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How common is precocious puberty in patients with Williams syndrome?

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Williams syndrome is a multiple congenital anomaly syndrome associated with distinctive facies (so-called 'elfin facies') and mental deficiency (Preus 1984; Jones 1988; Morris et al., 1988). Cardiovascular disease (predominantly supravalvular aortic stenosis) (Williams et al., 1961; Morris et al., 1988) and hypercalcemia are additional variable clinical findings (Jones and Smith, 1975; Jones 1990). Recently, a submicroscopic deletion of chromosome 7q11.23 has been reported in about 90% of patients with Williams syndrome (Nickerson et al., 1995).

Precocious puberty in Williams syndrome patients has not been previously reported in the medical literature. Anecdotally, premature puberty does occur in individuals with this condition, as observed by personal experience, by other physicians treating Williams syndrome patients, and in conversations with other Williams syndrome families. We report herein on a young girl previously diagnosed with Williams syndrome and with onset of puberty at $7\frac{1}{2}$ years of age and menarche at $8\frac{1}{2}$ years of age.

Our patient is an 8 11/12 year old white girl who at birth weighed 2300 g (3rd centile) and had a length of 46 cm (3rd centile) after a full term gestation. Figure 1 shows frontal photographs of the patient at several ages. Her 14-year-old mother admitted to 'minimal' alcohol use during pregnancy and her 20-year-old father was an admitted drug user (marijuana, crack cocaine and phencyclidine). Her mother also smoked approximately 3 packs per day throughout the pregnancy. At birth she was noted to be hypotonic and was diagnosed with 'cerebral palsy'. The proposita has no known living siblings. She was adopted by her maternal great aunt at $2\frac{1}{2}$ months of age.

Her early development was marked by small size (height and weight below 5th centile) and developmental delay (crawled at 13 months, walked at 19 months). At the age of $3\frac{1}{2}$ years, she was referred for genetic evaluation because of her small size and developmental delay. At that time, she was noted to have epicanthal folds, stellate irises, prominent lips, a hoarse voice, 5th finger clinodactyly, mild hallucal valgus deformity, fine motor dyspraxia and hypoplastic tooth enamel. She was diagnosed with Williams syndrome. No cardiac or renal abnormalities were noted.

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At the age of $7\frac{1}{2}$ years, our patient began to show signs of precocious puberty, notably breast development and female Tanner II-III external genitalia with pubic hair development and increased pigment in the genital area. At that time, LH and FSH levels were obtained and were normal for her age (LH 3.1 MIU ml^{-1}, FSH 4.4 MIU ml^{-1}). Her height and weight were at the 50th centile for her age. At approximately $8\frac{1}{2}$ years of age, she developed menstrual periods and axillary hair growth. She continued her rapid growth, with her height and weight reaching the 75th centile for her age.

Chromosome studies were performed using fluorescence *in situ* hybridization (FISH) analysis with a probe which includes the elastin gene following the manufacturers' protocols (Oncor, Inc., Gaithersburg, MD). These showed a submicroscopic deletion of band 7q11.23 consistent with the diagnosis of Williams syndrome.

Although Williams syndrome and precocious puberty has not been previously associated or characterized in the medical literature, this child's condition, as well as anecdotal reports in other Williams syndrome families suggest that precocious puberty is not an unusual finding in this syndrome. Since intellectual and emotional development of children with Williams syndrome can be significantly delayed, pharmacological and hormonal intervention to delay puberty may be warranted to allow for further intellectual and emotional maturation. We urge reporting and undertaking studies of individuals with Williams syndrome and precocious puberty to discover the incidence, severity and cause in this classical genetic syndrome. In addition, this information would be helpful to the health care providers and families and to know the results of hormone repression therapy in individuals with precocious puberty and Williams syndrome.

References

Burn J (1986): Williams syndrome. J Med Genet 23: 389–395. [PubMed: 3537294]

Jones KL (1988): "Smith's Recognizable Patterns of Human Malformation". Philadelphia: W.B. Saunders.

Jones KL (1990): Williams syndrome: An historical perspective of its evolution, natural history and etiology. Am J Med Genet Suppl 6: 89–96.

Jones KL, Smith DW (1975): The Williams elfin facies syndrome. J Pediatr 86: 718–723. [PubMed: 1133652]

Morris CA, Dempsey SA, Leonard CO, Dilts C, Blackburn BL (1988): Natural history of Williams syndrome: physical characteristics. J Pediatr 113: 318–326. [PubMed: 2456379]

Nickerson E, Greenberg F, Keating MT, McCaskill C, Shaffer LG (1995): Deletions of the elastin gene at 7q11.23 occur in about 90% of patients with Williams syndrome. Am J Hum Genet 56: 1156–1161. [PubMed: 7726172]

Pagon RA, Bennett FC, LaVeck B, Stewart KB, Johnson J (1986): Williams syndrome: features in late childhood and adolescence. Pediatrics 80: 85–91.

Preus M (1984): The Williams syndrome: objective definition and diagnosis. Clin Genet 25: 422–428. [PubMed: 6723102]

Williams JCP, Barratt-Boyes BG, Lowe JB (1961): Supravalvular aortic stenosis. Circulation 24: 1311–1318. [PubMed: 14007182]

Fig. 1.

Frontal·photographs of our female patient with Williams syndrome and precocious puberty taken at 4 years of age (top, left), at 5 years of age (top, right) and at 9 years of age (bottom).