A case of familial Van der Woude syndrome and Popliteal Pterygium syndrome

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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 or palate, depressions (pits) near the center of the lower lip, which are 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, synechialty of fingers and toes, and a pyramidal skin fold over the hallux nail. The 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. Our goal is to report a familial case of these syndromes.

Methods
This is a case report.

Results
In our family, many clinical conditions due to the VW and PPS syndrome were identified. My partner had pits on the lower lip, troubles with salivary gland and speaking problems due to the healed up tongue. Our daughter also had pits on the lower lip, as well as troubles with salivary gland and hypodontia (4 missing teeth). Her first born child (born in 2011) had congenital palatoschisis, pits on the lower lip, troubles speaking and chriptorchism. Her second pregnancy in 2013 ended tragically with death of fetus at 36 weeks due to preeclampsia and placental abruption. Due to clinical features, foetus may have had PPS (picture 1 and 2). Her third pregnancy ended with a cesarean section at 32 weeks due to preeclampsia. The new-born had cleft upper and lower lips and pits on the lower lip. So far she is developing fine. At the age of 8 months she had reconstructive operation. 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 has PP syndrome.

Conclusion
Van der Woude syndrome and popliteal pterygium syndrome are autosomal dominant syndromes and both have mutation in gene IRF6. 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 has 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 will depend on severity of pterygium and if genital anomalies will cause infertility, otherwise prognosis of growth and intelligence is good.