

WILLIAMS SYNDROME - A CASE REPORT

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ABSTRACT

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Aim: The aim of this case report is to describe the medical and dental features of an 18 year old female diagnosed with Williams syndrome (WS).

Summary: Williams syndrome is a rare, genetically determined multisystem disorder involving the cardiovascular system, musculoskeletal system, dysmorphic facies, intellectual disabilities and dental anomalies.

Key learning points: The short term and long term dental management of patients with Williams syndrome is discussed.

Keywords: Williams syndrome, diagnosis, cardiovascular abnormalities, dentofacial characteristics

1. Introduction

Williams syndrome (WS), also referred to as Williams-Beuren syndrome is a congenital, multisystem disorder resulting from the de novo hemizygous microdeletion on chromosome 7 (7q11.23). In 1961, Williams et al reported a condition with supraaortic stenosis, mental retardation, and abnormal facial features, based on their experience with 4 patients.¹ The following year, Beuren et al reported similar findings independently and expanded the phenotype to include peripheral pulmonary artery stenosis and dental malformations.² The incidence is around 1:10,000 live births. There is no gender or race predilection. Familial cases can occur, but are far less common than de novo cases.³ The deletion involves 26 to 28 genes, including the *ELN* gene, which codes for the protein elastin. This has been demonstrated to be responsible for the vascular pathology in WS. The remaining deleted genes contribute to the phenotypic findings in these patients.⁴ The disorder is characterized by growth and developmental deficiencies, cardiovascular defects (supraaortic stenosis) dysmorphic facial features (Elfin facies), hypercalcemia, renal and gastrointestinal disorders, dental anomalies and several conductive and neurological abnormalities. The characteristic facial features include wide mouth, thick lips, full prominent cheeks,

depressed nasal bridge, long philtrum, heavy orbital ridges, stellate irises, small chin and low ear implantation.⁵ The dental anomalies include microdontia, abnormal tooth morphology, hypoplastic enamel defects, anterior crossbite, tongue thrusting, excessive interdental spacing and deep or open bite. Class II and III occlusions are also commonly seen in these individuals.⁶ The clinical diagnosis of WS is based on recognition of the typical dysmorphic facial features, cardiovascular anomalies (supraaortic stenosis, pulmonary stenosis), developmental delay and hypercalcemia.

This is confirmed by the FISH (fluorescent in situ hybridization) test which detects the deletion of the elastin gene on the long arm of chromosome 7.⁵

There is no specific treatment for WS. The treatment is multidisciplinary and an individualized approach is used to address the systemic disorders and developmental and cognitive disabilities. The aim of this report is to present an 18 yr old girl with WS; her clinical characteristics, diagnosis, treatment, dental anomalies, dental management and short term and long term prevention plan.

2. Case report

An 18.3 year old female, R.S, with a diagnosis of Williams syndrome presented herself to the European University College mobile screening van

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Figure 1. Frontal View



Figure 2. Profile View



Figure 3. Intraoral Frontal View

in Dubai, United Arab Emirates.

2.1. Medical History

The patient was of Palestinian descent and was the youngest in a family of five children. The parents reported a consanguineous marriage and had no other children that were affected. According to the mother, the pregnancy and delivery were both normal. The diagnosis of WS was suspected only when the child was 11 yrs old, based on her slow learning abilities and distinct facial characteristics. A cardiology evaluation revealed mild to moderate supravalvular aortic stenosis. A FISH test was requested by the pediatrician which showed a mutation on chromosome 7, location q11.23, gene *ELN*, which confirmed the diagnosis of WS. The patient presented the following features, characteristic of the disorder:

Medical: Supravalvular aortic stenosis, low weight, low muscle tone, constipation.

Physical facial features: Small upturned nose, wide mouth, full lips, long philtrum, small chin and puffiness around the eyes.

Personality: Very engaging, overly friendly, strong expressive language skills. She had exceptional musical abilities, played the flute and was a singer.

Developmental: Learning and attention difficulties, visual - spatial deficits and difficulty with fine motor movements.

2.2. Dental History

A detailed history, extraoral examination, intra oral examination and radiographic evaluation were conducted.

Extra oral examination revealed the characteristic 'elfin facies' with broad forehead, small upturned nose, wide mouth, long philtrum, full lips and cheeks, small chin and puffiness around the eyes. (Figs 1 and 2)

Intra oral examination revealed a full complement of permanent dentition with class III molar occlusion bilaterally; generalized plaque induced gingivitis; existing amalgam fillings in teeth 16, 27 and composite fillings in teeth 17, 15, 14, 11, 21, 24, 25, 26, 36, 46. (FDI Notation System). Teeth 12,



Figure 4. Upper Occlusal



Figure 5. Lower Occlusal



Figure 6. Right Lateral View



Figure 7. Left Lateral View

23, 36 and 44 had brownish discoloration on the facial surfaces, indicative of enamel hypoplasia, which is commonly seen in patients with WS.⁶ Recurrent caries were detected on teeth 25, 26 and 36 and deep fissures were noted on teeth 34, 35, 44, 45, 17, 27, 37 and 47. Vitality tests revealed all the teeth to be vital. There was no previous history of trauma reported (Figs 3-7).

The patient had very poor oral hygiene and brushed only once a day. Her diet consisted of sugary snacks throughout the day. She had been treated by a general dentist for the existing restorations prior to being evaluated by the authors. The treatment was accomplished under local anesthesia. According to the dental history reported by the parent, the patient had sporadic dental care through out and had not seen a dentist for the past two years. The family was very keen to reestablish dental care for the patient and decided to continue long term care with the European University College dental clinic.

2.3. Radiographic

A panoramic and bitewing radiographs were taken at the first visit. The panoramic radiograph revealed no signs of supernumerary teeth or of any pathology. The third molars were all present. No interproximal decay was noted on the bitewing radiographs. (Fig. 8)

Due to the systemic complications associated with the syndrome, the patient was referred to her physician for a medical consult prior

to proceeding with any dental treatment. A cardiologist was also consulted as the patient had a history of supravalvular aortic stenosis; no antibiotics were required for SBE prophylaxis.

An informed consent was obtained from the parents of the patient for the dental treatment. A comprehensive dental treatment plan was formulated. The short term dental plan included dental prophylaxis, scaling and fluoride varnish (Duraphat, 22600ppmF) application on all the teeth. Composite restorations were planned for teeth 25, 26, 36 and on the buccal surface of 44. Resin sealants were recommended for teeth 34, 35, 44, 45 and all second permanent molars.

The patient was very concerned about the brownish discolorations on her front teeth (12, 23) which were planned to be treated with microabrasion.

The treatment was accomplished using local anesthesia. An individualized preventive plan was put in place that included frequent follow ups every 3 months for dental prophylaxis and fluoride varnish application. Twice daily brushing with fluoridated toothpaste (1450ppm F) and flossing was recommended. Diet and nutrition counseling was provided. An orthodontic consultation was recommended due to the Class 3 malocclusion.

The behavior of the patient was rated as ++ on the Frankl behavior scale.⁷



Figure 8. Orthopantomogram

She was very friendly and engaging which is the characteristic 'cocktail party' nature of individuals affected by this syndrome. She also liked to sing after every visit.

3. Discussion

Williams syndrome is a rare, genetic disorder with the occurrence of characteristic physical and mental abnormalities. The incidence of the features noted in this condition are dysmorphic facies (100%), cardiovascular disease (most commonly supravalvular aortic stenosis [80%]), mental retardation (75%), a characteristic cognitive profile (90%), and idiopathic hypercalcemia (15%)⁵ The deletion of the elastin gene is responsible for the connective tissue phenotype, which includes a hoarse voice, soft skin, lax ligaments, vasculopathy, mainly supravalvular aortic stenosis, the impression of premature aging and stiffness of joints.^{5,8} The pathogenesis of other characteristics, such as hypercalcemia, mental retardation and unique personality traits may be explained by the loss of one or more genes contiguous to the *ELN* gene.⁵ Diagnosis is often made in mid-childhood when characteristic features, cognitive profiles and cardiac findings become more apparent.

Our patient was diagnosed late at 11 yrs of age because the mother noticed that the child was a very slow learner and she was not growing as fast as her siblings. The pediatrician suspected Williams syndrome based on the child's facial characteristics and made a referral to the cardiologist who diagnosed the presence of supravalvular aortic stenosis. The diagnosis was confirmed by the FISH test. The lack of advanced care facilities in the area where the patient was born and raised in early childhood led to the delay in diagnosis.

The characteristic facial features noted in most children with WS are similar and often become more apparent with advancing age. Infants have

full cheeks and a flat facial profile, whereas older children and adults often have a long narrow face and a long neck accentuated by sloping shoulders (8). Blue- and green-eyed children with WS have a prominent "starburst" pattern to their irises (stellate iris).^{5,8}

The reported patient did present the characteristic facial features such as small upturned nose, periorbital fullness, wide mouth, full lips and small chin, in addition to an aging facial appearance and presence of multiple white hairs. She also had low muscle tone, visual spatial defects, a slight developmental delay and a very engaging personality as seen with persons affected by this syndrome.

The patient was diagnosed with supravalvular aortic stenosis which did not require any surgery. A consultation was conducted by her cardiologist before any dental treatment was performed. According to the current AAPD guidelines,⁹ antibiotics were not required for SBE prophylaxis prior to dental treatment. Individuals with cardiac manifestations should be followed regularly by their cardiologist as supravalvular aortic stenosis is an often progressive condition that may require surgical repair. Peripheral pulmonary artery stenosis is often present in infancy and usually improves over time. Because the elastin protein is an important component of elastic fibers in the arterial wall, any artery may become narrowed.⁵

In infants with WS, the presence of colic, irritability, vomiting, muscle cramps and constipation can be attributed to hypercalcemia. Symptomatic hypercalcemia usually resolves during childhood, but lifelong abnormalities of calcium and vitamin D metabolism may persist.¹⁰ Multivitamins with Vitamin D are contraindicated in these patients.

The cognitive and behavior profile is one of the key elements of this syndrome. Patients often present mild intellectual disability, strong language skills

and weakness in visuospatial construction. They also exhibit personality traits such as empathy, overfriendliness, attention problems and anxiety.⁸ This is an important factor to consider in the behavior management of children during dental treatment.

Many studies have reported increased frequency of dental abnormalities including malocclusion, hypodontia, malformed teeth, taurodontism, pulp stones, increased space between teeth, enamel hypoplasia, and high prevalence of dental caries. Affected patients usually have normal periodontium and are not predisposed to increased periodontal destruction, despite the presence of elastin gene haploinsufficiency.^{6,11}

A high caries index is reported due to the enamel hypoplasia and hypomineralization which can be attributed to the hypercalcemia seen in these individuals.¹² The reported patient presented enamel hypoplasia, dental caries and a Class III malocclusion commonly seen in this condition. Periodontal evaluation revealed a healthy periodontium. Individuals with WS can exhibit hyperacusis, which is hypersensitivity to certain sound frequencies.¹³ This is of great significance in the dental environment where instruments like the dental hand piece, ultrasonic scalers and high volume section generate high pitched sounds. The Tell Show Do behavior management approach¹⁴ is very helpful where these instruments and their sounds are first demonstrated to the patient before being used. The patient was diagnosed with anxiety disorder for which she was undergoing psychological therapy. The Tell Show Do behavior

management technique and reassurance helped allay her anxiety and she was very cooperative during the dental treatment. The risk of sudden cardiac death is 25-100 times greater in patients with WS compared to the general population¹⁵, which confers a significant risk for patients undergoing general anesthesia. This is an important consideration for clinicians planning procedures requiring general anesthesia.¹⁶

Early dental examinations and parent counseling are important in the management of individuals with WS. Preventive and dietary programs must be customized for these patients and reinforced in children with severe enamel hypoplasia, high caries rates and vulnerable cardiac condition to help minimize the risk of infection in the oral cavity.¹⁶

4. Conclusion

There is no cure for Williams syndrome. The care for these patients is mainly symptomatic and supportive. Individuals with WS need regular monitoring for potential medical and dental problems by health care professionals who are familiar with the disorder. The dental treatment protocol may require alterations or necessary precautions to be taken due to the underlying medical conditions. The pediatric dentist thus plays an important role in the overall care of these patients.

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**CV**

Dr. Neeta Chandwani is an American Board Certified Pediatric Dentist with over 25 years of experience in both clinical and academic pediatric dentistry with a core focus on treating children with special health care needs and complex medical conditions.

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She is an Examiner for the American Board of Pediatric Dentistry certification exam and is involved in various dental organizations both locally and internationally.

She has been a guest speaker at various conferences and events.

Questions**Williams Syndrome is a result of:?**

- a. *De novo* deletion on chromosome 7 (7q11.23);
- b. *De novo* deletion on chromosome 11 (11q. 7.23);
- c. Autosomal dominant condition;
- d. Autosomal recessive condition.

Which is the most common cardiac condition in patients with Williams Syndrome?

- a. Supravalvular aortic stenosis, Tetralogy of Fallot;
- b. Pulmonary artery stenosis, Ventricular septal defect;
- c. Mitral valve prolapse, Supravalvular aortic stenosis;
- d. Supravalvular aortic stenosis, Pulmonary artery stenosis.

Which of the following are dental findings in Williams Syndrome patients?

- a. Microdontia;
- b. Hypoplastic enamel;
- c. Increased interdental spacing;
- d. All of the above.

A definite diagnosis for Williams Syndrome is obtained by?

- a. Fluorescence in situ hybridization (FISH)test;
- b. Distinctive facial features;
- c. Cognitive and behavior profile;
- d. Presence of cardiovascular anomaly.