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Congenital amyoplasia and maternal cocaine use

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Resumen

Introducción: La artrogriposis múltiple congénita (AMC) es un síndrome caracterizado por contracturas congénitas no progresivas de dos o más articulaciones. La forma clásica de AMC llamada amioplasia es siempre esporádica. En la artrogriposis neurógena, la forma más frecuente (90%), la afectación inicial se encuentra en las neuronas del asta anterior de la médula, las raíces nerviosas o el nervio periférico.

Casos clínicos: Se exponen dos casos de recién nacidos que desarrollaron una clínica similar de amioplasia. El primer niño tenía contracturas articulares, atrofia de los músculos de las extremidades inferiores e incontinencia. El segundo niño presentó paraplejía fláccida con atrofia muscular y atonía muscular abdominal. Las dos madres eran consumidoras de cocaína durante el embarazo. En ambos pacientes los exámenes neurofisiológicos demostraron una denervación a diferentes niveles de la médula espinal.

Discusión: Se ha postulado como causa de amioplasia congénita una necrosis de la médula espinal fetal debida a hipotensión sistémica. En adultos se han descrito casos de episodio cerebrovascular relacionados con el consumo de cocaína. Probablemente, los mecanismos están relacionados con la estimulación adrenérgica, la vasoconstricción cerebral y cambios bruscos en la presión arterial. En ambos casos las características clínicas descritas al nacer fueron debidas a denervación de la médula espinal a diferentes niveles. Los defectos encontrados en nuestros pacientes podrían estar asociados a consumo materno de cocaína durante el embarazo, que produciría vasoconstricción del pequeño lecho vascular e isquemia-infarto por alteración vascular en la médula espinal del feto.

Palabras clave

Amioplasia, artrogriposis, cocaína, neonato, patología del sistema nervioso

Abstract

Introduction: Arthrogryposis multiplex congenita (AMC) is a term used to describe a disorder characterized by multiple, nonprogressive joint contractures at birth. The classic form of peripheral AMC, referred to as amyoplasia, is always sporadic. In neurogenic arthrogryposis, the most frequent form (90%), the initial injury would be in the anterior horn cells of the spinal cord, the nerve roots or the peripheral nerve.

Case reports: We report the cases of two newborns who presented similar clinical signs of amyoplasia. One had joint contractures, muscle atrophy and incontinence. The other had flaccid paraplegia with muscle atrophy in lower limbs and abdominal muscle atony. Both mothers had consumed cocaine during pregnancy. In both patients, neurophysiological examination demonstrated denervation at different levels of spinal cord.

Discussion: Necrosis of the fetal spinal cord caused by systemic hypotension has been postulated as a cause of amyoplasia. The mechanism of cocaine-related cerebrovascular accidents in adults is probably related to adrenergic stimulation, cerebral vasoconstriction and a sudden surge in blood pressure. In our two cases, the clinical findings reported at birth were due to denervation at different levels of the spinal cord. Therefore, the defects in our patients may be associated with maternal use of cocaine during pregnancy, producing small vessel vasoconstriction and vascular disruption in the fetal spinal cord.

Keywords

Amyoplasia, arthrogryposis, cocaine, newborn, nervous system diseases

Introduction

Arthrogryposis multiplex congenita (AMC) is a term used to describe a highly heterogeneous disorder characterized by multiple, nonprogressive joint contractures at birth. The classic form of peripheral AMC, referred to as amyoplasia, is always sporadic. A distal form of AMC, with major involvement of the hands and feet, was attributed by Hall to autosomal dominant inheritance (OMIM: #108120; #301680; #108130)[1-3].The effects of prenatal exposure to cocaine on newborns are not fully known. Many studies have demonstrated that children of mothers who consume cocaine during pregnancy are born preterm, with low birth weight, reduced birth length and head circumference, and a high incidence of obstetrical complications[4,5]. Serious consequences, like cerebral, cardiac, skeletal, gastrointestinal

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tract and urinary tract malformations, have also been reported[6]. The newborns of cocaine-using mothers have been described as irritable and hypersensitive, with feeding difficulties[7], circumstance that apparently are indicative of neurological dysfunction. We report two newborns who displayed similar clinical signs of spinal injury.

Case reports

Case 1 (figures 1 and 2)
This patient is the product of the second pregnancy of a 38-year-old smoker who also consumed cannabis. The delivery, at 34.6 weeks, was uncomplicated, despite premature rupture of membranes. The mother had negative serologies for HIV, HCV, HBsAg, VDRL and *Toxoplasma*. The newborn was a boy with a birth weight of 1400 g, head circumference of 29.5 cm and birth length of 41 cm. His Apgar score was 9 at 1 minute and 10 at 5 minutes, and arterial cord blood values were pH 7.19 and base deficit –4.9. He was transferred to the neonatal intensive care unit because of respiratory distress, and required a single dose of surfactant and assisted ventilation. Extension of lower limbs, flexion of hips, clubfoot and muscle atrophy in lower limbs were observed. The urinary bladder became distended and suprapubic bladder compression was successful in emptying the bladder periodically. An increase in the frequency of defecation was also observed. The results of the initial blood test (glucose, electrolyte, creatinine and calcium concentrations and complete blood count with differential cell and platelet counts) were all normal. The cerebrospinal fluid was normal. He tested positive for cocaine in urine and his mother admitted her use of cocaine during pregnancy. The abdominal X-ray showed an enlarged bladder. Ultrasound showed a normal urinary tract and kidneys. A cranial ultrasound was normal. Cranial computed tomography revealed no evidence of blood loss or subarachnoid hemorrhage. Spinal cord magnetic resonance imaging (MRI) showed no abnormalities. Electromyographic analysis detected signs of bilateral denervation of the muscles of metameric segment S1-S2, with lesion of the spinal *terminal/trigeminal* tract.

Figure 1.

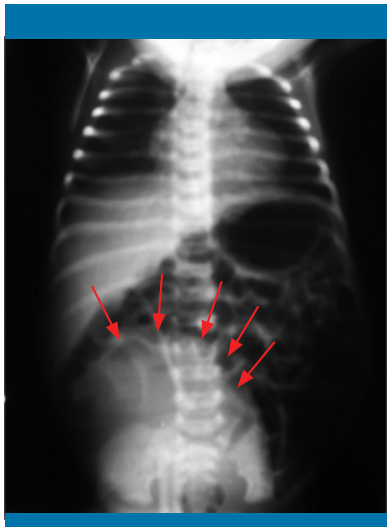

Figure 2.

Case 2 (figures 3 and 4)
The second case involved a male infant, born at 28 weeks' gestation of a 17-year-old mother. The mother had inhaled cocaine during pregnancy and had experienced a cocaine overdose one week before delivery. Premature rupture of membranes occurred 26 hours prior to delivery. As fetal monitoring during the 6 hours before delivery showed the infant to have multiple variable decelerations, cesarean section was performed. His birth weight was 1200 g, the head circumference was 26.5 cm and the birth length was 38 cm. The Apgar scores were 5 at 1 minute and 7 at 5 minutes. Arterial cord blood values were pH 7.29 and base deficit –2.6. The infant was transferred to the neonatal intensive care unit, where he required assisted ventilation for 56 hours. The initial physical examination revealed hypotonia, weak neonatal cry and absence of neonatal reflexes. Umbilical artery catheterization was not performed. The urinary bladder became distended and suprapubic bladder compression was successful in emptying bladder periodically. Flaccid paraplegia with muscle atrophy in lower limbs and abdominal muscle atony developed. Diagnostic evaluation included: blood glucose, electrolyte, creatinine and calcium concentracions and complete blood cell count and platelet count, all of which were normal. HIV antibodies, HIV antigen and VDRL were negative. X-ray of the thoracic and lumbar portion of the spine and electroencephalography were normal. Cerebrospinal fluid evaluation at 24 hours of age showed 9600 red blood cells and 20 white blood cells per microliter, glucose 71 mg/dL, protein 0.42 g/L and negative Gram stain. Cerebral ultrasonography appeared normal. Spinal cord MRI did not show macroscopic abnormalities. Electromyographic analysis detected central denervation between L2-L4.

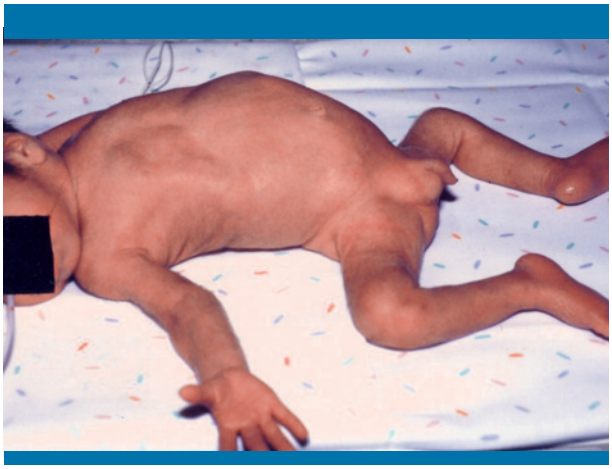

Figure 3.

Figure 4.

Discussion

Arthrogryposis multiplex congenita is a syndrome that can be inherited or acquired. It can be caused by poor muscle development. The muscles develop during embryogenesis through the impulse of nervous fibers and motor neurons. The etiology of arthrogryposis is multifactorial and, in one third of the cases, it is possible to identify a genetic cause[8]. In neurogenic arthrogryposis, the most frequent form (90%), the initial injury would involve the anterior horn cells of the spinal cord, the nerve roots or the peripheral nerve. The muscle is replaced by fibroadipose tissue. In myopathic arthrogryposis, the initial injury affects the muscle or muscle synapses. The incidence is minor, around 7%. This occurs in some genetic diseases, often inherited, in which the contractures are associated with a disease such as congenital muscular dystrophy and congenital myopathy[9]. An electrophysiological study can be performed to assess muscle activity and determine whether muscle, peripheral nerve or spinal cord are affected. The combination of nerve conduction and electromyographic studies and muscle biopsy provides valuable diagnostic information[10].

Cocaine acts at the peripheral level, inhibiting nerve conduction, preventing norepinephrine uptake at the nerve terminal receptors and increasing norepinephrine levels[11]. This mechanism causes vasoconstriction, tachycardia and abrupt changes in blood pressure. Higher rates of early pregnancy loss and third-trimester placental abruption appear to be major complications of maternal cocaine use[12]. Cocaine crosses the placental barrier by simple diffusion, a circumstance that allows a concentration of up to 80% of the plasma concentration of the mother to reach the fetus[13]. Retrospective works in children exposed to cocaine have suggested an increasing incidence of periventricular hemorrhage and leukomalacia[14,15]. The necrosis of the fetal spinal cord produced by systemic hypotension has been postulated as a cause of amyoplasia. This would cause cellular ischemia of anterior horns in the fetal spinal cord. The effects of prenatal exposure to cocaine on the structure and function of the central nervous system of the newborn are still not clearly demonstrated[16]. Cocaine or opiate exposure during pregnancy has been shown to increase the risk for manifesting a constellation of central and autonomic nervous system anomalies[17]. Norepinephrine, serotonin and dopamine are the neurotransmitters present at early stages of fetal brain development. Cocaine increases the circulating levels of all three neurotransmitters in the fetus. Numerous cases of cerebrovascular diseases associated with cocaine abuse have been reported in adults. Di Lazzaro et al.[18] reported the first case of spinal cord transient ischemic attack related to cocaine misuse, as well as two cases of spinal ischemic infarction. The MRI in spinal cord stroke can be normal despite profound neurological deficits, especially if performed acutely. The mechanisms of cocaine-related cerebrovascular accidents in adults are probably related to adrenergic stimulation, cerebral vasoconstriction and a sudden surge in blood pressure at all levels of the central neuraxis (including spinal cord). In our two cases, the clinical findings reported at birth were due to a denervation in different spinal cord levels. Therefore, the defects in our patients may be associated with maternal use of cocaine during pregnancy, producing small vessel vasoconstriction and vascular disruption in the fetal spinal cord.

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