A FAMILY PRESENTING GOLTZ SYNDROME (FOCAL DERMAL HYPOPLASIA) IN THREE GENERATIONS*

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SUMMARY: Seven M, Suyugül Z, Yüksel A, Geçkinli B, Hacıhanefioğlu S, Cenani A. (Genetic and Teratology Research Center, İstanbul University, İstanbul, Turkey). A family presenting Goltz syndrome (focal dermal hypoplasia) in three generations. Turk J Pediatr 1998; 40: 593-601.

In this report we present three affected females of the same family in three generations. The cases have features of focal dermal hypoplasia (Goltz syndrome). One of the three affected females is the index case and the others are her mother and her grandmother. We performed skin biopsies on them. According to histopathological examinations skin lesions were compatible with Goltz syndrome. These cases exhibited focal dermal hypoplasia (FDH) manifestations including skin, dental and skeletal abnormalities. The affected females were seen in three generations of the same family which pointed to its X-linked dominance. *Key words: focal dermal hypoplasia, Goltz syndrome, X-linked dominant.*

Focal dermal hypoplasia (FDH, Goltz syndrome) is a rare inherited dermatological disorder which is commonly associated with skeletal, dermal, ocular, oral and soft tissue abormalities.

This syndrome includes varying degrees of cutaneous lesions. These lesions show dermal hypoplasia with widespread pigmentation and depigmentation in a cribriform or linear arrangement which follows Bloschko's lines.

The syndrome is presumed to be transmitted in an X-linked dominance with lethality in males. There are a few cases of surviving affected males who may be mosaics or possibly carry a new mutation. We report three generations of females with FDH.

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Case Report

Our case, a five-year-old girl with skin abnormalities and varying mesodermal defects, is the first child of nonconsanguineous parents (Fig. 1). Physical examination revealed the areas of underdeveloped and thinned skin, localized herniations of subcutaneous fat through the attenuated dermis, areas of hypopigmentation of the skin, telangiectases and papillomas on the base of perianal area (Figs. 2 and 3). There was also regional baldness, sparse and brittle scalp hair and enamel defects (Fig. 4). Nails were poorly developed, dystrophic, spooned and hypopigmented (Fig. 5).

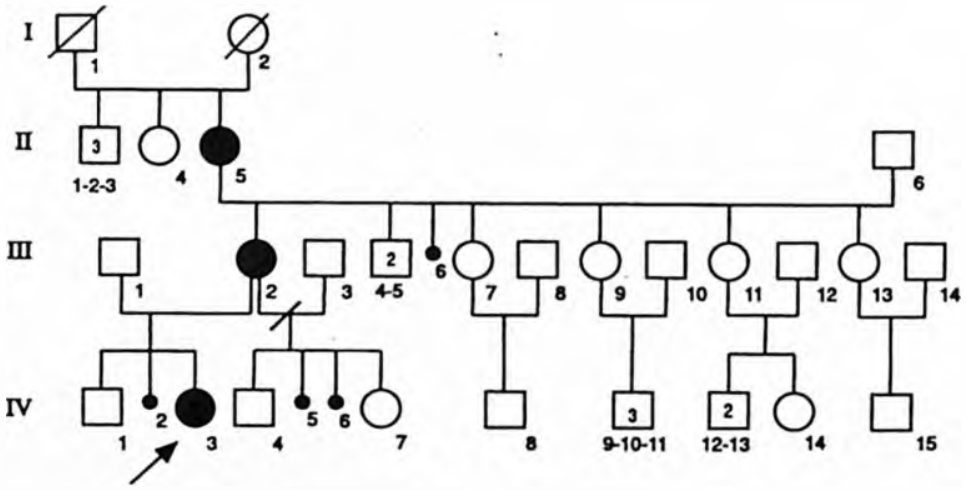


Fig. 1: Pedigree of family.

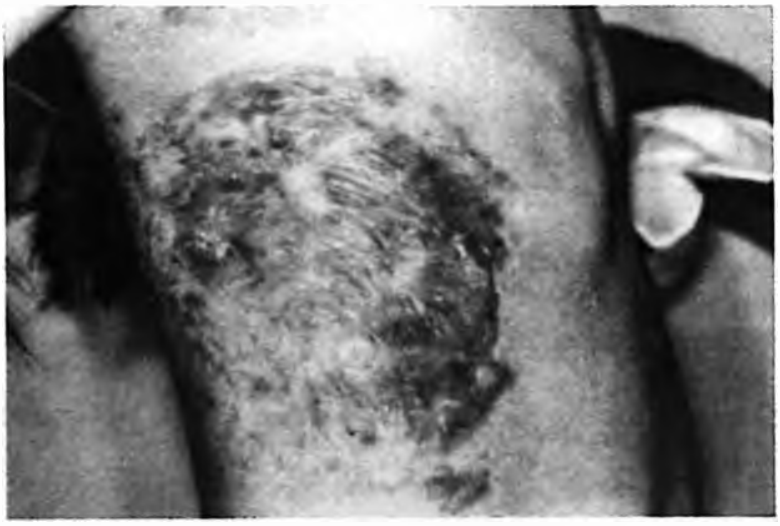


Fig. 2: Shows areas of underdeveloped and thinned skin in the patient (IV-3).

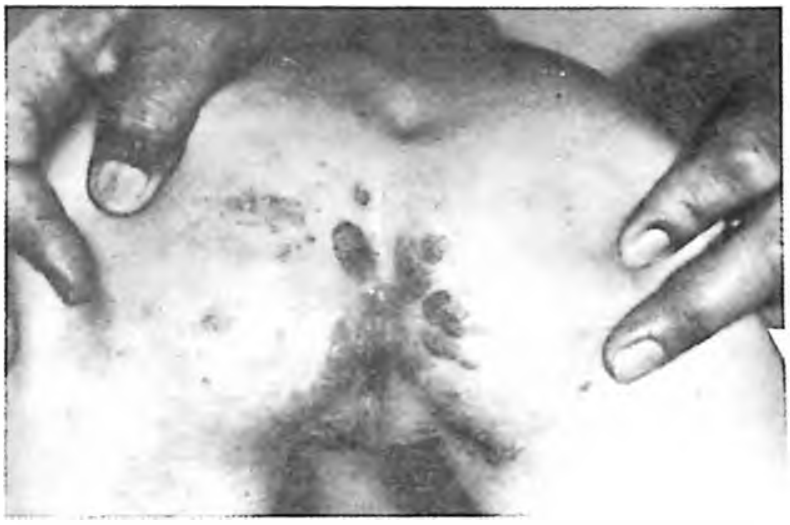


Fig. 3: Shows papillomas of patient's (IV-3) perianal area.

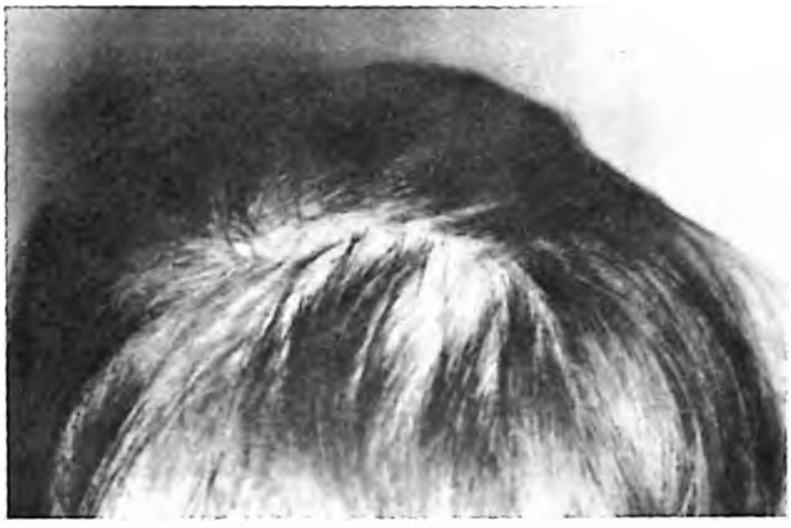


Fig. 4: Shows regional baldness, and sparse and brittle hair in the patient (IV-3).

In addition, some ocular abnormalities were discovered such as ptosis, blue sclera, irregularity of pupils, and heterochromia iridis. Skeletal abnormalities seen included scoliosis, high-arched palate and asymmetric face, trunk and extremities. An inguinal hernia was also present.

Detailed history of the case revealed the presence of cutaneous lesions, papillomas increasingly expanding in size, slight developmental delay and recurrent respiratory tract infections since birth. The papillomas were seen in the histopathologic examination of skin biopsy specimen (Fig. 6).

X-ray examination disclosed dorsal scoliosis and characteristic linear striations and cortical thinning of the long bones (Fig. 7).

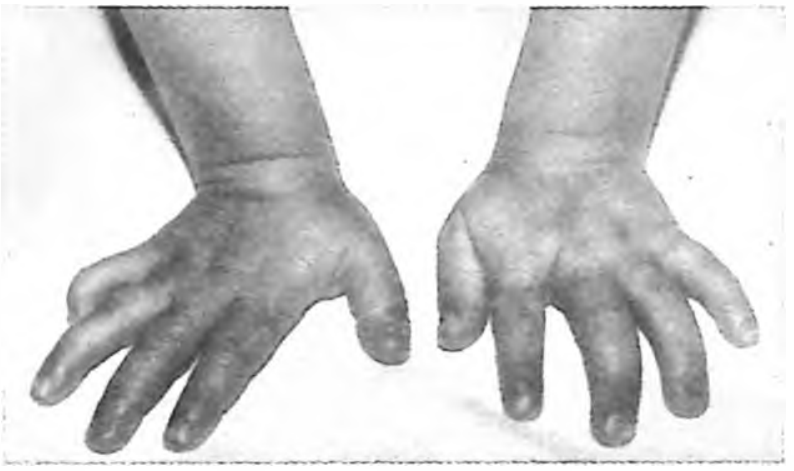


Fig. 5: Shows poorly developed, dystrophic nails and comptodactyly in the patient (IV-3).

Fig. 6: Histology of the surface showed stratified squamous epithelium with acanthosis and papillomatous hyperplasia (H.E. X40) (IV-3).

Results of complete blood cell counts, renal and liver function tests, urine analysis, total serum proteins, serum calcium and phosphorus levels were normal, but serum immunoglobulin A level was 21 mg/dl (normal range 51 ± 19 mg/dl). The other immunglobulin levels were normal.

Some of the varying anomalies of Goltz syndrome were also present in our patient's mother and grandmother. Our patient's mother had multiple papillomas in her inguinal, left scapular and axillary areas. She also had slightly erythematous, red and brown pigmented areas on her extremities and gluteal region (Fig. 8). Mild dystrophy of the toenails (Fig. 9a) and thumbnails, thinning of the hair, dental caries and scattered telangiectases were noted. Long bone x-ray and

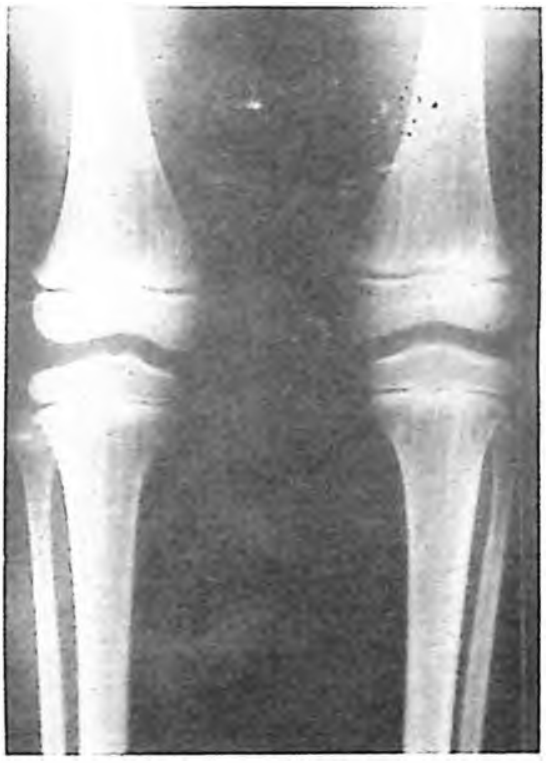


Fig. 7: Shows linear and vertical thinning and longitudinal striation of the long bones in the x-ray of the patient (IV-3).

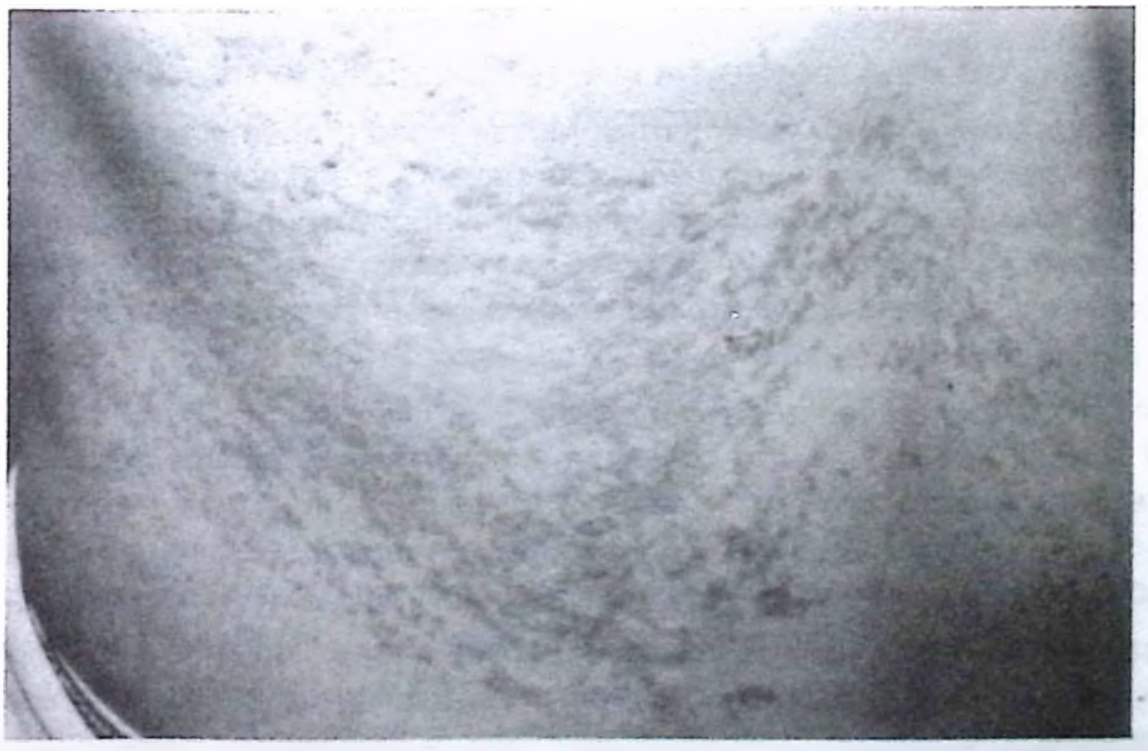
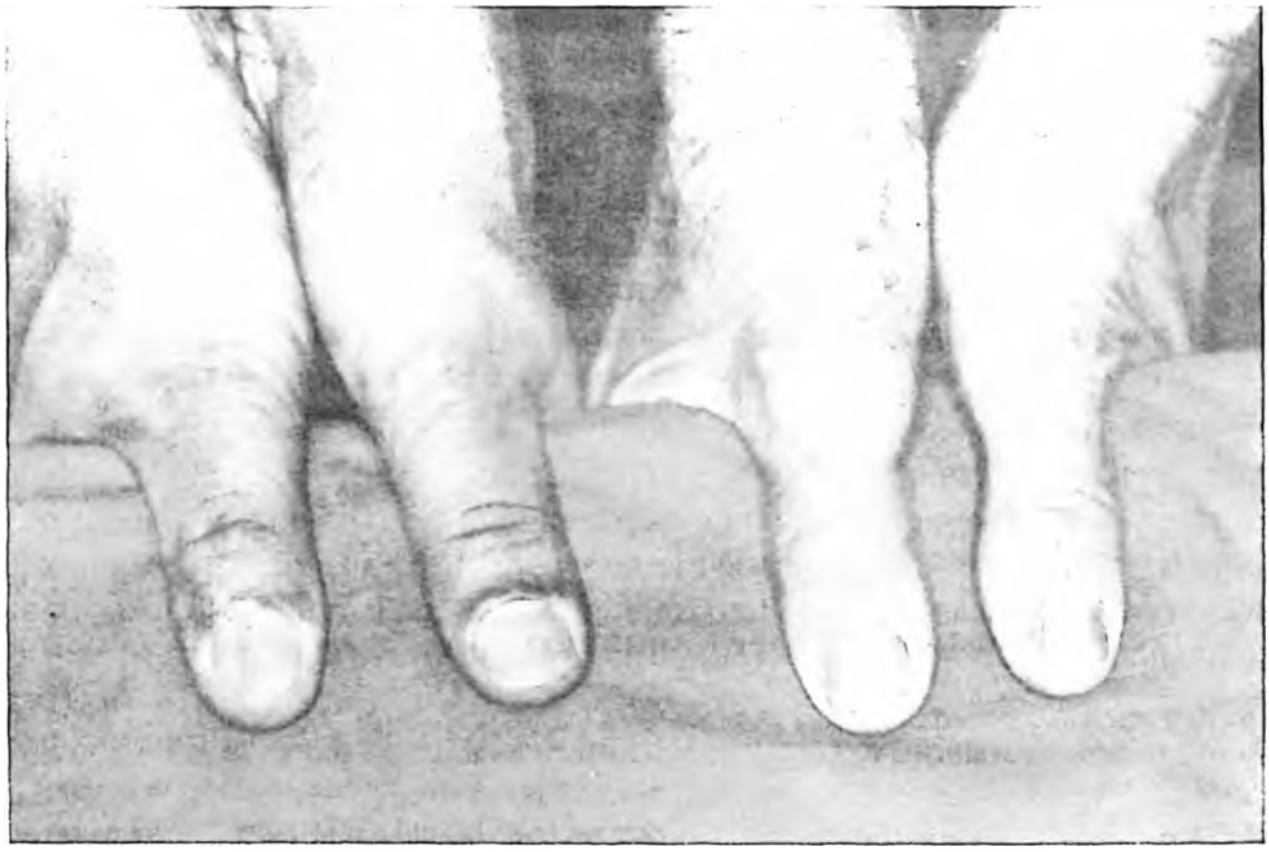


Fig. 8: Shows slightly erythematous, red and brown pigmented areas on back and abdominal area of mother (III-2)



(a) (b)

Fig. 9: Shows mild dystrophy of the nails in (a) mother (III-2) and (b) grandmother (II-5).

immunoglobulin A levels were normal. Mother's and grandmother's skin biopsy results were the same as our patient's. Our patient's grandmother had papillomas on her tongue and inguinal area since childhood (Fig. 10), and now has papillomas below her breasts. She also had red pigmented areas starting from both her axillary areas toward her arms. Also present was nail dystrophy on her left thumb (Fig. 9b).

Family history of the kindred revealed that II/4, III/7, III/9, III/11 and IV/7 cases had similiar skin lesions. We could not examine these patients because they were living in Italy.

Discussion

Focal dermal hypoplasia is a rare disorder characterized by widespread mesodermal and ectodermal dysplasia. This syndrome is an inherited dermatological disorder commonly associated with skeletal, dental, ocular and soft tissue defects. This syndrome was first described in 1962 by Goltz et al.[1] who reported four generations of female subjects in one family.

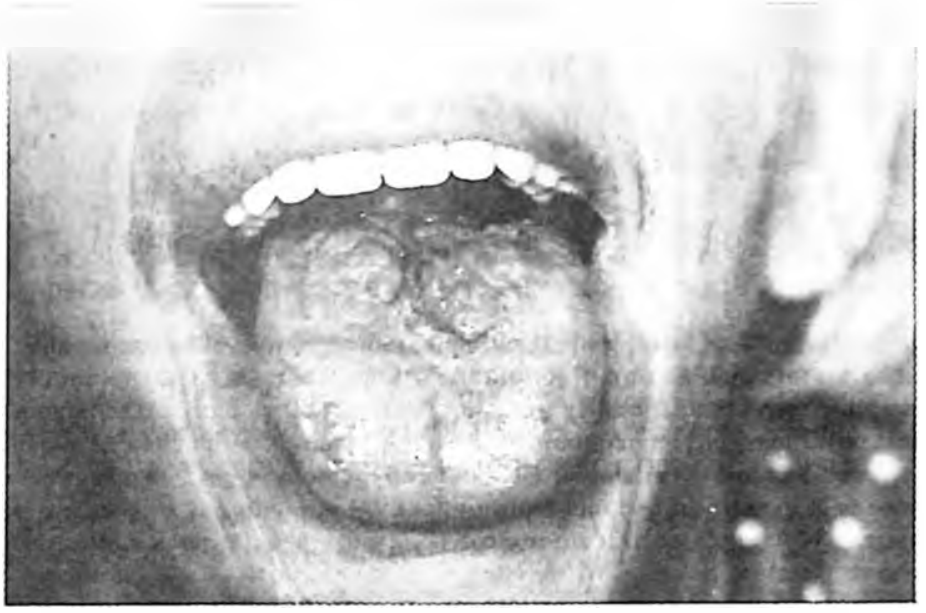


Fig 10: Shows the papilloma on grandmother's (II-5) tongue.

More than 200 cases of FDH have been reported in the literature. Most cases are seen in females and affected females have an increased incidence of spontaneous miscarriages of male fetuses. Therefore, it has been assumed that the mode of inheritance in most of the cases in an X-linked dominant trait with lethality in males. However, more than 30 affected males have also been reported[2-4]. Alternatively, an autosomal dominant mode of inheritance was based on the observations of affected males with father-to-daughter transmission[5,6]. Surviving affected males survive may be mosaics or might have Klinefelter's syndrome.

Although 95 percent of Goltz syndrome cases have been estimated as new mutations, families that were affected in four or three generations have been described in the literature[1,7]. Wechsler et al.[7] reported females with varying expressions of FDH in the same family. They have postulated that early inactivation of the X chromosome bearing the mutant gene responsible for FDH is the cause of variable expression.

In this report we describe affected females with Goltz syndrome in three generations. We also observed an excess of affected women who have spontaneous abortions. Abort material may be male fetuses. Because of this, we suspect that FDH is an X-linked dominant trait with male lethality.

The cutaneous abnormalities consist of atrophic hyperpigmented and hypopigmented macules and erythematous lesions. These lesions showed a characteristic linear or reticular distribution. Linear distribution followed Bloschko's lines. Telangiectasia was a common feature. Other cutaneous abnormalities

including lipomatous nodules and papillomatous lesions, and laryngeal and esophageal papillomas have also been described in the literature[8]. Our three cases (II-5, III-2, IV-3) had papillomas in the perianal area and on the back of the tongue. Atrophic hyperpigmented and hypopigmented lesions were also seen in their axillary areas. The skin biopsy specimens were obtained from the papillomatous lesions of the three affected cases (II-5, III-2, IV-3). The lesions showed acanthosis and papillomatous hyperplasia of the epidermis. Nail dystrophy and thinning of the hair were also noted in the three affected females. The mother (III-2) and her child (IV-3) had tooth anomalies.

Other abnormalities were skeletal anomalies including spinal anomalies such as kyphosis, scoliosis, spina bifida, anomalies of vertebrae, and rudimentary tail. Anomalies of hands and feet included hypoplasia or absence of digits, polydactyly, syndactyly, camptodactyly and clinodactyly. Radius and clavicle deformities and generalized osteoporosis were also found. The most constant radiographic sign in FDH is osteopathia striata involving longitudinal striation of long bones[9]. Index case's (IV-3) x-ray examination disclosed dorsal scoliosis and characteristic linear striations and also cortical thinning and longidutinal striation of the long bones.

Ocular abnormalities frequently found in patients with FDH include microphthalmos, anophthalmia and colobomas. Our index case (IV-3) had ptosis, blue sclera and heterochromia, but the other cases (II-5, III-2) had no ocular abnormalities.

According to the mapping studies of FDH, gene locaiton is in the region Xp22-31[10]. Naritomi et al.[10] reported two girls with terminal deletion of Xp. These patients had Aicardi's and Goltz syndrome. The two genes for Goltz and Aicardi's syndromes might be contiguous genes. Zuffardi et al.[11] demonstrated a girl having several signs of Goltz syndrome with deletion of the chromosome 9q32-qter. They concluded that in at leas some of the cases of FDH the inheritance was autosomal, although X-linked dominant inheritance cannot be ruled out in others. According to us, these results may represent a genetic heterogeneity of FDH.

In this report, the index case, her mother and her grandmother had clinical and histopathological findings compatible with Goltz syndrome. The pedigree data in this family were as follows: three affected females in three generations, with some of them having one or more abortions. Abortion material, which was not analyzed, may have been male fetuses. Thus, we suspect inheritance of this syndrome is most probably an X-linked dominant trait with lethality in males.

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