Case Report

Popliteal pterygium syndrome: case report from rural India

Vasav D. Desai^{1*}, Gayatri S. Desai², Nirav Raulji¹

¹Consultant Pediatrician and Neonatologist, ²Department of Obstetrics and Gynecology, Kasturba Hospital, Jhagadia, Gujarat, India

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*Correspondence:

Dr. Vasav D. Desai,

E-mail: vasav.d.desai007@gmail.com

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ABSTRACT

The popliteal pterygium syndrome is a congenital malformation that includes orofacial, musculoskeletal and genitourinary anomalies. It is also known as faciogenitopopliteal syndrome. It is autosomal dominant disorder. It has highly variable expressivity and incomplete penetrance. The incidence of the popliteal pterygium syndrome is 1/300000, which makes it an extremely rare condition. The most striking characteristic of this syndrome is popliteal pterygium, which consists of a net of connective tissue spreading from the ischial tuberosity to the calcaneus. In this study, authors present the case of a 1 day old male patient with cleft upper lip, cleft palate, bifid scrotum, popliteal pterygium and congenital talipes equinovarus (CTEV).

Keywords: Autosomal dominant disorder, Bifid scrotum, Cleft lip, Cleft palate, Congenital talipes equinovarus, Popliteal pterygium syndrome

INTRODUCTION

Popliteal pterygium syndrome is a rare congenital condition involving craniofacial and genitourinary anomalies as well as malformation of the extremities. Its incidence is approximately 1 in 300000 live births. This syndrome was first described by Trélat in 1869 and received its current designation from Gorlin in 1969.¹

A more descriptive term suggested for this condition, on the basis of incomplete expression of the features of the syndrome, is faciogenitopopliteal syndrome.² Affected individuals may also have webbing or fusion of the fingers or toes, characteristic triangular folds of skin over the nails of the large toes, or tissue connecting the upper and lower eyelids or the upper and lower jaws.

They may have abnormal genitals, including unusually small external genital folds (hypoplasia of the labia majora) in females. Affected males may have

undescended testes (cryptorchidism) or a scrotum divided into two lobes (bifid scrotum).

CASE REPORT

A male baby was born at Kasturba hospital, SEWA rural which is situated in rural area of Gujarat state of India by vaginal delivery at full term and weighed 2.8 kg. The index case was the first child of the couple. The mother reported no occurrence of previous miscarriages. The pregnancy had been detected at 8 gestational weeks. The mother started taking folic acid and iron supplements in the fifth gestational month. The main malformations found in the patient were as follows: bilateral cleft in the upper lip (Figure 1); middle lower lip cleft with ectopic salivary glands (Figure 2) similar to that found in Van der Woude syndrome; cleft palate; bifid scrotum (Figure 3) and bilateral CTEV (Figure 3). In addition to all these anomalies, the child also had popliteal pterygium (Figure 3), which is sine qua non of the syndrome in question.

Figure 1: B/L Cleft lips.

Figure 2: Red arrow shows middle lower lip cleft.

Figure 3: Red arrow shows bifid scrotum, blue arrow shows popliteal pterygium, black arrow show CTEV.

DISCUSSION

The clinical features of the syndrome are highly variable. Among the craniofacial anomalies involved in this syndrome, cleft lip and/or cleft palate are commonly found. In addition, small lower lip pits, which the salivary ducts flow into; syngnathia, represented by congenital bands of tissue between the maxilla and the mandible; and ankyloblepharon filiforme adnatum, which is fusion of the eyelid margins by small threads of abnormal tissue, can also be observed. The most striking characteristic of this syndrome is popliteal pterygium, which consists of a net of connective tissue spreading from the ischial tuberosity to the calcaneum (Table 1).

This pterygium may severely limit extension, abduction and rotation of the leg. In some subjects it was reported to be so tight that the heel almost touched the buttocks, while in other cases it could just be felt as a tight string without any severe limitation of the range of movements.³

Table 1: Frequency of anomalies in popliteal pterygium syndrome.

Anomalies	Frequency (% of cases)
Cleft Lip	93
Cleft palate	57
Syngnathia	40
Lip pits	45
Ankyloblepharon	17
Popliteal web	57
Syndactyly	50
Intercrural web	8
Talipes equinovarus	14
Digital reduction defects	12
Genital anomalies	36
Nail anomalies	33

Genitourinary alterations are present in both genders. In females, hypoplasia of the labia majora is the most common alteration, with hypoplasia of the vagina and womb as well as hypertrophy of the clitoris also being described. In males, unilateral or bilateral cryptorchidism and absent or bifid scrotum may be present, with the penis usually being normal.

No alterations have been observed in growth and intellect. Other deformities associated with popliteal pterygium syndrome include scoliosis, clubfoot, hidden spina bifida, a small sternum, and bifid rib. In the absence of a positive family history, the minimal diagnostic criteria for popliteal pterygium syndrome are any three of the following.⁴

- Cleft lip/palate
- Popliteal pterygium
- Paramedian lower lip sinuses
- Genital anomalies
- Toenail anomalies.

In index case, first four anomalies were present from aforementioned clinical diagnostic criteria.

Autosomal dominant transmission is usually the cause of familial cases, with decreased penetrance and large intrafamilial phenotypic variation being associated with the syndrome. The ratio of male:female patients is 1:1. The condition is usually diagnosed when typical manifestations of the syndrome are observed.^{3,5} The variability in the expression of this syndrome may lead to a retrospective diagnosis in previous generations that showed less evident signs of popliteal pterygium syndrome.^{6,7} A new spontaneous mutation could explain the sporadic nature of popliteal pterygium syndrome. The location of the responsible gene is still unknown; however, Lees et al, showed that there is a consistent connection with the mutation of the IRF6 gene located on chromosome 1q32 locus (also known as the Van der Woude syndrome locus).⁵ Mutation of RIPK4 gene on chromosome 21 has been identified to be the cause of autosomal recessive PPS. Most reported cases are sporadic; advanced parental age is found in a number of these cases, suggesting new mutations.⁸

The pathogenesis of popliteal pterygium syndrome is partially understood, and several hypotheses have been raised, such as primary microvascular abnormalities associated with edema, leading to a disturbance of the epithelial tissues and resulting in the formation of secondary adhesions, excessive epithelial growth leading to fusion and secondary mesenchymal involvement, primary collagen defects, and loss of the apoptotic mechanism. In the popliteal pterygium, displacement of muscles and tendons occurs. The underlying mechanism

for the popliteal pterygium syndrome is thus clearly different from the mechanism in multiple pterygium syndrome, where no displacement of muscles is found and the pterygia formation is attributed to limited intrauterine joint mobility. The congenital sinuses of the lower lips are thought to be a remnant of the lateral sulci originating from a genetic defect. Genetic and histopathological studies are required to further elucidate the nature of this syndrome.⁵

However, most reported cases are sporadic, and the first-degree relatives of these patients must be carefully investigated to detect minimal anomalies that may be present, such as syngnathia or ankyloblepharon, in order to exclude hereditary transmission.³ In this reported family, parents are normal. None of parents are having advanced age. No other person in maternal or paternal pedigree is affected with same syndrome which suggests a new mutation in the index patient.

Differential diagnosis includes two groups; the syndromes with similar orofacial anomalies and disorders with similar limb defects.^{9,10} The first group includes cleft lip and palate syndromes, van der Woude's syndrome, which presents with paramedian lower lip pits and cleft lip/palate and is inherited as an autosomal dominant trait.^{9,10} The second group includes lethal PPS and PPS with ectodermal dysplasia. Both are autosomal recessive disorders. The multiple pterygium syndrome and lethal pterygium syndrome also need to be considered in the differential diagnosis.^{10,11} However, they are usually clearly distinguished by pterygia formation across various other joints or additional, mainly vertebral anomalies (Table 2).

Table 2: Differential diagnoses in the popliteal pterygium syndrome.

Syndrome	Cleft lip/ palate	Lip pits	Syngnathia	Popliteal pterygium	Other	Inheritance
Cleft lip/ cleft palate Syndromes	+	-	-	-	Various	AD
van der Woude syndrome	+	+	-	-		AD
Cleft palate/ lateral synechia syndrome	-/+	-	+	-	Hypoplastic lower jaw and tongue short upper lip	AD
Lethal popliteal pterygium Syndrome	+	-	+	+	Microcephaly corneal aplasia, ectropion, bony fusions, hypoplastic nose,absent thumbs	AR
Popliteal pterygium syndrome with ectodermal dysplasia	+	-	+	+	Woolly hair, brittle nails, ectodermal anomalies, fissure of sacral vertebra	AR

The overall prognosis of the popliteal pterygium syndrome is good. Patients need to undergo a series of operations for correction of the congenital anomalies. Cleft lip and palate repair can be done in consecutive sessions starting around 2-3 months of age. An artificial palate can be placed temporarily if feeding is difficult. Speech and hearing problems may develop secondary to the clefting abnormality. If salivation from the lower lip pits is severe, these need to be surgically removed. Early surgical intervention for the popliteal webs appears to be important with respect to long term results. During the operation special attention needs to be given to the vessels and nerves within the pterygium.¹²

Prenatal detection of cleft lip and palate by ultrasound is possible. In severe cases, the popliteal pterygium can also be disclosed by ultrasound because of abnormal movements and lack of ability to stretch the knee. However, in view of the good overall prognosis and the usually normal intelligence, ethical questions need to be taken into consideration if termination of pregnancy is requested by the parents.

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