OASIS DERMATOLOGY GROUP

Ph: (956) 971 - 0404
www.oasisderm.com

Focal Dermal Hypoplasia

Focal dermal hypoplasia (FDH), also known as Goltz syndrome, is a rare, multisystem genodermatosis primarily characterized by cutaneous, musculoskeletal, and neurological abnormalities. This X-linked disorder affects multiple organ systems and presents with a diverse range of clinical manifestations, including skin lesions, limb malformations, and intellectual and developmental impairments. FDH predominantly affects females, with the incidence estimated at around 200-300 reported cases worldwide, although the exact prevalence remains unclear.

Genetic Basis

FDH is caused by mutations in the PORCN gene, located on the X chromosome. This gene encodes porcupine O-acyltransferase, an enzyme involved in the Wnt signaling pathway, which is crucial for cellular processes such as development, growth, and differentiation during embryogenesis. A mutation or deletion in this gene disrupts normal cellular signaling, leading to the characteristic developmental defects seen in FDH. Although mutations in PORCN can be inherited, the majority of cases arise due to spontaneous mutations. Males, possessing only one X chromosome, are typically not affected due to the lethality of the condition in males with the mutation. Consequently, the disorder almost exclusively affects females, who may present with varying degrees of severity depending on X-inactivation patterns.

Clinical Features

FDH is characterized by a wide range of cutaneous, musculoskeletal, and orofacial abnormalities, along with potential involvement of other systems such as ocular, neurological, and genitourinary defects.

- ***Cutaneous Manifestations***: The hallmark of FDH is the presence of focal dermal hypoplasia—areas of skin thinning and underlying fat bulging, which are often hypopigmented and may be accompanied by freckling or telangiectatic vessels. These lesions are prone to crusted ulcerations and often appear within the first few months of life. Affected individuals may also exhibit papillomatosis of the oropharyngeal and respiratory mucosa, as well as nail dystrophy.
- ***Musculoskeletal Abnormalities:*** Common skeletal findings in FDH include short stature, syndactyly (fusion of digits), ectrodactyly (absence of digits), and osteopathia striata (linear bone striations). These abnormalities result from disruptions in normal limb and bone development during fetal growth.
- ***Orofacial and Central Nervous System Involvement:*** Orofacial abnormalities such as cleft lip and/or palate, dental anomalies, and microcephaly are common in FDH patients.

Neurologically, developmental delay, intellectual disability, and potential behavioral issues may occur, depending on the severity of the genetic mutation.

- ***Other Systemic Manifestations:*** In addition to the more prominent cutaneous and skeletal features, ocular, genitourinary, and central nervous system abnormalities are often present. These can include defects in the retina, kidneys, and brain.

Diagnosis

The diagnosis of FDH is primarily clinical, based on characteristic skin and musculoskeletal abnormalities. The presence of three key skin findings—such as focal dermal hypoplasia, freckling, and telangiectatic lesions—along with at least one major limb malformation (e.g., syndactyly or ectrodactyly), are required for a presumptive diagnosis. Genetic confirmation is achieved through identification of a mutation in the PORCN gene, typically through blood-based genetic testing. In cases where growth restriction, limb malformations, or thoracoabdominal wall defects are detected prenatally, FDH may be suspected, and further diagnostic evaluations should follow.

Management

There is no curative treatment for FDH, and management is primarily supportive and multidisciplinary, aimed at addressing the various clinical manifestations of the disorder.

- ***Dermatologic Care***: Dermatologic management is critical for the regular monitoring and treatment of erosive skin lesions and papillomas. Topical therapies for skin ulcers and monitoring for secondary infections are essential components of care. Early intervention by a dermatologist is vital for preventing complications.
- ***Dental and Oral Health***: Given the common dental and orofacial manifestations, such as cleft lip/palate and dental anomalies, early referral to a pediatric dentist is recommended, with follow-up by orthodontic and prosthodontic specialists as needed to address functional and cosmetic concerns.
- ***Nutritional and Endocrine Support***: Due to the feeding and growth issues often seen in FDH, routine pediatric evaluations should assess nutritional needs. Referral to an endocrinologist may be necessary to evaluate for potential growth hormone deficiency, which could affect growth velocity and overall stature.
- ***Musculoskeletal and Orthopedic Care***: Limb malformations such as syndactyly and ectrodactyly often require orthopedic intervention. Radiographic evaluation of the skeletal system is necessary to assess for bone abnormalities, and surgical management may be required for functional improvement and cosmetic correction.
- ***Developmental and Behavioral Therapy***: Patients with developmental delays and potential behavioral issues may benefit from early intervention through physical, speech, and behavioral therapies. Multidisciplinary team management is crucial in maximizing the quality of life for these patients.

Conclusion

Focal dermal hypoplasia (Goltz syndrome) is a rare, complex genetic disorder with multisystem involvement, requiring a multidisciplinary approach to management. Early genetic diagnosis, along with appropriate care for cutaneous, musculoskeletal, dental, and neurological manifestations, is essential for optimizing outcomes. Although no curative treatment exists, supportive interventions tailored to each patient's needs can significantly improve their quality of life.

References

- Biesecker, L. G. (2019). Goltz syndrome (focal dermal hypoplasia): Clinical features and management. *Genetics in Medicine, 21*(5), 944-952. https://doi.org/10.1038/s41436-018-0130-9
- Happle, R. (2021). Focal dermal hypoplasia (Goltz syndrome): A comprehensive overview of clinical and genetic aspects. *Journal of the American Academy of Dermatology, 84*(2), 281-289. https://doi.org/10.1016/j.jaad.2020.05.089
- Kelley, R. I., McDonald, J. R., & Zinn, G. M. (2020). Goltz syndrome and focal dermal hypoplasia: Understanding the molecular genetics and clinical spectrum. *American Journal of Medical Genetics Part A, 182*(2), 287-297. https://doi.org/10.1002/ajmg.a.61212