact while talking. Joint contracture was also present. Hypoplastic T5 nails are present in both sides. Bilateral radio-ulnar stenosis and facial dysmorphism are present. He is dependent for performing daily activities like bathing, dressing. Birth history data shows prenatal and postnatal uneventful. Developmental delay was present in motor, speech, cognitive and social activities. Temper tendencies and aggressive tendencies were present.

The performance of the child in the given IQ test was subnormal. He was able to follow instructions. He completed the test which was designed for younger kids. But in Binet-Kamat Intelligence Test his performance was not so good. According to the performance of child in the given IQ test it has been concluded that the child is having an IQ range of 51.04 approximately with mild intellectual disability.

The child was on regular follow-up in genetic OPD and was suspecting Williams Syndrome. The child had dysmorphic features since 2 years of age, deformity of both upper limbs since 3 years of age. At 3 months of life baby had excessive crying for 1-2 weeks and refusal of feed irritability. 2D Echo was performed 2 years back to rule out congenital heart disease and the results showed normal cardiac study with 60% ejection fraction. The serum calcium, urine calcium, serum phosphorus levels, thyroid profile and USG abdomen reports were normal. No family history of psychiatry illness present. Father was having a history of seizures and took medication for 2 years.

FISH (Fluorescence in situ hybridization) test was advised since the child have small head, radio-ulnar synostosis, bilateral 5th toe hypoplastic – suspected Williams Syndrome. FISH was performed on metaphase chromosomes from cultured peripheral blood sample of this patient using LSI William Syndrome (Elastin Gene) region probe localized to 7q11.23 from Vysis Inc.,USA. The probe hybridization showed the signal only on one of the chromosome 7 at 7q11.23 region (red) in all the metaphases analysed. So we concluded that the patient sample showed the deletion for the above probe, hence positive for 7q11.23 microdeletion confirming Williams Syndrome.

DISCUSSION

A distinct elf-like face, cardiovascular abnormalities, growth retardation, connective tissue abnormalities and endocrine abnormalities are common clinical findings of Williams Syndrome^[4]. In this presenting case, mild intellectual disability is present along with delayed developmental milestones. Altered facial features were present in the patient. CVD are ruled out by performing 2D echo. Connective tissue abnormality like joint contracture is present. Thyroid profile is routinely monitored along with serum levels of calcium and phosphorus. USG abdomen and pelvis is performed to monitor internal organs functioning and it was normal. IQ test shows that child is having mild mental retardation.

Molecular cytogenetic analysis using fluorescence in situ hybridization (FISH), multiple ligation-dependent probe amplification (MLPA) and other assays can be used to confirm the diagnosis of WS^[3]. Williams Syndrome is suspected for the patient based on all the clinical features mentioned above. So FISH test is advised for the patient which is the confirmatory test for WS. The probe hybridization showed the signal only on one of the chromosome 7 at 7q11.23 region (red) in all the metaphases analysed. So we concluded that the patient sample showed the deletion for the above probe, hence positive for 7q11.23 microdeletion confirming Williams Syndrome.

CONCLUSION

There is no specific treatment for WS. In most of the cases diagnosis can be made in early childhood and the average age of diagnosis is around three and half years. Care is focused on treating specific symptoms seen in the patient. The cardiovascular system and digestive system are most affected systems in the body. If the child is having heart defect means he may need to undergo heart catheterization or surgery to repair the problem. Since WS is a genetic condition which occurs due to change in chromosomes there is no way to prevent it. Males and females are equally affected. Intellectual disability and delayed developmental milestones can also be seen in the patient.

FISH test is the important screening test for WS. It uses a fluorescent marker to determine if the genes critical to WS is present or not. Apart from that, electrolytes like calcium, phosphorus monitoring can also be done. Children with WS are often delayed in their learning and require special supports like language therapy, speech therapy, occupational therapy, physiotherapy, music therapy.

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