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Fevre-Languepin Syndrome Popliteal Pterygium Syndrome a Case Report

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Case Report

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Abstract

Popliteal Pterygium Syndrome is characterized by congenital malformations that affect the face, extremities and genitalia. Autosomal dominant inheritance with variable expressivity and incomplete penetrance is widely accepted. This disorder is very rare. The incidence is 1/300.000. Affects both gender at same rates. The features of the syndrome are highly variable and may show a wide range of expressivity; even within families. The minimum diagnostic criteria are three of the following:

1. Cleft lip/palate.
2. Popliteal Pterygium.
3. Paramedian lower lip pool.
4. Genital abnormalities.
5. Abnormalities in nails.

The differential diagnosis is very important in sporadic cases and those with only mild expression. The overall prognosis of the Popliteal Pterygium Syndrome is good. The pathogenesis of the syndrome is only partially known. The analysis of chromosomes showed normal results, so at present there is no suggestion for a possible location of genes. The case presented below is a male 5 years old, from Caja Seca, Zulia State, Venezuela who is brought by the grandmother to the hospital Sor Juana Ines de La Cruz in the city of Mérida for presenting high respiratory infectious process, he is valuated and hospitalized to be managed by multidisciplinary assessment and for the respective surgical correction. The case reported has all the minimum criteria.

Keywords: Popliteal Pterygium; Autosomal Dominant Inheritance

Introduction

Popliteal Pterygium Syndrome is characterized by congenital malformations that affect the face, extremities and genitalia. Gorlin et al. coined the term "Popliteal Pterygium Syndrome" on the basis of the most peculiar anomaly, the popliteal webs [1,2].

In some publications the names of Fevre and Languepin [3] are used as an eponym. A more descriptive term has been suggested based on the condition of incomplete expression of the characteristics of the syndrome, which is "Facio-genito-popliteal syndrome"[4] However, the most commonly used for this condition is "Popliteal Pterygium Syndrome". It is widely accepted autosomal dominant inheritance with highly variable expressivity and incomplete penetrance. The term Popliteal Pterygium Syndrome has also been used for two inherited autosomal recessive conditions, however, they are clinically distinguishable [5,6].

Historical Notes

The formation of membrane tissue through the popliteal fossa is a rare event. The first reports of this anomaly in medical journals date back to the second half of the 19th century. The first report is attributed to Trelat in 1869 [7] Wolff reported to the Society of Surgeons in Berlina patient with popliteal membrane and other birth defects, including a caudal appendage and reduction defects of the toes. He compared the few common membranes with pterygium in some animals and noted that the popliteal pterygium had never been described in animals [8] Basch reported a patient 4 months old with popliteal pterygium, who died in infancy, and gave a very detailed description in the report of necropsy and drawing abnormal placement of tendons and muscle insertions in the pterigion [9] Kopits described four cases, three of them belonging to the same family, and gave details of the surgical techniques he used [10] Up the date a minimum of 81 patients with PPS are published in medical reports and at least 22 families with the disorder have been described. The diagnosis has been made in various ethnic groups that includes caucasians, Japanese [11] and black [12,13].

Incidence

This disorder is very rare and its incidence figure is difficult to calculate. Among the 21.170 cases in an orthopedic clinic, Kopits [10] had observed four cases of two families. Assuming that both families had been diagnosed with PPS, an incidence of 0-9/10.000 is calculated. Hecht and Jarvinen from 14 of 594 cases with cleft lip or cleft palate born between 1954 and 1963 in Oregon, USA; they only describe a family with two affected siblings with PPS. The incidence of cleft/lip palate in the general population varies between 10 and 18/10.000 [14] Calculated from this, the incidence of PPS would be 1/300.000, making it very rare.

Clinical Features

The characteristics of the syndrome are highly variable and can display a wide range of expressiveness, even within families, which can range from oro facial, skin, musculo-skeletal and genital anomalies.

Oro facial Anomalies

Cleft palate, with or without cleft lip have been found to be the most frequent anomaly in the PPS and is present in 91 – 97% of cases [2,11] All grades of severity of the cleft have been described, ranging from bilateral cleft lip and palate to only a cleft uvula. Paramedian lower lip pits occurs in 45 – 46% of cases. Intraoral tissue bands (syngnathia) were found in 42 – 46% of cases. These can seriously affect the opening of the mouth and must be removed surgically in the first year of life, or directly after birth if the limitation of mouth opening is so severe that feeding problems occur. Ankylo blepharonfili formeadnatum is located in approximately 20% of cases.

Skin and Musculoskeletal Abnormalities

The most important clinical feature is the popliteal pterygium, it is reported in 89 to 96% of cases [11]. This is probably an overstatement, given that the diagnosis of the syndrome is usually done through the appreciation of a popliteal membrane in the patients. In cases with family links, this anomaly is found in 56 – 58%. The popliteal membrane may contain a palpable cord of connective tissue, and may contain the popliteal artery and perineal nerve. The cord normally runs from the heel to the ischial tuberosity. It can seriously limit the 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 may be felt as a tight rope without limiting the range of motion. Absence of abnormal muscles or abnormal insertion of the muscles and tendons can occur. In the surgical procedure, care should be taken to not cut the vessels or nerves that supply the lower leg. Thorough preparation tissue from the plastic surgeon with elongation tendons and skin Z plasty is usually followed by a number of casting processes [15,16]

Additional pterygium through the inguinal fossa may occur in about 9% of the cases.

A very distinctive anomaly of the nailsis characterized by a pyramidal fold extending from the base to the outer portion of the nail, and is described by up to 33% of cases. Other nail abnormalities, such as nail hypoplasia, appear mostly in the toes. Syndactyly occurs in 50%, usually it affects the second and third toe, but sometimes the toes 2 to 5. Reduction defects of the fingers are rare, such as bifid or hypoplastic hallux or pollux or absence of thumbs [17] Other skeletal abnormalities include talipesequinovarus, hidden spina bifida, bifid ribs and short sternum. Hyperpigmentation of the cord of the popliteal fossa has been mentioned in two patients.

Genitourinary Anomalies

Abnormalities of the genitals are presented in both female and male patients. In women, the most common findings are hypoplastic labia majora, hypoplastic vagina and uterus also, and hypertrophy of the clitoris. In men, uni- or bilateral cryptorchidism, scrotum bifida or absent, but usually a normal-sized penis. In severe cases, genital abnormalities can result in reduced reproductive capacity. Inguinal hernias are occasional.

Mental Growth and Development

There is no recognizable problem with growth. Weight and height at birth, as well as in head circumference, usually reported as normal. Intelligence is usually normal. Some cases with reduced intelligence have been notified.

In the case described by Kopits [10] reference to additional clinical abnormalities such as contractures of the upper extremities, epicanthal folds, facial hemangioma, or dysplastic ears, and hidden spina bifida, are suggestive of the “Multiple Pterygium Syndrome”. In the women described by Wolff [8], additional unusual abnormalities included a caudal appendage. Intellectual deficit, however, was attributed to the lack of education in this patient. The patient of Hackenbroch [18] also had two rows of teeth, epicanthal folds and hidden spina bifida. The diagnosis in these three cases is uncertain. In all other cases with confirmed diagnosis of PPS intelligence is normal.

Range of Manifestation

Although most sporadic cases and indexed in familial popliteal pterygium cases had affected relatives who often only had cleft palate, cleft/lip palate, ankyloblepharon or pits on the lips or both. Probably they had not been identified as carriers of PPS if they had been the only ones affected in the family.

Minimal diagnostic criteria for PPS are three of the following [19]:
1. Cleft/lip palate.
2. Popliteal pterygium.
3. Paramedian lower lip pits.
4. Genital abnormalities.
5. Nail abnormalities.

Differential Diagnosis

The differential diagnosis is very important in sporadic cases and those with only mild expression. Two groups of disorders should be considered:

1.-Syndromes with similar orofacial anomalies [20,21] and
2.-Limb disorders with similar defects [5,6,22] The first group includes cleft palate inherited as an isolated anomaly, cleft lip and palate syndromes, the Van der Woude [23] Syndrome presented with paramedian lower lip pits and oral clefts, is inherited as an autosomal dominant trait, the syndrome cleft palate/sinequia which is also autosomal dominant and the syndrome of congenital syngnathia with no cleft palate and is also transmitted in an autosomal dominant condition [21] The combination of a hypoplastic thumb and cleft lip and palate also can be found in Juberg-Hayward Syndrome [24] which also is presented with microcephaly, syndactyly and hypo plastic genitals and it can also be seen in the Fraser Syndrome [25] however, never presented with popliteal pterygium, but in the classical form there is unilateral or bilateral cryptophthalmos. Among the disorders that have similar defects in the extremities the most important differential diagnosis is described by Bartsocas & Papas [5] in a consanguineous family. This condition occurs with popliteal membranes, facial clefts, syngnathia, ankyloblepharon, aplasia of thumb, syndactyly, hypoplasia of labia majora, microcephaly, corneal aplasia, hypoplasia of nasal wings. In other cases of this autosomal recessive hereditary disease, ectropion and severe reduction of metacarpals and metatarsals in complete sindactilias have been described [17].

Another distinctive syndrome with popliteal pterygium also shows genitourinary malformations including absence of a kidney, cracks in the sacral vertebrae, epithelial lesions and dystrophic scalp, tinea, dull hair, dystrophic nails and subungual hyperkeratosis with enlargement and thinning of the sheet. Mental

retardation, ectodermal dysplasia and scar atrophy of the scalp are the most important characteristics for differentiation of this inherited autosomal recessive syndrome.

Multiple Pterygium Syndrome [26] and Lethal Pterygium Syndrome [27] should also be considered in the differential diagnosis. However, they are usually clearly differentiated by the formation of pterygium in other joints or additional vertebral anomalies.

Natural History and Management/ Treatment

The overall prognosis of PPS is good. Patients often undergo a series of plastic surgery operations, usually from neonatal period and extend until puberty. In the neonatal period the ankyloblepharon and oral sinequia are excised to allow the eye opening and best feeding. Repair of cleft lip and palate are made according to the latest correction procedures.

An artificial palate, can be temporarily place if feeding is difficult. A cleft palate is usually closed in the first year of life. Speech and hearing problems can develop secondary to the fissure. If severe salivation is due to the holes on the lower lip, they must be surgically corrected.

Surgical intervention at an early age of the popliteal membrane appears to be important with respect to long-term results. Operations include the spin-off of the band, mobilization of nerves and vessels, Z plasty of skin and tendon removal. During the operation should be taken special attention to the vessels and nerves in the pterygium. Postoperatively, plaster casts and physical therapy are used to maximize long-term results. Cryptorchidism may require surgery within the first three years of life.

Heritage

The subjects affected in consecutive generations by transmission men to men have been reported so likely as auto somal dominant [14,28-30] The male: female ratio is 1:1 [14] Although all those affected have the same disorder, they differ considerably in the expression pattern of malformations.

Monozygotic twins with different characteristics of PPS have been observed [31] the variable expression occurs between generations, but brothers show a trend similar phenotypic expression. In incomplete expressions the syndrome is often recognized only if a family member fully expresses the condition of a popliteal birth membrane.

Most cases are sporadic, however, information about family history is very incomplete in most sporadic cases. Mutations in the IRF6 gene affect the development and maturation of tissues in the face, skin, and genitals, resulting in the signs and symptoms of PPS.

Genital abnormalities can cause infertility and thus affect reproductive fitness of the subject. This, and the high number of sporadic cases, suggests a high rate of new mutations. Advanced paternal age is in a series of sporadic cases, suggesting new mutations.

Prenatal Diagnosis

Prenatal detection of cleft/lip palate with ultrasound is possible. In severe cases, the popliteal pterygium can also be revealed by ultrasound, due to abnormal movements and the inability to extend the knee. However, in view of the good overall prognosis and normal intelligence, ethical issues for pregnancy termination if requested by parents must be taken into account.

Pathogenesis

The pathogenesis of the syndrome is known only in part. Membranes and thready intraoral ankyloblepharonadnatum suggest excessive proliferation of the epithelial layer of the blastomere of the lower jaw and eyelids, occurring in the early first trimester of pregnancy [32,33] In the popliteal pterygium displacement of muscles and tendons occurs [15]. The mechanism for PPS is clearly different from the mechanism of Multiple Pterygium Syndrome, when the movement of muscles and pterygium formation can be attributed to the limited intrauterine mobilization [27]. The lower lip pit is believed to be a remnant of the lateral grooves from a genetic defect [4]. It has been found in a patient with a deletion of chromosome 1q,46 which, in addition, had developmental delays, hearing loss, microcephaly, and various facial dysmorphic anomalies, but without cleft palate or pterygium.

Clinical Case

The case presented below is a 5 year old male, born and from CajaSeca, Zulia State, Venezuela who is led by the grandmother to Hospital Sor Juana Ines de la Cruz of the city of Merida for presenting upper respiratory tract infectious process, he is valuated and hospitalized to be

managed by multidisciplinary assessment and for the respective surgical correction.

a) Prenatal and obstetrical history: Product of a mother of 33-year-old, fifth pregnancy, obtained vaginally, mother does not remember the number of obstetric consultations, there were no complications during pregnancy neither the delivery. Birth weight 3.000 g, birth length 46 cm. He remained hospitalized for two months for respiratory complications (not specified).

b) Family background: Grandmother denies other diseases or malformations in other family members.

c) Functional Review: Do not walk (due to functional limitation), only crawl. Dysarthric speaking, nasal speech. Adequate level of intelligence according to age and social status.

d) Physical Exam: Vital signs normal. Weight: 16.5 kg Size: 99.8 cm approximate (using bony prominences as reference points).In stable clinical conditions, mild skin and mucosa paleness, normocefalus, right incomplete unilateral cleft lip according to Millard or Byrd, hard and soft palate cleft, partial edentula, multiple caries, flat abdomen, without visceromegalies, or herniations. Penis normal configuration, no scrotum, each testicle housed in the ipsilateral popliteal pterygium edge at 4,6 cm from the base of the penis, anus permeable unaltered, undamaged spinal column, upper extremities unchanged, lower limb external rotation, abduction and attitude sustained bending both knees in 45° angle with limited extent in whole, bilateral extensive skin fold seen from the ischial region to posterior ipsilateral ankle with a delta-shaped, translucent with display of arteriovenous elements throughout its whole extension, range of articular motion of both hips is full, position of both feet in equinovarus with adduct of bilateral forefoot, varus bilateral midfoot, shortening of bilateral tendon of Achilles giving attitude equinovarus, hallux bilateral bifida, left hallux in an attitude of sustained extension, syndactyly of second and third bilateral finger, persistence of interdigital fold between I and IV bilateral, nail hypoplasia in the lower limbs. Neurologic preserved for age (bone and tendon reflex and aquiliano not valued due to restrictions skin fold).

Discussion

The minimum criteria for diagnosing a PPS rest in the presence of at least three of the five aforementioned criteria, in this medical case the presence of four of these criteria, are given by: popliteal pterygium, cleft lip and palate, genital abnormalities and nail abnormalities, as can be seen in the images of Annex. As described in the literature reviewed, these abnormalities were present from birth and no history of consanguinity. Nor alterations in other organs and systems were found, no alteration of intelligence and memory.

No chromosomal studies were conducted to the patient and even that is described that this congenital abnormality is transmitted from one patient affected to their offspring, in this case the parents or another family member of the affected child showed no phenotypicanomaly.

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