Spectrum of Features in Pterygium Syndrome

Sanjay Y. Parashar, Peter J. Anderson, Neil McLean, Marzoeki Djohansjah and David J. David, Australian Craniofacial Unit and Institute, Adelaide, South Australia, and 1Department of Plastic Surgery, School of Medicine, Airlangga University, Indonesia.

Pterygium syndrome is a complex and rare congenital deformity that consists of contractures involving multiple flexural surfaces and associated craniofacial anomalies. It often has associated conditions, including anomalies of the cardiovascular, respiratory, gastrointestinal and genitourinary systems. It may present in different forms, including multiple pterygium syndrome of Escobar, lethal multiple pterygium syndrome, popliteal pterygium syndrome, lethal popliteal syndrome (Bartsocas-Papas syndrome) and arthrogryposis multiplex congenita. The clinical presentation, multidisciplinary management and the long-term outcome in three patients with this condition are presented.

Key Words: congenital deformity, pterygium syndrome

Introduction

Pterygium syndrome has a wide spectrum of presentation. Multiple pterygium syndrome (MPS) of Escobar is an autosomal recessive malformation consisting of growth retardation, multiple pterygia involving neck, fingers, antecubital, popliteal, intercrural and craniofacial anomalies. The typical craniofacial features are downslanting palpebral fissures, epicanthal folds and small mandible. This syndrome is clearly distinguished from popliteal pterygium syndrome (PPS) that classically involves contractures of the lower extremities with associated craniofacial and genitourinary anomalies. PPS is autosomal dominant with variable expressivity and incomplete penetrance. The incidence of all forms of pterygium syndrome is uncertain and they are frequently nonspecifically termed as arthrogryposis.1 There have been previous reports of the entity, but most are individual case reports.2-3 A highly variable presentation of this anomaly has been reported with a wide range of severity. A very severe form is the lethal MPS and lethal PPS with a high incidence of fetal death, and it is presumed that the pterygia may result from embryonic onset of fetal akinesia.4 Other theories such as abnormal collagen and aplasia of developing muscle fibres have also been proposed.2-5 We reviewed the clinical presentation of three cases of this group of anomalies managed from early childhood, and report on the outcome of the multidisciplinary management of this condition.

Case reports

Case 1

A 3-year-old European male presented to the Australian Craniofacial Unit (ACFU) with MPS, Pierre Robin sequence and undescended testes. An antenatal ultrasonography at 20 weeks’ gestation had reported multiple pterygium, cleft palate and cystic hygroma. Fetal distress led to an emergency caesarean section at full term.

The clinical features included extensive pterygia of the neck extending from the chin to the sternum with the chin tethered to the chest. The contractures involved all the joints of the upper and lower limbs; deformities included multiple syndactyly, intercrural pterygia, congenital hip dislocation, and rocker bottom feet (Figures 1 and 2). He was unable to walk, had difficulties using the wheel chair, and was unable to lie supine. The facial anomalies included microglossia with restricted mouth opening, cleft of the soft palate, hypoplastic
tongue, enophthalmos, bilateral epicanthal folds and antimongoloid slant (Figure 3). Other anomalies present included chest wall deformity with hypoplastic nipples and thoracolumbar scoliosis. Detailed radiological investigations revealed fusion of the cervical spine at the C1 and C2 level, and incomplete fusion of C3–4 vertebrae. The mandible was hypoplastic with an obtuse gonial angle and hyperplastic coronoid process extending into the temporal fossa (Figure 4).

A multidisciplinary team that included specialists in craniofacial, paediatric and orthopaedic surgery, orthodontics, dentognathic surgery, otorhinolaryngology, enophthalmos, bilateral epicanthal folds and antimongoloid slant (Figure 3). Other anomalies present included chest wall deformity with hypoplastic nipples and thoracolumbar scoliosis. Detailed radiological investigations revealed fusion of the cervical spine at the C1 and C2 level, and incomplete fusion of C3–4 vertebrae. The mandible was hypoplastic with an obtuse gonial angle and hyperplastic coronoid process extending into the temporal fossa (Figure 4).

His neonatal period was complicated by the presence of airway obstruction and feeding difficulties. These were managed conservatively by the speech pathologist and respiratory physician. His ventilation was improved with the use of continuous positive airway pressure. Following this, at the age of 3 years, a review by the respiratory physician and formal polysomnogram revealed significant episodes of airway obstruction. He underwent linear and angular distraction of the mandible (Figure 5) to improve his airway, feeding, mouth opening and permitted repair of the cleft palate. Subsequently, at the age of 10 years, he underwent multistaged surgical release of the neck contracture with the use of split thickness skin graft in addition to several orthopaedic procedures for his lower limb anomalies that included congenital hip dislocation, fixed deformity of the hip, knee contracture and rocker bottom feet. He is currently 12 years old, uses a wheelchair and has no trouble sleeping in the supine position (Figure 6). He will remain under multidisciplinary review until he reaches skeletal maturity.

**Case 2**

A European female patient was born with bilateral cleft lip and palate (CLP) with lower lip pits, popliteal contracture extending down to the ankle, preaxial polydactyly, simple syndactyly, calcaneovalgus deformity and hypoplastic labia majora. She was diagnosed with PPS. She underwent multidisciplinary assessment by a team that included specialists in craniofacial and orthopaedic surgery, orthodontics, dentognathic surgery, otorhinolaryngology, enophthalmos, bilateral epicanthal folds and antimongoloid slant (Figure 3). Other anomalies present included chest wall deformity with hypoplastic nipples and thoracolumbar scoliosis. Detailed radiological investigations revealed fusion of the cervical spine at the C1 and C2 level, and incomplete fusion of C3–4 vertebrae. The mandible was hypoplastic with an obtuse gonial angle and hyperplastic coronoid process extending into the temporal fossa (Figure 4).
tistry, speech pathology and physiotherapy. The CLP was managed according to the published cleft protocol of the ACFU. The cleft lip was repaired at 3 months and the palate at 9 months of age. A bilateral alveolar bone graft was performed at 11 years, and bimaxillary surgery and augmentation of malar bone at the age of 18 years. Final surgery included revision of the lip and augmentation rhinoplasty at the age of 20 years (Figure 7). The orthopaedic and physiotherapy team managed her knee and ankle deformities conservatively during her early childhood with splints for 2 years and achieved total correction without any residual functional deformity.

Case 3
A 3-month-old Asian male presented with PPS and a range of associated anomalies. The facial anomalies included complete midline cleft of the lip and palate with nasal deformity, ectropion of the upper eyelids, frontal hirsutism and bilateral choanal atresia (Figure 8). The associated upper limb anomalies were complete syndactyly of the second and third fingers, hypoplastic thumb, agenesis of the fifth digit of the right hand, and agenesis of three radial digits of the left hand. The lower limb deformities included bilateral popliteal pterygia, bilateral talipes equinovarus, intercrural webbing and agenesis of the lateral three digits (Figure 9). In addition, he had associated genitourinary anomalies that included bifid scrotum, micropenis and testicular agenesis.

Due to the multitude of anomalies, he underwent a multidisciplinary assessment. A radiological study detailed the skeletal anomalies and genetic testing revealed chromosome 14/5 translocation (Figure 10).

Clinically, the priority was management of bilateral ectropion of the upper eyelids that was causing damage to the cornea. This was treated by release with full thickness skin grafting. A large defect in the lip and nasal structures necessitated recruitment of tissues from the cheeks and forehead using tissue expansion (Figure 11). It is planned that he will undergo further coordinated reconstructive surgery for his hand, lower limbs and genitourinary anomalies. He is presently 3 years old and will remain under review until skeletal maturity.
PTERYGIUM SYNDROME

Discussion

MPS is a complex congenital deformity that consists of contractures of multiple flexural surfaces, anomalies involving the craniofacial region and extremities, and which often has associated systemic abnormalities. This condition may occur sporadically and is peculiar in that it may have autosomal dominant or recessive inheritance.

The genetic abnormality has not been detected for MPS, but a mutation in the \textit{IRF6} gene is the possible cause of PPS.\textsuperscript{7} The underlying pathogenesis is not clear, but it has been proposed that it is due to decreased fetal movement.\textsuperscript{4,5} A prenatal diagnosis can often be established with Escobar syndrome as in Case 1 of this report, and the presence of associated cystic hygroma is one of the typical signs of MPS.\textsuperscript{3,8} One report mentions that the severity of the disease may be indicated by the presence of a spinal anomaly.\textsuperscript{9}

Pterygium syndrome has a wide range of clinical presentations, and pterygia is consistently present involving several joints. PPS has characteristic involvement of the popliteal region, which may range from mild contracture as in Case 2 to extensive knee, ankle and crural pterygia as in Case 3. It is suggested that the presence of at least three of the following deformities including cleft lip and palate, popliteal pterygium, paramedian lower lip sinuses and genital anomalies are required for the diagnosis of PPS.\textsuperscript{10} Lower lip pit was seen in both our cases with PPS, and one of the reports indicates its incidence as 56% of PPS cases.\textsuperscript{11} Another report suggests that PPS and van der Woude syndrome are allelic and results from mutations in the \textit{IRF6} gene.\textsuperscript{7} On the other hand, MPS primarily consists of multiple contractures involving all the joints.
of the limbs and the neck as well. There are significant musculoskeletal anomalies and growth retardation.\textsuperscript{3,9} Associated craniofacial anomalies in MPS include micrognathia, cleft palate, low set ears, antimongoloid slant, and epicanthal folds. In MPS, primary pathology may be the pterygium, and the facial and limb anomalies may be secondary to the contractions, while in PPS, all the anomalies appear to be part of the multisystem involvement. The presence of hypertrophied coronoid processes in Case 1 in this series is a consequence of the force exerted by the temporalis muscle during mouth opening.

The range of associated anomalies leads us to undertake a multidisciplinary team approach. Airway and swallowing are often the functional problems encountered during the neonatal period. Case 1 had severe airway obstruction, and a mandibular distraction performed at the age of 3 years benefited him by improving his airway and feeding and permitted closure of the cleft palate. His neck pterygia involved shortening of all the tissue planes, however, releasing the skin and platysma resulted in a reasonable improvement in the neck movement. He is planned for a further stage of neck release. Any definitive surgery will be planned after the completion of his skeletal growth.

Case 2 has a mild form of PPS and has been managed throughout her developmental period. The bilateral CLP was managed according to the ACFU protocol until after the completion of her skeletal maturity. The lower limb pterygia was managed conservatively with complete functional recovery. At the other extreme, Case 3 represents a severe form of PPS with lower limb pterygia, multiple digital anomalies, and multiple facial and genital deformities.

The range of clinical features associated with multiple pterygium syndromes is peculiar. These highlight the benefit of multidisciplinary assessment and management to deal with multiple anomalies that are associated with this condition.

Due to the undetermined growth pattern of multiple pterygium syndromes (MPS of Escobar and PPS), it is suggested that all such patients should be longitudinally followed up at least until maturity.

Acknowledgements

We would like to express our special thanks to Louise Netherway (Research Officer) and Christopher Sprod (Clinical Photographer) for their support and assistance in preparing this manuscript.

References