# Van Der Woude Syndrome family tree

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## Objective

Van der Woude syndrome (VW syndrome) is an autosomal dominant syndrome that affects the development of the face. The cause is mutation in the IRF6 gene, which is located in the long arm of chromosome 1 (1q32. 3-q4). The gene provides instructions for making a protein that plays an important role in early development. The protein is active in cells that give rise to tissues in head, face, skin and genitals. Children with VW syndrome are born with a cleft lip of palate, depressions (pits) near the center of the lower lip, which is usually moist, due to the presence of salivary and mucous glands in the pits. Hypodontia (absent teeth) is the most common anomaly. They also have an increased risk of delayed language development, learning disabilities and other mild cognitive problems, but IQ is usually within normal ranges. The popliteal pterygium syndrome (PP syndrome) is autosomal dominant genetic malformative disorder characterized by cleft lip, with or without cleft palate, contractures of the lower extremities, abnormal external genitalia, syndactyly of fingers and toes, and a pyramidal skin fold over the hallux nail. Syndrome is associated with mutations in the IRF6 (1q32. 2-q32. 3) gene, involved in the formation of connective and epithelial tissues. Growth and intelligence are expected to be normal, corrective surgeries are available. However, the prognosis for physical activity depends on the severity of the pterygium. Genital anomalies may cause infertility.

### Methods

This is a case report.

#### Results

In our family, many clinical conditions due to the VW and PPS syndrome were identified. Grandmother had 6 daughters. 4 of them were stillborn, 2 were healthy. One of them had stillborn son. Another daughter had 4 children, one, girl, died 5 days after she was born, another girl was born healthy but has cognitive problems and learning dissabibilities. One son was born healthy, another have had pits on the lower lip, troubles with salivary gland, and speaking problems due to the healed up tongue. He has 2 children, one healthy son and one daughter. She had pits on the lower lip, troubles with salivary glands, hypodontia, 4 missing teeth. In both of them VW syndrome had been confirmed with genetic tests. She was pregnant three times. Her first born child (born in 2011) had congenital palatoschisis, pits on the lower lip, troubles speaking and chriptorchism. VW syndrome confirmed. Her second pregnancy in the year 2013 ended tragically, with death of foetus at 36weeks due to preeclampsia and placental abruption. Due to clinical features, foetus may have had PPS. Her third pregnancy ended with a c section at 32 weeks because of preeclampsia. The new-born had cleft upper and lower lips, and pits on the lower lip. VW syndrome confirmed. So far she is developing fine. At the age of 8 months she had reconstructive operation. Now she is even more beautiful girl. Genetic tests were made in previously described individuals. Mutations in gene IRF6 (16C>T) have been confirmed in 5 of them, 4 have VW syndrome, 1 have PP syndrome.

### Conclusion

Van der Woude syndrome and popliteal pterygium syndrome are an autosomal dominant syndromes, mutation in gene IRF6 is present. Both syndromes are clinically associated with cleft lips and palate, pits on lower lips and palate, salivary gland and speaking problems, missing teeth, learning disabilities and other mild cognitive problems. PP syndrome can affect extremities and external genitalia. In our family, mutation in gene IRF6 have been diagnosed with genetic testing, 5 members have been positive, 4 have VW syndrome, 1 have PP syndrome. Face development anomalies can be diagnosed early, in utero with ultrasound. When a child is at least 2-3 months old, oral and maxillofacial surgeries can fix palate, lips and dental anomalies. Today, the prognosis and treatment of individuals with VW syndrome is excellent.

Prognosis of individuals with PP syndrome depends on severity of pterygium, genital anomalities can cause infertility, otherwise prognosis of growth and intelligence is good.