# LENS SUBLUXATION WITH STRETCHED CILIARY PROCESSES IN A GIRL WITH GOLTZ SYNDROME

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## ABSTRACT

**Purpose**
To report lens subluxation with additional stretching of the ciliary processes as ocular features of Goltz syndrome.

**Methods**
Case report.

**Results**
A now 4-year old girl was diagnosed at birth with Goltz syndrome. Best-corrected visual acuity was 1/60 in both eyes. Slitlamp examination showed bilateral iris colobomata and inferior subluxation of the lens with abnormally stretched ciliary processes. Funduscopy revealed bilateral chorioretinal and optic disc colobomata.

**Conclusions**
Ocular anomalies are often associated with Goltz syndrome. Although ectopia lentis is a known ocular feature, this is the first case of lens subluxation with additional, abnormally stretched ciliary processes.

## KEYWORDS

Goltz syndrome, Lens subluxation, stretched ciliary processes

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## INTRODUCTION

Focal dermal hypoplasia (FDH), also known as Goltz syndrome, is a rare developmental multisystem disorder affecting tissues of ectodermal and mesodermal origin, causing a highly variable spectrum of anomalies (1). Characteristically, patients show a combination of dermal hypoplasia, skeletal, dental, genito-urinary and ocular anomalies (1, 2). Goltz syndrome is transmitted as a dominant X-linked trait. As such, a large majority of affected patients are female with heterozygous mutations or deletions of the PORCN gene (Porcupine), but male patients who are mosaic for a mutation in this gene have also been described (3, 4). Spontaneous abortions are more frequent in families with FDH (1).
In this case, we illustrate the different clinical features of Goltz syndrome with special focus on the ophthalmic features, which occur in 40% of cases (1, 6). The most frequent ocular findings are colobomata of the iris and chorioretina, and have been reported in one third of cases. Less frequent ocular signs include microphthalmia/anophthalmia, strabismus, nystagmus and ectopia lentis, as well as corneal clouding, aniridia, heterochromia, and optic atrophy.

## CASE REPORT

A 4 year-old girl was referred for an ophthalmic examination.
She was the first child of non-consanguineous parents, born after 37 weeks of gestation by spontaneous delivery with a birth weight of 2,435 grams and a length of 47 cm. The mother had not taken any medication during pregnancy, and there was no history of previous miscarriages.
The diagnosis of Goltz syndrome was made clinically at birth on the basis of the following congenital defects: linear dermal hypoplasia on the right side of the chest and abdomen, right elbow and left shoulder, brittle and sparse hair, ectrodactyly of the third ray of left hand, hypoplasia of the nails, clinodactyly of the 5th finger of the right hand, as well as syndactyly of the 4th and 5th finger of the left hand and left foot, notched gingiva and an anteriorly displaced anus.
A chest X-ray showed a midclavicular hypoplasia and ultrasonography of the kidneys revealed bilateral hypoplastic kidneys with vesico-ureteral reflux. Ultrasonography of the heart and brain MRI were normal.

Ocular examination at birth revealed mild facial asymmetry with hypertelorism. There was a horizontal nystagmus with a moderate esotropia of the right eye. On slitlamp examination, a bilateral inferior iris coloboma was seen. Fundoscopy showed bilateral chorioretinal colobomata, involving the optic discs.
The girl had a normal karyotype.

The diagnosis of Goltz syndrome was confirmed by molecular analysis: a de novo missense mutation was identified in exon 5 of PORCN gene (c.502G>A, p.G168R).
There were no other family members suffering from the same condition.

The girl had a normal psychomotor development: she started walking at the age of 15 months and the first spoken words came at the early age of 8 months. She has undergone a first stage surgical correction of the ectrosyndactyly of the left hand at the age of one year, with more surgery planned later.

An obstructed right lacrimal canal required silicone tubes in the lacrimal canal at the age of 6 months. They were taken out 3 months later.
At the age of 4 years, best-corrected visual acuity (BCVA) was 1/60 in both eyes. At that time, slitlamp examination revealed bilateral inferior lens subluxation in combination with abnormal elongated ciliary processes. Fundoscopy confirmed the chorioretinal coloboma with pale discs seen earlier.

## DISCUSSION

Focal dermal hypoplasia is a rare meso-ectodermal disorder that is transmitted as a dominant X-linked trait. About 90% of clinically affected subjects are female. There is a high frequency of spontaneous abortions in the offspring of heterozygous women, probably representing lethality in male foetuses; only somatic mosaicism seems compatible with life in

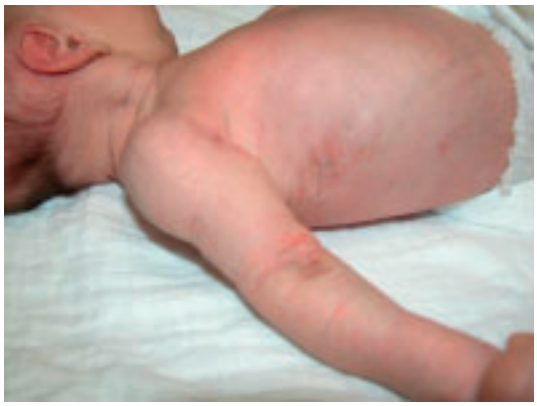


*Fig. 1:* Dermal hypoplasia with hyperpigmentation at birth

*Fig. 2:* Syndactyly of 4th and 5th finger, clinodactyly of 5th finger and hypoplasia of the nails at age 4

newborn males (1-6). In 2007, Grzeschik et al (3) and Wang et al (4) independently reported mutations in the gene PORCN at Xp11.23, segregating with FDH. The PORCN gene is a member of the porcupine (Porc) gene family that encodes Porc proteins, localized to the endoplasmic reticulum. They are membranebound O-acyltransferases that stimulate the secretion of wingless (Wnt) family of proteins through post-translational lipid modification (N-palmitoylation and Oacylation) (3, 4).

The hallmark of this disorder is *dermal hypoplasia,* found in all patients. Underdevelopment of dermal connective tissue results in localized herniations of subcutaneaous fat into the epidermis. These areas are often accompanied by hyperor hypopigmentation, telangiectasis, and linear streaking. The skin is thinned in these areas and is subject to ulceration following minor trauma (1-6). Our patient had linear dermal hypoplasia on the right side of the chest and abdomen, right elbow and left shoulder (*Fig. 1*).

*Skeletal abnormalities are* the second most common systemic features, noted in 70-80% of the patients (1,2,5). Syndactyly, brachydactyly, oligodactyly, short stature, osteopathia striata, scoliosis, and clinodactyly are among the more frequent skletetal defects that have been described in this syndrome.

Brachydactyly, ectrodactyly of third ray of the left hand, syndactyly of the 4th and 5th finger (*Fig. 2*) and toe, short phalanges, absent toenails and fingernails, and midclavicular hypoplasia were present in our patient.

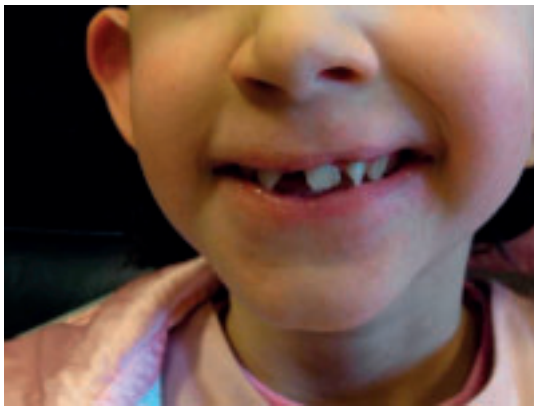


*Fig. 3:* Abnormal quality and positioning of teeth at age 4

*Fig.4:* mild facial asymmetry with hypertelorism at age 4

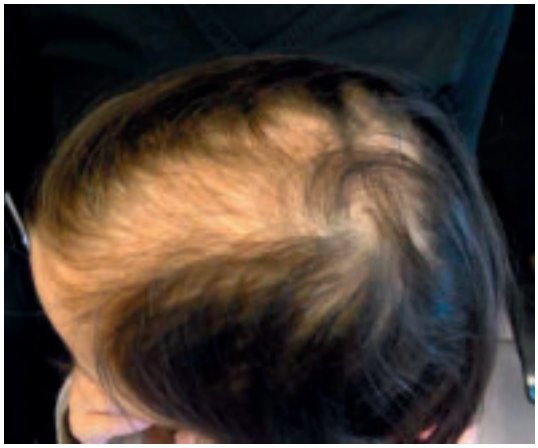


*Fig. 5:* Brittle and sparse hair at age 4

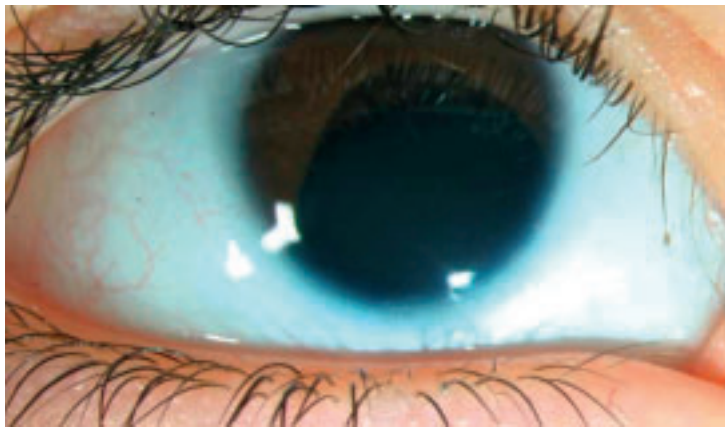
The *facial appearance* is characteristic in FDH. The face and/or skull are typically asymmetric and scalp hair is scarce and brittle. Mild facial asymmetry (*Fig. 4*) and brittle and sparse hair (*Fig. 5*) were seen in the patient reported herein.

*Mental retardation* has been noted in 12% of patients with FDH, while our patient had normal mental development (1). Central nervous system abnormalities include myelomeningocoele, hydrocephalus, and Arnold-Chiari malformation. Brain MR imaging in our patient was normal.

*Dental manifestations* (52%) include hypodontia, microdontia, developmental defects, and malocclusion. Our case had malpositioning of developmentally abnormal teeth (*Fig. 3*) and notched gingiva.

*Ocular abnormalities* in focal dermal hypoplasia are present in at least 40% of the cases (1-6). The common ocular findings are coloboma affecting the iris, choroid and optic disc, microphtalmia/anophtalmia, ectopia lentis, strabismus, photophobia, obstructed lacrimal canals, aniridia, and conjunctival papillomas. Recently peripheral subepithelial corneal opacification was reported in a mother and daughter with FDH.

Our case had microcornea, an obstructed right tear duct, iris, chorioretinal, and optic disc coloboma and ectopia lentis with stretched ciliary processes (*Fig. 5-10*). It is possible that the latter were already present at birth and were missed during the immediate postnatal examination.



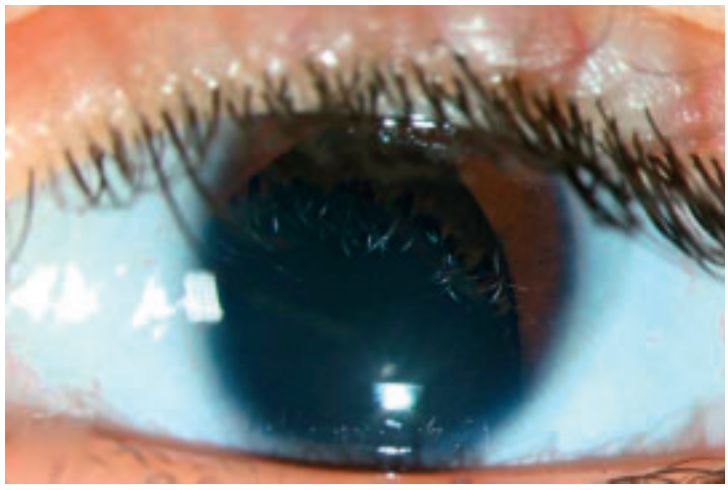
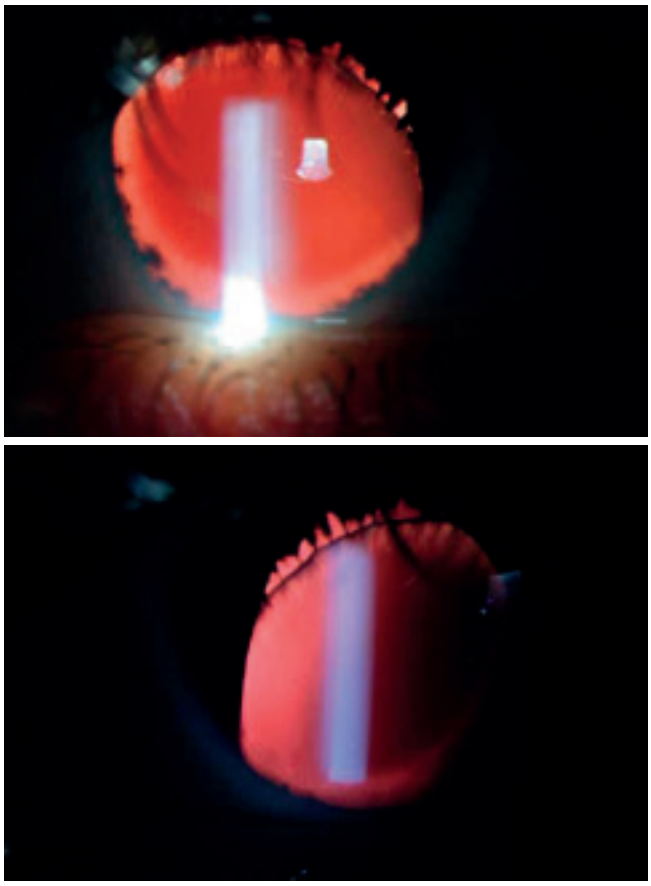


*Fig. 6-7:* Inferior iris coloboma of Right eye (RE) and Left eye (LE) at age 4



◀ *Fig. 8-9:* stretched ciliary processes in retro-illumination of RE and LE at age 4

ture of FDH, and is probably related to the colobomatous malformation of the globe. However, to the best of our knowledge this is the first report on stretched ciliary processes in FDH. Some of these seem to insert directly onto the lens equator, whereas others connect to the lens via shortened zonular fibers (*Fig. 6-9*). This is true for ciliary processes around the full 360° of the equator, with additional abnormal opacification of the inferior portion of the lens (*Fig. 8*). It is possible that the inferior displacement of the lens plays a role in the stretching of the superior ciliary processes, potentially due to a pull mechanism from zonules at the colobomatous side of the ciliary body, and/or the effect of gravity. Other conditions with ectopia lentis, in which the quality of the zonular fibers is affected, such as Marfan syndrome and ectopia lentis et pupillae, are generally not associated with stretching of the ciliary processes. However, as these can be seen around the whole equator in our case, it is more likely that the abnormally stretched ciliary processes are another sign of developmental anomalies specific to Goltz syndrome.

*Genitourinary system* abnormalities including hydronephrosis, bifid ureter and renal pelvis, horseshoe kidney, hypoplasia of the genitalia, and hypotrichosis have been reported in Focal dermal hypoplasia (5). Our patient had hypoplastic kidneys with vesico-ureteral reflux.

## CONCLUSION

Ocular anomalies are often associated with Goltz syndrome and contribute in a major way to the disease morbidity. Strabismus and colobomata are common findings.

In this case, an additional inferior lens subluxation was found in addition to abnormally stretched ciliary processes. Lens subluxation is a known fea-

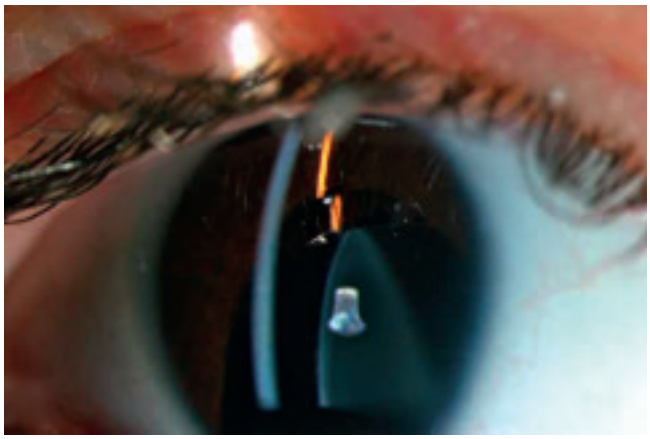


*Fig.10:* Inferior displaced lens at age 4

## REFERENCES


(1) Goltz RW – Focal dermal hypoplasia syndrome - An update. *Arch Dermatol* 1992; 128(8): 1108-1111.
(2) Temple IK , MacDowall P, Baraitser M, et al – Focal dermal hypoplasia (Goltz syndrome). *J Med Genet* 1990; 27 (3): 180-187.
(3) Grzeschik KH, Bornholdt D, Oeffner F, et al – Deficiency of PORCN, a regulator of Wnt signaling, is associated with focal dermal hypoplasia. *Nat Genet* 2007; 39(7): 833-835.
(4) Wang X, Reid Sutton V, Omar Peraza-Llanes et al – Mutations in X-linked PORCN, a putative regulator of Wnt signaling, cause focal dermal hypoplasia. *Nat Genet* 2007; 39: 836-838.
(5) Knockaert D, Dequeker J – Osteopathia striata and focal dermal hypoplasia. *Skelet Radiol.* 1979; 4: 223-227 (6).
(6) Lueder GT, Steiner RD – Corneal abnormalities in a mother and daughter with focal dermal hypoplasia. *Am J Ophthalmol* 1995; 120: 256-258.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