Focal dermal hypoplasia: Unusual presentation in Saudi Arabia

Awadh Alamri, Mazin Al Jabri

King Abdulaziz Medical City-Jeddah, Saudi Arabia

Received 6 September 2015; accepted 23 November 2015

Available online 11 December 2015

Abstract

Focal dermal hypoplasia (Goltz syndrome) is a rare genetic multisystem characterized by multiple abnormalities of ectodermal and mesodermal origin. It is found predominantly in females. We report a case of a two month-old baby girl who had dermal hypoplasia, atrophic skin lesions with telangiectasia in a linear pattern, fat herniations, papillomas and cleft of the upper lip, ectrodactyly, claw hands, microphthalmia and unusual association of gastrointestinal omphalocele.

1. Introduction

Focal dermal hypoplasia syndrome (FDHS), also known as Goltz syndrome, is a rare congenital mesoectodermal disorder which was first described in 1962 (Goltz et al., 1962).

This syndrome is characterized by cutaneous defects consisting of thinning of the skin, herniations of adipose tissue in the form of yellowish papules and abnormal skin pigmentation. Patients with FDHS also may present with skeletal, dental, ocular, hair and nail anomalies (Goltz et al., 1962, 1970).

There is strong evidence that it is inherited as an X-linked dominant condition. It has a female preponderance and there is an increased frequency of miscarriage in male fetus in affected female. However a few cases have been documented in male and these have been attributed to half chromatid mutations or autosomal dominant inheritance affecting the germ cells (Giam and Khoo, 1998; Mahé et al., 1991; Paller, 2007).

There are several 100 cases described in the literature but only a very few cases from Saudi Arabia and Middle East. We describe a rare case of Goltz syndrome along with unusual presentation of gastrointestinal omphalocele which is up to our knowledge the first case reported in Saudi Arabia with this association.

2. Case report

A two month old baby girl was seen in Jeddah, Saudi Arabia with skin lesions in a form of hypopigmentations since birth.

She is a product of full term pregnancy; antenatal history was unremarkable, with a negative family history. She is the 3rd offspring of nonconsanguineous parents, and has healthy brother and sister.

She had a gastrointestinal omphalocele that was repaired at age of 2 days (Fig. 1).

On examination, the patient had microcephaly, low set ears, wide nasal bridge and clefted upper lip. Eye examina-
tions reveal microphthalmus of left eye, blue sclera, total coloboma of the optic nerve and retina and downward subluxation of lenses (Fig. 2).

Cutaneous examination shows multiple erythematous soft papules (Raspberry-like papilloma) over lips (Fig. 3), gingiva and perineum. She has multiple atrophic erythematous to hypopigmented linear streaks on trunk, back and lower extremities along the lines of Blaschko (Fig. 4). She has hypoplastic nails and nail dystrophy involving fingers and toes nails, hair was normal.

Musculoskeletal examination shows syndactyly, oligodactyly and ectrodactyly on the feet (Fig. 5), and syndactyly, clinodactyly and claw hands (lobster-claw) on the upper limb (Fig. 6).

Laboratory studies showed normal hematology and blood chemistry. A skeletal survey and MRI brain were done and they were normal.
Histopathology of skin showed the absence of dermal collagen and the accompanying appearance of adipose tissue in the dermis (Fig. 7).

3. Discussion

Goltz syndrome is a rare neurocutaneous disorder characterized by widespread dysplasia of mesodermally and ectodermally derived structures (Goltz et al., 1962, 1970).

Goltz et al reported three females in 1962 with a mesoectodermal condition which they called focal dermal hypoplasia (FDH); this rare, multisystem condition is now often referred to as Goltz syndrome (Goltz et al., 1962).

Focal dermal hypoplasia genetic defect has been associated with at least 24 different mutations in the PORCN gene on the X chromosome. Even though the biochemical functions of the human PORCN gene are not well characterized, PORCN is known to target Wnt signaling proteins that are key regulators of embryonic development (Giam and Khoo, 1998; Bornholdt et al., 2009).

Of focal dermal hypoplasia cases, 90% occur in females, and the variability in the severity of expression is due to the random X-chromosome inactivation (lyonization). This results in functional mosaicism with anomalies of the skin and bone following the lines of Blaschko. Approximately 10% cases occur in males; postzygotic somatic mosaicism accounts for the findings in these affected males. Postzygotic somatic mosaicism is also postulated for the sporadic female cases with negative family pedigree analysis (Giam and Khoo, 1998; Mahé et al., 1991; Paller, 2007).

Although the cutaneous features predominate in most reports and have given the condition its name, characteristic abnormalities are also frequently present in the nails, hair, skeletal system, and eyes.

It is a rare condition with fewer than 300 cases reported, most of whom are females. However, males living with this syndrome were reported (Temple et al., 1990; Begovic and Zergollern, 1989).

It presents with characteristic abnormalities of the skin, eyes and teeth and may also have effects on the skeletal, gastrointestinal, genitourinary, neurological, and cardiovascular systems (Begovic and Zergollern, 1989).

Our patients had dermal hypoplasia, atrophic skin lesions with telangiectasias in a linear pattern, fat herniations, and papillomas of the upper lip. These are among the most common cutaneous abnormalities of FDH reported in the literature with dermal hypoplasia (61.6%), fat herniations (46.4%), and papillomas (46.4%) of the lips, gums, perianal and perioral areas that may develop within the first few months of life (Hall and Terezhalmy, 1983).

Typical cutaneous abnormalities are almost invariably present from birth. Initially, the most prominent type of lesion comprises pink or red, angular, atrophic macules, which may be slightly raised or depressed, and which often show reticulate grouping. The lesions may be a few millimetres or-several centimeters across. Occasionally they are blistered or eroded at birth (Ayme and Fraser, 1982; Daly and Vermont, 1968), and, in such cases, they have occasionally been described as cutis aplasia. Telangiectasia is commonly present. In racially pigmented skin, the lesions may be hypo- or hyperpigmented rather than erythematous. These lesions generally have a rather obvious and highly characteristic linear and asymmetrical distribution, and they may be found on any part of the body. The linear patterning follows Blaschko’s lines (Jackson, 1976), and is often most prominent on the legs, especially the thighs, on the forearms, and on the cheeks where single lines often radiate from the angle of the mouth. The intensity of the erythema tends to fade with age, so that the atrophic areas eventually appear white.

Soft, pinkish-yellow to brown saccular nodules provide the second characteristic type of skin lesion in FDH; these are the so called ‘fat herniations’.

These can occur anywhere, but they are perhaps most commonly found on the limbs, particularly in the popliteal...
and antecubital fossae. They may appear at any time during childhood.

The third characteristic type of skin lesion is a raspberry-like papilloma which can appear at any time during the patient’s life. Such lesions may be multiple.

They occur most frequently at junctions between mucosa and skin, on or around the lips, in the vulval and perianal areas, and around the eyes, but they may be seen at other sites, including the ears (both on the pinnae and in the middle ears), the fingers and toes, the groin and umbilicus, inside the mouth (on the gums and at the base of the tongue), and even in the oesophagus (Brinson et al., 1987).

In addition, there is a tendency for mild generalized xerosis associated with a degree of pruritus, which can be a troublesome symptom, and some patients are photosensitive.

The hair is frequently somewhat sparse and brittle. Localised areas of absence of hair are not uncommon in the scalp and in the pubic area.

Dystrophy or anonychia occurs when nails are contiguous with linear skin lesions.

Histology of the first two types of skin lesion shows marked reduction in the thickness of the dermis, with attenuation of the collagen fibres. Fat cells extend virtually to the epidermis, interspersing among which may be strands of dermal connective tissue (Goltz et al., 1962). The epidermis appears normal (Boente et al., 2007; Howell, 1969).

Electron microscopy shows numerous fine filamentous structures in the dermis, believed to represent immature collagen (Tsuji, 1982), and it is possible that while collagen synthesis may occur at a normal rate (Uitto et al., 1980), the collagen does not form mature bundles in the normal way. Multilocular fat cells have been seen ultrastructurally in the lesional fat, and these are considered to be an immature form of adipocyte (Uitto et al., 1980).

There is a debate as to whether the defect is primarily an atrophy of the dermis, with secondary fat ‘herniation’, or a
complex developmental abnormality of connective tissue causing both dermal hypoplasia and the development of fat hamartomata (Howell, 1969). The frequent presence of dermal elements, including collagen and elastin fibres, below the superficially situated fat, and the ultrastructural demonstration of immature adipocytes within this fat, tend to support the latter view.

The histological features of the raspberry-like papilomata closely resemble those of the angiofibromata of tuberous sclerosis and those of the so called solitary fibrous papule of the nose, with acanthosis and papillomatosis of the epidermis, and dilated capillaries in the dermal core (Boente et al., 2007).

The ears are thin and protruding, often simple, low set, and sometimes asymmetrical. The nose has a narrow bridge and a broad nasal tip, sometimes with a unilateral notch of the ala nasi. The chin is pointed. Asymmetry of the face with mild hemihypertrophy has been described.

Ectodactyly “lobster-claw” deformity was present and is considered an important musculoskeletal feature.

Findings in the skeletal system are variable and usually asymmetrical. The hands and feet are affected in 60–70% of reported cases. Abnormalities include syndactyly, absence or hypoplasia of digits, also ectodactyly and polydactyly, in any combination.

The spectrum includes the absence of the whole or part of an extremity. A ‘lobster claw’ type of deformity is perhaps particularly characteristic. Asymmetry in the size and shape of the face, trunk, or limbs has been reported in 30% of cases, and scoliosis in 15–20%.

X-rays can be helpful. In 1972, Larregue et al. (Larregue et al., 1972) noted longitudinal striations in the metaphyses of long bones (‘osteopathia striata’) in nine patients.

This finding is not pathognomonic, but is found in approximately 20% of gene carriers and can be a useful feature, particularly if the condition is suspected in minimally affected subjects.Vertebral anomalies including spina bifida occulta and clavicular dysplasia are additional findings.

There was right microphthalmia. Ocular abnormalities have been present in approximately 20% of reported cases, and may make a major contribution to the handicap associated with this condition. Reported ocular abnormalities are: blocked tear, ducts (Goltz et al., 1970), coloboma, or congenital defects of the iris, retina, choroid and optic nerve, strabismus, nystagmus, cloudy cornea, anophthalmia and microphthalmia (Manzi and Magli, 1990). The ears were low set and deformed and this was reported before in 2 reviews.

One of gastrointestinal abnormalities that occur in people with focal dermal hypoplasia is an omphalocele. In the literature review we found similar case reported by Gordon (1975). Samejima et al. reported similar association of focal dermal hypoplasia with omphalocele in 1981 (Samejima, 1981) and according to their paper that was the second reported case of such association. Recently in 2011 Ho Won Lee et al reported similar cases in Korea (Ho Won Lee et al., 2011).

Abnormalities of the genitourinary tract such as bifid ureter, bifid renal pelvis, horseshoe kidney, and hypoplastic or absent kidney can be present. Ectopic kidney is an important urologic finding with a reported incidence of 9% in the literature (Hall and Terezhalmy, 1983).

Conflict of interest

None.

References


