

# Lymphatic, tooth and skin manifestations in Turner syndrome

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**Abstract.** Turner syndrome is a chromosomal disorder due to an absent or abnormal X chromosome. The two most typical features are short stature and gonadal dysgenesis. There is a wide range of other phenotypic features, many of which are thought secondary to lymphedema during embryogenesis. Reviewed are common sequelae of lymphatic obstruction, as well as common tooth and skin findings. © 2006 Elsevier B.V. All rights reserved.

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## 1. Introduction

Embryonic lymphatic obstruction is thought to be responsible for the pathogenesis of many of the common phenotypic features seen in Turner syndrome, and troublesome lymphedema can persist after birth. Tooth development is also affected, and dental changes seen in Turner syndrome must be taken in to account when considering orthodontic procedures. There are many skin findings that seem to be more prevalent in Turner syndrome than in the general population.

## 2. Lymphatics

Most conceptuses with a 45,X karyotype (approximately 98%) are spontaneously aborted. The pathogenetic mechanism for early death in 45,X embryos and fetuses is unknown. It may be related to vascular abnormalities or to abnormal fluid balance, leading

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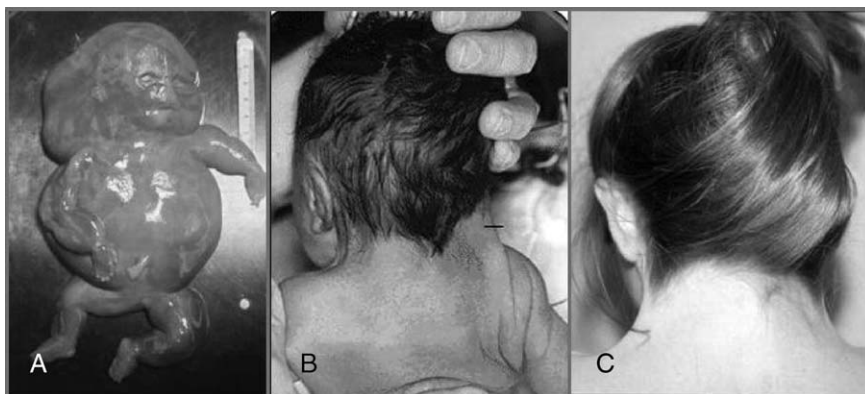


Fig. 1. Fetal hydrops due to lymphatic obstruction often leads to fetal demise (A). For those that survive, the sequelae of lymphedema leads to many of the phenotypic features described in Turner syndrome, including the pterygia colli seen in infancy (B), and the distinctive web-neck and low-set hairline (C). (Panel B reprinted with permission from *Turner Syndrome: A Comprehensive Guide*, Eli Lilly and Company.)

to disturbed embryo–placental circulation, and excess fluid volume in the fetus [1]. Lymphatic obstruction is thought to be due to hypoplasia or agenesis of the lymphatic ducts [2], which, when severe, leads to hydrops fetalis and fetal demise (Fig. 1). For those girls that survive, many of the phenotypic features are believed to be due to the deforming effects of in utero edema. Edema may also contribute to the development of renal and cardiac anomalies [3]. Often jugular lymphatic obstruction causes cystic hygroma formation during embryogenesis. The cystic hygroma resolves before birth, leaving the redundant nuchal folds (pterygia colli) seen in the newborn and later as the webbed neck and low-set hairline which are signature features of Turner syndrome (Fig. 1). Lymphedema is more commonly seen in individuals with the 45,X karyotype, than in those with mosaic or other karyotypes [4].

Lymphedema, particularly of the dorsum of hands and feet, is present at birth in upwards of 60% of infants with Turner syndrome and is the reason for early diagnosis in

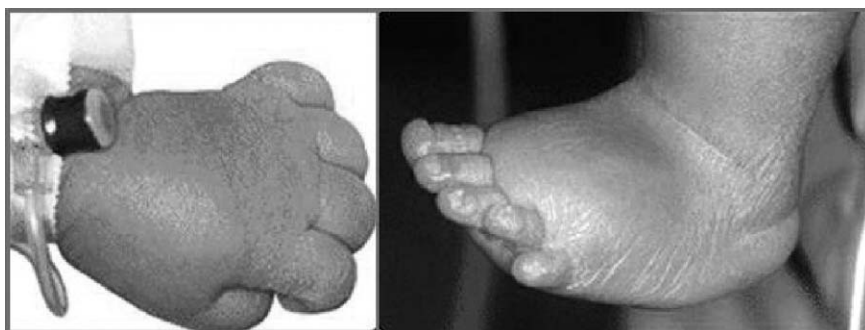


Fig. 2. Lymphedema of the dorsum of hands and feet can be a presenting feature of Turner syndrome at birth. (Reprinted with permission from *Turner Syndrome: A Comprehensive Guide*, Eli Lilly and Company.)

approximately one-third (Fig. 2) [5]. The presence of lymphedema in a female newborn should always suggest the diagnosis of Turner syndrome. The lymphedema seen at birth usually resolves by 2 years of age without therapy [2]. Infrequently, lymphedema may occur or reoccur at any age and may be associated with the initiation of therapy with GH or estrogen and may require support stockings and elevation for treatment. Long-term treatment with diuretics should be avoided because of its marginal efficacy and problems with fluid and electrolyte imbalance [6]. Vascular surgery should also be avoided. For severe or refractory cases, complete decongestive physiotherapy (CDP) may be appropriate. In our experience, this is rarely needed.

### 3. Orthodontics

Several abnormalities in tooth development and morphology have been described in Turner syndrome, including reduced tooth size, thinner enamel, and less dentine [7], the clinical significance of which is unknown. Girls with TS are at greater risk for root resorption, which can lead to tooth loss, especially during orthodontic treatment. In addition, micrognathia is often present, which can cause crowding of the lower teeth. The high arched and narrow palate common in girls with Turner syndrome also contributes to dental malalignment. Orthodontic evaluation should be considered for all girls with Turner syndrome when permanent teeth have erupted. Growth hormone treatment can alter craniofacial proportions and all girls with TS treated with GH should receive periodic orthodontic follow-up [8].

### 4. Skin manifestations

Numerous cutaneous findings are observed in Turner syndrome (see Ref. [2] for a review). There are an increased number of melanocytic nevi in many individuals with Turner syndrome, mostly acquired in late childhood. Large or dysplastic nevi are uncommon [9], but a propensity for halo nevi has been reported [10]. Growth hormone treatment has been reported to increase the growth of nevi in children with Turner syndrome



Fig. 3. The deep set, and up-turned nails that are common in Turner syndrome.



Fig. 4. Hypertrichosis of the upper and lower extremities is sometimes seen in Turner syndrome. It was the presenting complaint in the 9-year-old girl above (left). It is unclear whether there is an intrinsic increased risk of hypertrophic scarring (keloid formation) in Turner syndrome, or whether it is more a reflection of the common sites of surgery in this population (right). Note the acquired nevocytic nevus along the jawline. (Right panel reprinted with permission from *Turner Syndrome: A Comprehensive Guide*, Eli Lilly and Company.)

[11], but this has been disputed by others [12]. Despite the increased number of nevi, there does not appear to be an increased risk of melanoma [13].

The nails in girls with Turner syndrome are often deeply set, hyperconvex or concave and appear to grow upwards at the free edge of the nail plate (Fig. 3). The toenails are usually more affected than the fingernails and the deep-set upturned toenails may cause recurrent paronychia or cause pain when wearing shoes, requiring frequent clipping of the nails. This growth pattern does appear to improve somewhat with age.

Other cutaneous findings have included neonatal cutis verticis gyrata, alopecia areata and vitiligo. Premature aging of the facial skin has been reported [5]. Luxuriant hair growth on the arms and legs has been described. Hypertrichosis was the presenting complaint leading to the diagnosis of Turner syndrome in at least one case in the authors' personal experience. Facial hair is not usually abnormal. Acne seems to be less of a problem in adolescents with Turner syndrome than in their unaffected counterparts, perhaps due to a relative decrease in androgen exposure due to gonadal failure [2].

An increased risk of developing hypertrophic scars (keloids) has long been thought intrinsic to Turner syndrome (Fig. 4). However, this propensity for keloid formation may be a reflection more of the sites at which individuals with Turner syndrome commonly undergo plastic surgery (head, neck and upper chest) rather than an intrinsic risk peculiar to Turner syndrome. Among 92 patients with Turner syndrome who had undergone 103 surgical procedures, only two developed hypertrophic scars/keloids [4]. The risk of keloid formation should be carefully discussed with the patient before any surgery, particularly elective or cosmetic procedures.

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