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Case Reports

Focal Dermal Hypoplasia (Goltz Syndrome) in a 4-Year-Old Girl: A Rare Case Report

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Abstract

Background: Focal dermal hypoplasia (FDH) is a rare X-linked dominant genetic disorder characterized by dermal hypoplasia along Blaschko's lines and multisystem involvement.

Case Presentation: We reported a 4-year-old girl who presented with facial asymmetry, alopecia, polydactyly, oral papillomas, and linear hypopigmented atrophic skin lesions following Blaschko's lines, along with nystagmus and proptosis of the eyeball. Whole exome sequencing, performed in the patient and both parents, identified a heterozygous chrX:48372971 NM_203475.3:c.904G>T (p.Val302Phe) variant in the *PORCN* gene, which is essential for Wnt protein secretion and signaling.[1] The variant was absent in both parents, indicating a de novo event. According to the American College of Medical Genetics and Genomics (ACMG) criteria, the variant was classified as a Variant of Uncertain Significance (VUS) due to limited available evidence.[2] However, the strong phenotypic concordance with FDH and the de novo occurrence support its potential pathogenicity and may justify reclassification toward likely pathogenic.

Conclusion: The clinical and genetic findings support a diagnosis of FDH (Goltz syndrome). This case represents the first reported case in Indonesia and highlights the importance of integrating genotype and phenotype in interpreting VUS and contributes to the expanding spectrum of *PORCN* mutations.

Keywords: *Focal dermal hypoplasia; Goltz syndrome; Facial asymmetry; Papilloma*

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INTRODUCTION

Focal dermal hypoplasia (FDH), also known as Goltz syndrome, is a rare genetic disorder with an X-linked dominant inheritance pattern. It was first described by Liebermann in 1935 as *atrophodermia linearis maculosa et papillomatosis congenitalis* (linear atrophic macular and papillomatous congenital dermatosis), and the term "FDH" was later coined by Goltz in 1962.[3] The condition is characterized by dermal hypoplasia following Blaschko's lines, subcutaneous fat herniation, telangiectasia, hypopigmentation, skeletal anomalies such as split hand or foot ("lobster claw"), ocular abnormalities, and oral manifestations including dental and mucosal defects.[4] FDH is usually lethal in male fetuses, making it predominantly a disease of females.[5] The estimated prevalence ranges from 1.2 to 1.6 cases per million. In a previous case report, the patients' ages ranged from 4 to 27 years. Among four patients with different confirmed PORCN variants, three cases were identified as *de novo*.[6,7]

This report describes the first genetically confirmed case of FDH in Indonesia, highlighting her distinctive clinical features. Pediatric FDH is infrequently documented, particularly in this region. The identification of a heterozygous PORCN variant emphasizes the novelty of this case and the importance of integrating genetic and clinical findings for accurate diagnosis.

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CASE REPORTS

This is a single-patient case report of a 4-year-old girl diagnosed with Focal Dermal Hypoplasia (FDH). She was referred to our pediatric nutrition and metabolic disease clinic for evaluation and monitoring of multiple congenital anomalies. Comprehensive clinical evaluation, including physical examination, imaging studies, and genetic testing, was performed. Whole exome sequencing was conducted on the patient and both parents. Written informed consent was obtained from the patient's parents for publication of clinical data, genetic findings, and clinical photographs. This case report was conducted in accordance with institutional and ethical standards.

She had presented with left-sided facial asymmetry since birth, difficulty opening her left eye, and a smaller left eyeball. An extra finger was noted on her left hand, and the skin on the left side of her body had been prone to wounds and abrasions since birth. She experienced intermittent oral lumps and difficulty gaining weight. There was no close relationship between the patient's parents. Both of the patient's siblings were female, and there were no previous or current cases of similar conditions in the family other than the patient. On anthropometric examination, the patient weighed 8.3 kg and was 97 cm tall, with an upper arm circumference of 11.5 cm. According to WHO anthropometric curve, the patient was severely underweight, underheight, and malnourished.

Physical examination revealed a progeroid facial appearance and rib cage deformity. A characteristic physical examination of this patient revealed low-set ears, sparse eyebrows, flattened malar bones, short palpebral fissures, facial asymmetry, protruding ears, short philtrum, downturned corners of the mouth, thin vermillion upper lip, mandibular prognathism, sparse scalp hair, and preaxial polydactyly of the thumb and overlapping toes. The patient had recurrent oral papillomas despite previous excision located on the lip mucosa, inside the oral cavity, and in the pharynx. Histopathological examination confirmed squamous papilloma. Skin examination revealed macules and atrophic hypopigmentation patches with a linear pattern following Blaschko's lines on the front and back of the trunk and on the extremities.

Ophtalmological evaluation identified nystagmus, microcornea, and proptosis bulbi. Hearing assessment using BERA revealed profound sensorineural hearing loss. Plain CT scan of the patient's head was within normal limits. Bone survey demonstrated multiple lytic lesions in the calvaria and linear opacities in the femur and tibia, forming a zebra stripe sign or osteopathia striata. Echocardiography examination showed mild PR and no other abnormalities. Complete laboratory tests, electrolytes, liver and kidney function were within normal limits, and urine analysis was also normal.

Genetic testing via whole exome sequencing was performed on the patient and both parents, with results indicating PORCN gene findings pointing to focal dermal hypoplasia and additional findings of the SARS1 gene pointing to neurodevelopmental disorder with microcephaly, ataxia, and seizures (Nedmas). However, the combination of clinical findings, supporting examinations, and the patient's whole exome results point more toward a diagnosis of FDH or Goltz syndrome. The patient continues regular follow-up to visit the nutrition and metabolic disease clinic for monitoring of their condition, nutritional status, growth and development, and supportive management.

DISCUSSION

Focal dermal hypoplasia (FDH), or Goltz syndrome is an X-linked dominant disorder that is lethal in males in utero. Approximately 90% of affected individuals are female, usually carrying heterozygous or mosaic mutations in the *PORCN* gene, while male cases are rare and typically result from mosaic mutations.[8] Mutations in *PORCN*, which encodes a protein essential for Wnt signaling, disrupt dermal development and lead to the wide spectrum of clinical manifestations observed in FDH. Most cases arise de novo, with familial inheritance reported in only a small proportion of patients (only about 5%).[8] The prevalence statistics are summarized in Table 1.

Genetic testing identified the NM_203475.3:c.904G>T (p.Val302Phe) variant in the PORCN gene, which is a missense mutation causing a substitution of valine to phenylalanine at position 302 of the protein. The proband is heterozygous, while this variant is not found in the parents (NA), suggesting a possible de novo mutation. This variant has not been previously reported and is classified as a Variant of Uncertain Significance (VUS) according to the criteria of the American Society of Medical Genetics and Genomics (ACMG), meaning that its clinical status is currently not fully understood. Despite the VUS classification, the patient's phenotype is compatible with FDH, highlighting the relevance of genotype–phenotype correlation in interpreting novel variants.

Dermatological manifestations in FDH are variable. Linear atrophic skin lesions following Blaschko's lines are common, while papillomas of the lips and oral mucosa are reported in nearly half of patients.[9,10] Alopecia is frequent but variable feature, and fat herniation lesions occur in roughly 46% of cases, although some patients may lack this finding. The heterogeneity in cutaneous presentation emphasizes the importance of evaluating each patient individually and considering genotype–phenotype correlations when interpreting novel or uncertain genetic variants.

Findings in the skeletal system in FDH are variable and usually asymmetrical. Approximately 60–70% of cases report involvement of the hands and feet, with abnormalities such as syndactyly, hypoplasia or absence of fingers, ectrodactyly, and polydactyly, either singly or in combination. A characteristic deformity that is often encountered is the "lobster claw" type. Additionally, approximately 30% of patients exhibit asymmetry in the size and shape of the face, trunk, or extremities, and 15–20% experience scoliosis. Radiological examination can help detect abnormalities, such as osteopathia striata (longitudinal lines on the metaphysis of long bones), which is reported in approximately 20% of gene carriers; although not pathognomonic, this finding can aid in the

diagnosis of patients with minimal symptoms. Vertebral abnormalities such as spina bifida occulta and clavicle dysplasia may also be found in some cases, while long bone reduction defects, limb length differences, and giant cell bone tumors have been reported in some patients.[9,11] The phenotypic spectrum is broad, and some patients may not exhibit all features, reflecting the heterogeneity of FDH. Our patient's skeletal features fall within this reported spectrum, illustrating the heterogeneity of FDH.

Other manifestations of FDH can involve the genitourinary, gastrointestinal, nervous, and ear-nose-throat (ENT) systems. Genitourinary abnormalities, arising during the 4th–6th week of embryogenesis, may include renal agenesis, renal ectopia, and uterine malformations such as bicornuate uterus.[12] ENT involvement may present as mixed hearing loss from congenital ossicular abnormalities, dysphagia, or airway obstruction due to mucosal papillomas.[13]

Growth, nutritional, and gastrointestinal disorders are common. Children and adults with FDH often have lower birth weight and length, with reduced head circumference, height, weight, and body mass index (BMI) compared to the reference population. About 75% of patients experience one or more issues, including short stature, underweight, oral motor dysfunction, gastroesophageal reflux, gastroparesis, or constipation. These findings confirm that growth disorders in FDH are chronic and not solely the result of progressive growth decline, but rather have been present since early life.[14]

Neurocognitive function is usually normal, but approximately 15–20% of cases show mild to moderate intellectual impairment, sometimes accompanied by structural brain abnormalities or epilepsy.[15,16] Histologically, skin lesions show dermal thinning from connective tissue hypoplasia, superficial penetration of subcutaneous fat, increased vascularization in the papillary dermis, and epidermal hyperplasia in papillomatous areas, explaining the characteristic atrophic skin, fat herniation, and papillomas.[11,17]

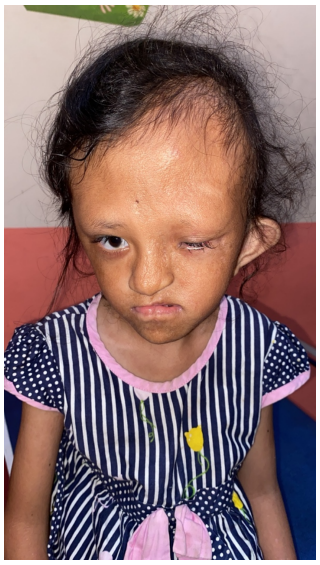

Figure 1. Facial asymmetry in the patient, accompanied by sparse eyebrows, malar flattening, protruding ears, short philtrum, thin upper vermillion lip, sparse scalp hair, and proptosis of the eyeball.

These features correspond to the patient's condition, including profound bilateral hearing loss (planned for BERA evaluation), malnutrition, and short stature. Cognitive function appears normal based on parental reports, though formal IQ testing has not been performed, and a skin biopsy has not yet been conducted.

Comparison with previously reported cases from South and East Asia shows that the clinical features of FDH observed in this patient are consistent with those described in other Asian populations. A case from India reported a 5-year-old girl with typical cutaneous findings including linear skin atrophy, fat herniation, papillomas, and skeletal anomalies such as polysyndactyly, facial asymmetry, and osteopathia striata, while systemic involvement was variable.[18] Similarly, a Taiwanese girl presented with hypopigmented atrophic macules along Blaschko's lines, fat lobule-like protrusions, nail dystrophy, syndactyly, and ear deformities, although no PORCN mutation was detected, highlighting possible postzygotic mosaicism or intronic/splice-site variants. These reports support that FDH manifestations are broadly comparable across Asian populations, though some phenotypic variations such as the presence or absence of specific skeletal or mucocutaneous anomalies may occur.[17]

From a clinical management perspective, this case highlights the importance of a multidisciplinary approach, including regular monitoring of growth and nutritional status, as well as evaluation for potential systemic involvement such as hearing, skeletal, and gastrointestinal abnormalities. Early supportive interventions are essential to optimize long-term outcomes. In addition, genetic counseling is recommended for the family. Although the identified variant is likely de novo, the possibility of germline mosaicism cannot be completely excluded; therefore, counseling regarding recurrence risk and future pregnancies is important.

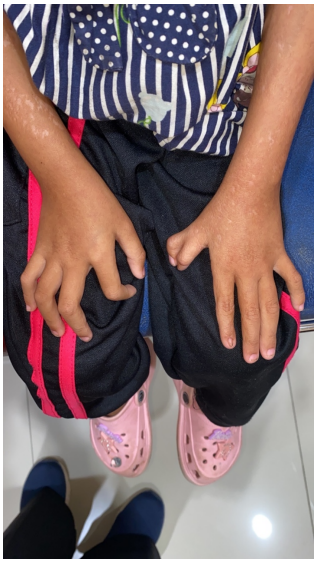

Figure 2. Polydactyly of the patient's life hand

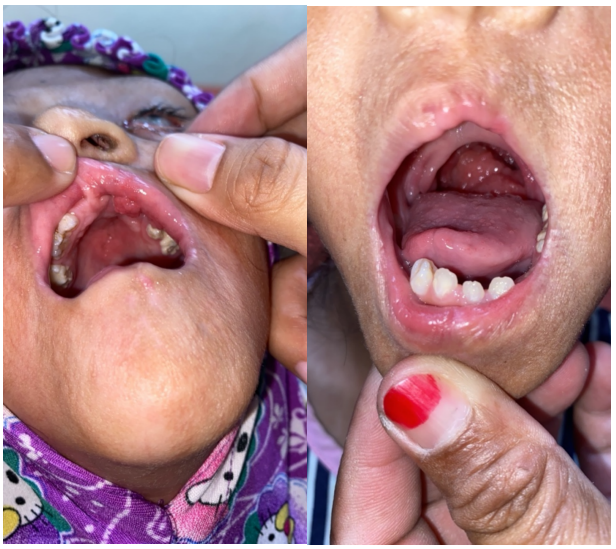

Figure 3. Ruccerent paillomas in the oral, lip mucosa, and extending to the pharynx

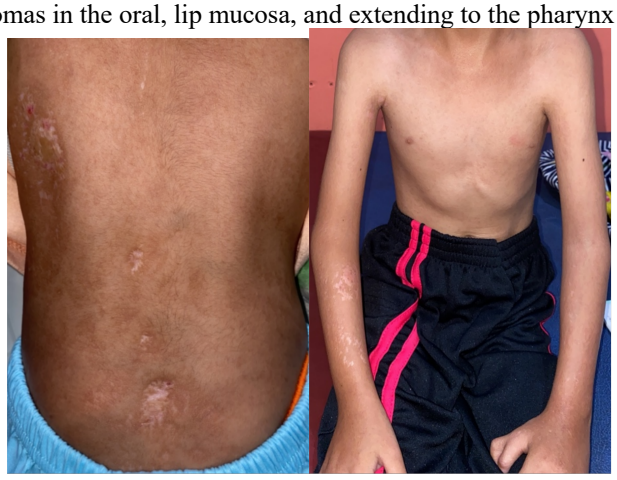

Figure 4. Macules and antrophic hypopigmented patches arraged in linnear pattern following Blaschko's lines

Table 1. Clinical Features of FDH: Literature vs. This Case

Clinical Feature	Literature Prevalence / Notes	Findings in This Patient	Comments / Variability
Sex	Female ~90%, Male rare (usually mosaic)	Female	Consistent with expected prevalence
Inheritance	De novo ~95%, Familial ~5%	Likely de novo (parents negative)	Variant classified as VUS
Skin lesions	Linear atrophic lesions along Blaschko's lines, papillomas ~50%, fat herniation ~46%, alopecia variable	Linear atrophic lesions, recurrent oral papillomas, alopecia; fat herniation absent	Highlights phenotypic heterogeneity
Skeletal anomalies	Hands/feet 60–70%, "lobster claw" type, facial/trunk asymmetry 30%, scoliosis 15–20%, osteopathia striata 20%	Polydactyly of left hand, facial asymmetry, osteopathia striata	Within reported spectrum, illustrating variability
ENT / Hearing	Mixed hearing loss occasionally reported	Profound sensorineural hearing loss	Matches literature, though rare
Growth / Nutrition	Short stature, underweight common	Severely underweight and underheight	Chronic growth disorder consistent with FDH
Neurocognition	Mostly normal; 15–20% mild-moderate impairment	Appears normal per parents	IQ not formally tested yet
Other systemic anomalies	GU, GI, cardiac anomalies possible	None reported	Absence shows variable expressivity

This case report has several limitations. First, the identified variant is classified as a Variant of Uncertain Significance (VUS), and functional studies were not performed to confirm its pathogenicity. Second, some evaluations, including formal cognitive assessment and skin biopsy, were not conducted. Despite these limitations, the combination of clinical features and genetic findings provides valuable insight into the phenotypic spectrum of FDH and supports the importance of genotype–phenotype correlation in rare disorders.

Informed consent was obtained from the patient's guardians. Formal ethical approval was not required according to our institutional guidelines.

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CONCLUSION

FDH has no causal therapy; management is supportive and multidisciplinary. This case reports the first genetically confirmed pediatric FDH in Indonesia, demonstrating classical cutaneous and skeletal features with a heterozygous PORCN variant. Despite VUS classification, genotype–phenotype correlation supports the clinical relevance.

As the first genetically confirmed pediatric FDH case in Indonesia, this report highlights the importance of genetic testing in rare multisystem disorders for accurate diagnosis and counseling. It also emphasizes the need for multidisciplinary management and long-term follow-up to optimize patient outcomes, as well as genetic counseling for family members regarding recurrence risk.

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