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CASE REPORT

Pfeiffer syndrome type 2: a case report

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Abstract

Objective: Report a rare case of Pfeiffer's syndrome type 2 in a male newborn. **Case Report:** Newborn male, preterm term of 33 weeks and 2 days, serial ultrasound suggesting presence of craniosynostosis and other abnormalities such as irregular and narrow vertebrae, pachygium, and ventriculomegaly in the second trimester, being confirmed later with magnetic resonance imaging. There was no need for obstetrical medications and maneuvers for the birth. Apgar score 4, heart rate less than 100bpm, precarious respiratory evolution, orotracheal intubation, umbilical venous catheterization and orogastric tube were required. With 2 hours of life presented bradycardia along with hemodynamic instability evolved to a cardiorespiratory arrest with no success in cardiopulmonary resuscitation. He passed away 3 hours after birth. **Comments:** Pfeiffer's syndrome is rare, being type 2 the most lethal because it has a clover-shaped skull. It is associated with the genetic mutations in fibroblast growth receptors FGFR1, FGFR2, and FGFR3. Premature fusion of the cranial sutures prevents normal skull growth by interfering with the shape of the face and head. The prognosis is associated with the severity of the anomalies and the early diagnosis through the gestational and family history, through detailed physical examinations and images (three-dimensional ultrasonography and MRI). The patient should have multidisciplinary treatment at birth.

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INTRODUCTION

Classified as an autosomal dominant syndromic craniosynostosis with complete penetrance of hereditary or sporadic origin, related to advanced paternal age, Pfeiffer syndrome is rare and affects one in 100,000 people[1,2]. It was described by Rudolf Arthur Pfeiffer in 1964[3], materialized by the presence of deviated thumbs and large and wide hallux associated with craniofacial malformations[3,4].

In most cases, it is related to genetic mutations in three of the four fibroblast growth factor receptors FGFR1 locus 8p11.2-p11.1 and FGFR2 locus 10q26. Studies show that, among craniosynostosis, a higher proportion of cases are caused by mutations in the FGFR2 gene, followed by FGFR3 and finally FGFR1[5]. Genetic variability is defined as "differences in mutant gene expression (differences in clinical severity, for example) that may result from the same mutation in two individuals due to differences in genetic background or environmental experience"[4].

There are three subtypes for the syndrome according to the severity of its manifestations[8]. The so-called "classic" or type 1 Pfeiffer syndrome manifests itself in a milder form, so that it is possible to observe cases of brachycephaly, hypoplasia of the midface, broad fingers and toes, and normal neurological and intellectual development, being this is the most common subtype. In type 2, with a worse prognosis, there are upper airway malformations, developmental delay, extreme proptosis, toe and finger abnormalities, elbow ankylosis, cloverleaf-shaped skull - trigonocephaly - and hydrocephalus, with severe neurological impairment. . Finally, type 3 presents abnormalities similar to type 2, except for the cloverleaf-shaped skull[9].

CASE REPORT

Newborn male, child of healthy, non-consanguineous parents, with no history of congenital malformations or heredofamilial diseases. Pregnancy assisted in another service, with serial ultrasounds, suggesting the presence of craniosynostosis, irregular and narrow vertebrae, pachygyria and ventriculomegaly in the second trimester, later confirmed with gestational magnetic resonance imaging. Negative maternal serologies. Mother admitted in expulsive labor, at 33 weeks and two days of pregnancy, without the need for medication or obstetric maneuvers for birth. This was the second pregnancy preceded by a miscarriage of twins, weighing 2,325 grams, 40 centimeters, with an Apgar score of four in the first minute. Received in sterile fields, taken to a warm crib, dried, exchanged fields, aspirated the airways and monitored (saturation and heart rate). Heart rate was less than 100 beats per minute. Positive pressure ventilation was started, with an initial oxygen concentration of 21%, at a rate of approximately 40 breaths per minute. After 15 seconds, it did not reach the desired frequency even with adequate chest movements. Positive pressure was maintained with an increase in oxygen supply to 100%, followed by orotracheal intubation, umbilical venous catheterization and orogastric tube. He was referred to the neonatal intensive care unit, coupled to mechanical ventilation, laboratory tests were performed, and chest and abdomen X-rays were performed.

The physical examination revealed the presence of multiple malformations: alteration of the craniofacial configuration, with trigonocephaly - "cloverleaf skull" (figure 1), hypertelorism, ocular proptosis, low implantation of the ears, thoracic and lumbar scoliosis (figure 2), ankylosis of the elbows, synostosis of the humerus, radius and ulna, and extremities with varus and broad thumbs and halluxes with syndactyly in hands and feet.

At two hours of life, he had bradycardia with hemodynamic instability. Hypothermia, hydroelectrolytic, acid-base, coagulation and anemia disorders were excluded. She received volume expansion with crystalloids and dopamine was started. He evolved with cardiorespiratory arrest, and cardiopulmonary resuscitation was instituted without success. He died three hours after birth.

DISCUSSION

The premature fusion of the cranial sutures (craniosynostosis), mainly the coronal, sagittal and lambdoid, ends up preventing the normal growth of the skull and can lead to an increase in intracranial pressure, causing the rupture of allometric growth and resulting in interference in the shape of the entire skull. the face and head[10].

There may be hearing loss due to complete or partial occlusion of the external auditory canal, visual abnormality due to ocular proptosis, central nervous system malformations (Arnold-Chiari syndrome), seizures, consolidation of vertebrae, cleft palate, and choanal atresia. Maxillary hypoplasia can lead to corneal damage and restriction of air and food passage. Regarding the feet and hands, we can find from broad and radially deviated thumbs to big fingers and brachydactyly. Cardiac malformations, although rare, may be present[8,9].

The natural course of neuropsychomotor development in these patients is unknown, since cranial compression limits



Figure 1. - Clover-shaped craniosynostosis. Craniofacial changes typical of type 2 Pfeiffer syndrome.



Figura 2. Radiological aspects of bone alterations.

brain growth, exposes the eyes over shallow orbits and prevents the development of the midface[11,12]. Although there are still clinical failures and limited corrective surgeries, it is possible to obtain a successful outcome from prenatal diagnosis[4].

The evaluation of craniosynostosis begins with the gestational and family history and detailed physical examination, however, the definitive diagnosis requires confirmation by imaging methods performed during pregnancy, three-dimensional images in cases where no cranial anomalies are found, and magnetic resonance imaging in order to to quantify bone defects, brain, muscle and airway malformations (choanal atresia/stenosis and laryngotracheal anomalies), allowing for an early approach and treatment[13]. As the reported patient was followed up at another service, it was only during the interview carried out in the delivery room that the syndrome became known. In the case presented, trigonocephaly was diagnosed on gestational ultrasound, however, it alone does not fulfill the diagnostic criteria for type two syndrome. Carriers of the severe form of the disease can progress to intrauterine death or death in the first hours of life, preventing molecular evaluation, considered a complement to diagnostic confirmation, given the high clinical variability of the disease. About 67% of affected individuals have mutations in the FGFR2 gene, of which 5% of patients with type one of the syndrome have mutations in the FGFR1 gene[14].

Early treatment (performed in the first three months of life) aims to decompress the brain mass and remodel the skull, expanding the bone orbits, reducing exophthalmos and expanding the airways[11]. These interventions are related to a reduced risk of secondary complications, increased survival and should be analyzed individually[12].

Multidisciplinary care should be instituted at birth, aiming to improve the development of physiological functions, better aesthetic and functional post-surgical results. On the other hand, surgeries during the growth of the facial region tend to present poor results, requiring new approaches in the future. As for skeletal malformations, surgical techniques are limited and, when possible, reserved for correction and improvement of the limitations caused by the disease[12-14].

Complications are common in patients with type two Pfeiffer syndrome[9]. Among them, the following stand out: aspiration pneumonia, hearing loss, intracranial hypertension, seizures, infections and chronic hypoventilation, in addition to complications resulting from the surgeries. The prognosis of these patients is directly related to the severity of cranial and respiratory anomalies, and to early diagnosis and treatment. Those with type 1 usually have a good evolution, while those with types 2 and 3 are associated with early death[9].

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