Intrafamilial Variability of Popliteal Pterygium Syndrome: A Family Description

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Popliteal pterygium syndrome is one of the autosomal dominant limb pterygium syndromes. It has incomplete penetrance and extreme phenotypic variability that leads to difficulty in diagnosis. A case is presented to emphasize the variable phenotype of this disorder. The absence of pterygia in the family members led to the misdiagnosis of van der Woude's syndrome. However, the presence of a pyramidal fold of skin over the nail of the hallux in family members suggested the diagnosis of popliteal pterygium syndrome. It is concluded that the presence of this distinctive nail abnormality in infants with cleft lip, cleft palate or both suggests the diagnosis of the popliteal pterygium syndrome.

A number of limb pterygium syndromes have been described (Hall et al, 1982). Popliteal pterygium syndrome is the most common form of the dominantly inherited types of limb pterygium syndromes. The name popliteal pterygium syndrome was suggested by Gorlin et al (1968) for a group of anomalies, including popliteal pterygia, orofacial defects, (including lip pits, cleft lip, cleft palate, or both, and syngnathism) and digital anomalies (syndactyly, hallucal nail folds).

A newborn female is presented who had cleft palate and associated ectodermal defects. Initially she was thought to have a syndrome of cleft lip-palate with ectodermal defects. However, further investigation of the family suggested the diagnosis of popliteal pterygium syndrome.

CASE REPORT

The proband (subject II-6) is the product of a 36 week gestation. The mother is a 27-year-old Caucasian female, G_6P_4. She had one elective and one spontaneous abortion. The mother smoked two packs of cigarettes daily but denied excessive ethanol intake or drug abuse. There was history of gonococcal infection and syphilis 11 years prior to this pregnancy. The father is a 33-year-old Caucasian male who had been in good health except for minimal high-frequency hearing deficit on the left. He had a partial repair of a cleft palate. Consanguinity was denied. A family pedigree diagram is shown in Figure 1.

Physical Examination. The proband was a newborn white female infant with a birth weight of 2.86 kg (75th percentile), head circumference 33.5 cm (75th percentile), and length 48.5 cm (45th percentile). Examination of the skin revealed a capillary hemangio-

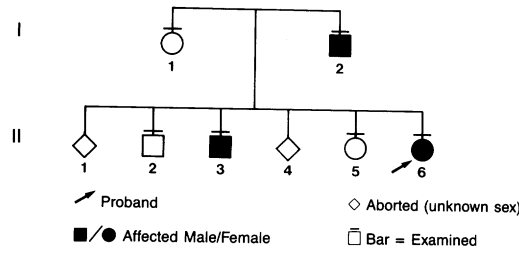

Figure 1 Pedigree diagram of the family.

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ma, 3 cm in diameter, over the occiput but was otherwise unremarkable. Scalp hair appeared to be normal in texture and distribution.

The eyes were normally spaced, the interpupillary distance being 4 cm (50th percentile). The palpebral fissures were not slanted and were normal in length, both being 2 cm. A 3 to 4 mm wide fibrous band was noted between the left upper and lower eye lids. This band restricted the opening of the left eye lids to 2 to 3 mm. The rest of the ophthalmic examination including funduscopic examination was normal.

The bridge of the nose was depressed. The intercanthal distance was 2 cm (50th percentile). The ear lobules were normal in size and shape, and the ears were not low set or posteriorly rotated. There were no ear tags noted. The philtrum and the vermilion border were normal and examination of the lips did not reveal any clefts, lip pits, or conical elevations. The chin was slightly micrognathic.

At birth there was fusion of the gingiva of the mandible and maxilla from the canine tooth area back to the maxillary tuberosity. This was surgically divided and revealed bilateral intraoral bands that restricted the oral opening to 1.0 cm anteriorly. These bands extended from the floor of the mouth to the palate just behind the alveolar margins. They were approximately 1 cm in diameter and 1.5 cm apart and prevented the tongue from normal anterior protrusion. In addition, a bilateral cleft of the hard palate was palpable.

Examination of the neck and chest was unremarkable. The nipples were normally spaced, and no supernumerary nipples were noted. Abdominal examination revealed the umbilical cord to have a single umbilical artery, and the labia majora were hypoplastic.

Examination of the upper extremities was normal. There were no supernumerary digits, syndactyly, or clinodactyly. The palmar creases were normal.

Examination of the lower extremities revealed complete soft tissue syndactyly between the second and third toes of the left foot. In addition, partial soft tissue syndactyly between the second and third toes of the right foot was present. A pyramidal fold of skin was noted over the right hallux extending over the base of the nail (Fig. 2). Examination of the popliteal angle did not reveal any pterygia nor was any fibrous band palpable over the popliteal area.

Investigations. A cord blood IgM level was normal, and an FTA:ABS study was also nonreactive. Abdominal ultrasonography revealed normal kidneys and collecting system. Audiology screening did not reveal any gross hearing deficit. A peripheral leucocyte banded chromosome analysis was normal. The primary dentition appeared to be normal on radiographs, and no conical teeth were noted. Bilateral cleft of the hard palate was confirmed radiographically. Light microscopy of the hair shafts was unremarkable.

Family Descriptions. A 6-year-old male sibling (subject II-3) had minimal conductive hearing deficit secondary to bilateral otitis media. He also had a bilateral cleft of the lip and palate which had been surgically repaired. A median lip pit was noted on the lower lip. Examination of the popliteal area was unremarkable as was the rest of his physical examination.

The father (Subject I-2) denied having eye abnormalities or intraoral bands at birth. On examination his hair appeared to be normal; no cleft lip or lip pits were noted. His cleft palate was mentioned earlier. Partial syndactyly between the second and third toes of the right foot was noted. Both the hallucal toenails were also dystrophic with a fold of skin extending over the base of the nails. No limb pterygia or fibrous bands were noted over the popliteal region in any of the family members.

Discussion

The variability of findings within this family emphasizes the difficulty in correctly assigning the diagnosis. Prior to the birth of the proband, the sibling was labeled as having van der Woude's syndrome. Initially, with the multiple anomalies noted in the proband, it appeared that the family represented an extended phenotypic variation of van der Woude's syndrome. However, extensive review of the literature suggests the most likely diagnosis is popliteal pterygium syndrome, even though none of the subjects had any evidence of popliteal pterygia.

Lip pits or fistula labia inferioris congenita have been described as early as 1845 by Demarquay (1845). The syndrome of lip pits with cleft lip and palate was described by Anne van der Woude (1954) when the 80 percent association with cleft lip and palate was established. Cervenka et al (1967) presented an extensive review

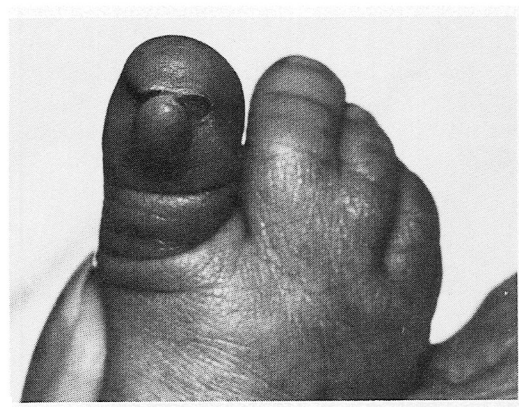

Figure 2 The proband's right foot showing the hallucal nail dystrophy.

TABLE 1 Comparison of Popliteal Pterygium Syndrome, van der Woude's Syndrome, and Features Noted in our Pedigree

Physical Findings	*Popliteal Pterygium Syndrome*	*van der Woude's Syndrome*	*Our Pedigree*
Autosomal dominant transmission	+	+	+
Cleft lip and palate	+	+	3/3
Lip pits	+	+	1/3
Ankyloblepharon	+	+	1/3
Intraoral bands	+	+	1/3
Syndactyly	+	+	2/3
Genital anomaly	+	−	1/3
Nail dystrophy	+	−	2/3
Popliteal pterygia	+	−	0/3

establishing equal sex ratio, autosomal dominant transmission with 80 percent penetrance and variable phenotype of van der Woude's syndrome. A number of other anomalies may be associated (Table 1).

Trélat (1869) is credited with reporting the first case of popliteal pterygium syndrome which was later named as such by Gorlin et al (1968). Rintala and Lahti (1970) proposed "facial-genito-popliteal syndrome" as being more descriptive; however, popliteal pterygium syndrome remains the more widely used designation. Autosomal dominant transmission is generally accepted in familial cases. A number of reports have emphasized the marked phenotypic variability of popliteal pterygium syndrome. Gorlin et al's (1968) report mentioned the variable expressivity of the syndrome. Other family descriptions (Hall et al, 1982; Hecht and Jarvinen, 1967; Pashayan and Lewis, 1980) have also emphasized the intrafamilial variability of popliteal pterygium syndrome. Bixler et al (1973) reported monozygous twins who were affected with different features of popliteal pterygium syndrome.

As shown in Table 1, both syndromes may have very similar physical findings in addition to the cleft lip and palate. Both have been associated with ankyloblepharon, syngnathia, and syndactyly. However, the rather characteristic finding of the popliteal pterygium syndrome, the dystrophic toenails, has not been reported in association with van der Woude's syndrome. Characteristically, it is a pyramidal fold of skin extending over the base of the nail, usually the hallux. It was described in Gorlin et al's (1968) initial report and a number of other reports including those of Klein (1962), Hecht and Jarvinen (1967) (seven of eight cases) and Hall et al (1982) (45% of cases). In the family presented, the father (Subject I-2) had the characteristic dystrophic hallucal toenails bilaterally. The proband had the toenail dystrophy on the right hallux.

The absence of pterygia in cases of popliteal pterygium syndrome has been well documented. In Pashayan and Lahti's (1980) pedigree report, the proband had a fibrous popliteal scar. However, the sibling had a popliteal scar only unilaterally, and the affected father had none. In a series of 48 cases (Hall et al, 1982), popliteal pterygia were absent in 16 percent of the cases. In Hecht and Jarvinen's (1967) series, only six of eight cases had popliteal pterygia. In a pair of affected monozygous twins (Bixler 1973), only one had popliteal pterygia; the other had a "forme fruste". These reports confirm that popliteal pterygia are not invariably present in the popliteal pterygium syndrome. Therefore, the absence of pterygia in our pedigree is not without precedence. In the pedigree presented, even though none of the family members had popliteal pterygia, the rather characteristic finding of the dystrophic toenails in association with cleft lip and palate and other associated defects suggests the diagnosis of popliteal pterygium syndrome.

IMPLICATIONS

Popliteal pterygium syndrome is one of approximately 133 syndromes associated with cleft lip and palate (Cohen, 1978). Many of the syndromes with cleft lip and palate have incomplete penetrance, genetic heterogeneity, and variable expression, making it difficult to ascertain the correct diagnosis. The genetic liability of isolated cleft lip and palate is different from that of a syn-

drome with associated cleft lip and palate. Hence, it is essential to obtain a detailed family history and a thorough physical examination in all cases of cleft lip and palate, in order to ascertain the correct diagnosis and provide appropriate genetic counseling.

In conclusion, we recommend that all cases of cleft lip and palate should be thoroughly evaluated to exclude a syndrome with associated cleft lip and palate. We also believe, as others have suggested, that the presence of pterygia is not an invariable feature of popliteal pterygium syndrome. Finally, the presence of this hallucal nail dystrophy in association with cleft lip and palate and other associated defects suggests the diagnosis of popliteal pterygium syndrome.

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