Arthrogryposis Multiplex Congenita: Report of two cases

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ABSTRACT

Arthrogryposis Multiple Congenita (AMC) is a rare syndrome that represents a group of congenital conditions characterized by joint contractures in two or more joints, non-progressive, usually symmetrical, of unknown etiology and which may be associated with other malformations, such as visceral and neurological. We present two isolated cases with characteristic features of AMC, seen in a high-risk pediatrics outpatient clinic in a city in western Paraná. Case 1: infant, female, 14 days old, with reduced fetal movements reported by the mother, presenting malformations involving only the limbs, seen immediately after birth. **Case 2:** infant, male, four months old, diagnosed with fetal hypokinesia on 23-week obstetric ultrasound, at birth, presents limb contractures and central nervous system dysfunction. The diagnosis of arthrogryposis is complex and essentially clinical, requiring a meticulous anamnesis, including an assessment of pregnancy, delivery, family history and a thorough physical examination, classifying what types of contractures, involved limbs, presence of altered musculature and neurological changes to differentiate AMC from other syndromes that also have joint contractures. The aftercare and treatment of infants with arthrogryposis must occur in multidisciplinary follow-up due to the varied manifestations that the disease may present and the characteristic of recurrence over the years.

KEYWORDS: Arthrogryposi, Immobilization, Contracture, Integrality in health.

INTRODUCTION

A rare syndrome of unknown etiology, Arthrogryposis Multiplex Congenita (AMC) was described by Otto as congenital muscular dystrophy in 1841 and named AMC by Stern in 1923[1-3]. With an estimated prevalence ranging from one in every 3,300 to 12,000 live births in both sexes, AMC is used to describe a group of congenital conditions, characterized by several joint contractures in two or more joints, which are non-progressive and generally symmetrical[4-5]. In addition to limb involvement, it may also manifest facial asymmetry, micrognathia, saddle nose, thin skin, muscle atrophy, scoliosis, degeneration of the nervous and urinary systems, pulmonary hypoplasia, immature and/or short intestine, and osteoporosis of long bones[5,7].

The etiopathogenesis of AMC is multifactorial and, although the exact cause is still unknown by some professionals, it results from genetic, parental, environmental factors and/or abnormalities during fetal development that affect the mother and the concept, such as: drugs, infections, oligohydramnios, polyhydramnios, uterine alteration, chronic diseases, and trauma[5,7].

Clinically, AMC is classified by Hall[7] into three categories, in order of severity: limb involvement only, limb involvement with another abnormality, and limb involvement with central nervous system (CNS) dysfunction. Cognition, which includes aspects of perception, attention, memory, as well as language development, may be affected if the CNS is involved due to the association between the MCA and genes related to neural cell development and differentiation[8]. The dysfunction may manifest itself through delayed psychomotor development, microgyria, microcephaly, seizures, hydrocephaly, lissencephaly and absence of the corpus callosum[8].

The objective of this study is to report two cases of arthrogryposis, to highlight AMC among the differential diagnoses of other syndromes that

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also evolve with joint contractures, as well as to emphasize the importance of multidisciplinary work in the diagnosis of the disease and prognosis of affected children, since adequate treatment can provide a better quality of life for children and the opportunity for a life with fewer limitations.

CASE REPORT

CASE 1

Female, 14 days old, born in 2019, caucasian, referred to a high-risk outpatient clinic for hand and foot malformations, visualized immediately after delivery, for multidisciplinary support.

Mother, 29 years old, third pregnancy, without complications, gestational infections or trauma, being preceded by a surgical delivery and a six-week gestational miscarriage followed by curettage. Mother with history of Legg-Calvé-Perthes syndrome and asthma, using inhaled corticosteroids, denies uterine malformations and absence of consanguinity between parents.

Family history of paternal aunt with hydrocephalus and a later death, natimortality of a paternal uncle in a late twin pregnancy, without cause investigated. The older sister has no congenital or developmental abnormalities.

Maternal report of little intrauterine movement, especially in the third trimester. Morphological ultrasonography (USG) showed polyhydramnios. Newborn of 39 gestational weeks, weighing 2,950 kg, 42 cm length, 36 cm cephalic perimeter, Apgar 9 and 10, delivery by cesarian section. Extended neonatal biological screening, neonatal hearing screening and red reflex test without changes, karyotype 46, XX.

Physical exam with age-appropriate muscle mass, no need for further investigations, hips with limited abduction, feet with bilateral vertical talus, rigid and limited plantar flexion. Hands with deformities, in dorsal wrist flexion, extended interphalangeal joints, with ulnar deviation and micrognathia. Adequate neurological development for age.

Hip ultrasonography shows a reduction of the alpha angle and hip radiography shows subluxation on the right. Radiographies of right and left hands with deformity of hand bones. Radiographs of the right and left feet show changes in the phalanx arrangement from the 2nd to the 5th toe with overlapping toes, signs of talus verticalis feet and accentuation of the plantar arch (figure 1). Total abdomen ultrasound and echocardiography without changes.

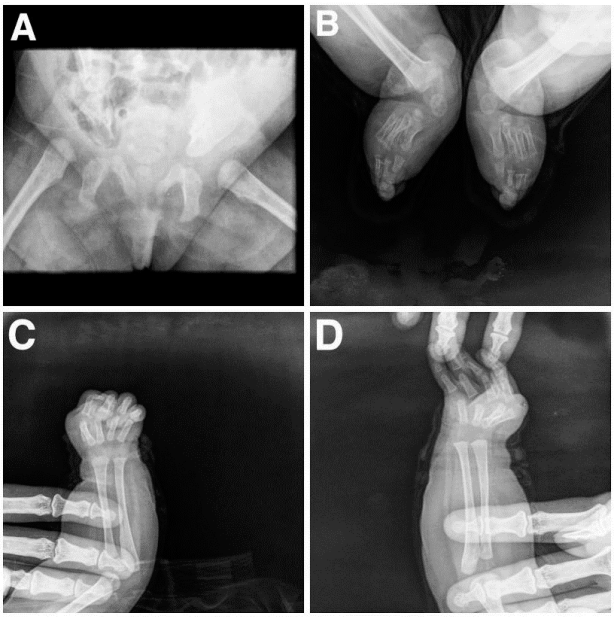

Figure 1. Radiography of the first case. A: Upper right hip dislocation, with suggestive signs of hip development dysplasia. B: Lower limbs showing signs of talus verticalis feet and bending position of the pododactyles with accentuation of the plantar arch. C: Upper right limb at rest. D: Upper right limb with passive extension of the chirodactyls. Both positions (C and D) have stiffed contractures in the wrist and chirodactyls.

The newborn was referred to the pediatric reference hospital in Latin America, where the diagnosis of distal arthrogryposis was confirmed. The infant used plaster immobilization in lower limbs for two months, using orthosis in the hands, requested correction surgery for the feet, and procedure in the waiting line. After physiotherapy, she presented functional improvement. Evaluation with speech and oral-maxillofacial therapy was pending.

CASE 2

Male, four months and three days old, referred to the high-risk ambulatory for multidisciplinary care due to AMC diagnosis.

History of first trimester gestational morphological USG with altered nuchal translucency (0.57 mm). The second morphological USG showed fetal hydropsia, cystic hygroma-type lymphangioma and polyhydramnios. The pregnant woman was referred to Curitiba, where fetal akinesia, moderate micrognathia and presence of contractures were identified in USG: closed hands, overlapping fingers of the left hand, thighs joined and parallel, with flexion over the trunk and hyper-extension of the knees, a picture compatible with AMC.

Mother of 31 years, third pregnancy and history of two cesarean sections, denies gestational complications, trauma or infectious diseases. Does not use alcohol, tobacco or other drugs and denies previous diseases, gestational pathologies, uterine alterations or natimortality. No family history of malformation or other diseases. Fourth degree of consanguinity between parents is reported.

Infant, born in 2018 from cesarean section, with 37 gestational weeks, 3.240 kg, the cephalic perimeter of 36 cm, Apgar 5 and 7 (by hypoactivity and apnea), neonate without sucking reflex and swallowing at birth. Evidence of small cystic hygroma in the cervical region, without the need for investigation and interventions. Altered neonatal hearing screening, being requested a Brainstem Auditory Evoked Potential test with normal bilateral results. Biological enlarged neonatal screening without alterations and a 46, XY karyotype. Examination of the eye fundus showed bilateral and diffuse pre retinal hemorrhages in the posterior pole, in fundoscopy presence of single micro-hemorrhage in the macular region, in reabsorption.

He was referred to the Neonatal Intensive Care Unit (NICU), where he remained for 45 days, and required mechanical ventilation, nasogastric tube and subsequent gastrostomy. Evidence of patent foramen ovale, dislocation of hips and knees. An electroencephalogram was performed and evidenced frequent epileptiform activity in the front-center-temporal regions, without clinical evidence, treated with clonazepam and phenobarbital. There were signs of cerebral volumetric loss in computed tomography of the skull, areas of hypoattenuation in the periventricular white substance and semi-ovals with non-specific aspects.

At four months old the infant starts to keep his eyes open, however he does not open and close his hands and has a restriction of movements in the upper limbs. There is no movement in the knee joint, it moves with the help of the abdominal musculature (Figure 2).

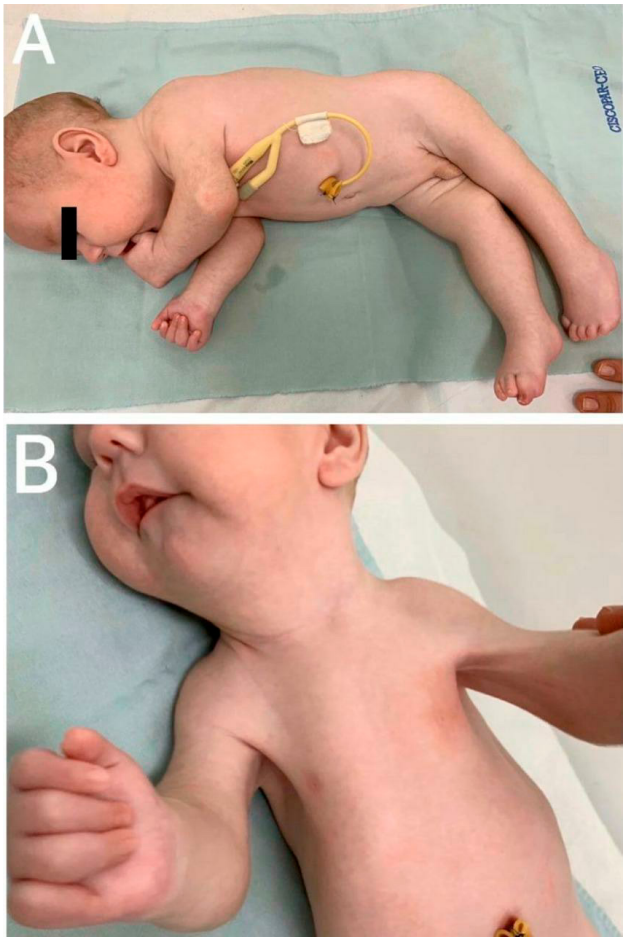

Figure 2: Patient of the second case. A - Resting position: there are contractures in the upper limbs and changes in the chirodactyl disposition. In the lower limbs, fixed contracture, hip extension, hyperstretched knees and pododactyl overlap are visualized. B - Upper limbs in passive extension: fixed contracture and movement limitation are observed. The figure shows micrognathia on the face and gastrostomy pouch.

The mother reported an improvement in motricity and neck support after treatment with physiotherapy and phonotherapy, but reported that at 16 months old the infant swallows small doses of water offered with a syringe and does not keep his mouth closed. The infant is referred to the Latin American Pediatric Reference Hospital, where he is treated by a gastroenterologist, neurologist,

orthopedist and geneticist. He remains in the use of clonazepam, phenobarbital and oxcarbazepine for the treatment of tonic-clonic seizures.

Both children follow in multidisciplinary monitoring by Primary Care in conjunction with the High-Risk Outpatient Model for Chronic Conditions Attention (MACC).

According to Circular Letter No. 166/2018-CONEP/SECNS/MS, this report of two cases was approved by the CEP/SCS/UFPR in the consolidated opinion number 4,219,939.

DISCUSSION

Akinesia or fetal hypomobility, the main etiological finding of arthrogryposis, may be related to myogenic factors, tissue diseases adjacent to the fetus's environment, maternal diseases, mechanical, vascular or nutritional factors and neurogenic factors[5,7,9-10]. Joint contracture is a clinical sign present in over 400 diseases, regardless of the pathology underlying the appearance of this hypomobility[5].

There is an early clinical relationship at the beginning of fetal hypomobility and the severity of sequelae[7]. Association stated in the case reports described above: in case 1 the mother felt the decrease in intrauterine movements on the third gestational trimester and was diagnosed as distal arthrogryposis I, Hall type 1[7]; in the second case, the mother identified hypokinesia in a period prior to 23 gestational weeks and the newborn presented sequelae with greater severity, being classified in the third type of Hall, due to involvement in the CNS[7,9,11].

When arthrogryposis exclusively affects the limbs, palmar flexion with ulnar deviation of the hand, vertical foot, hip dislocation, and finger contracture can be identified as the main manifestations[1,7,9]. In these situations, the severity of each AMC situation depends, among other clinical conditions, on how many joints in the body are affected and their level of stiffness[5]. Other non-joint abnormalities are also frequently associated with arthrogryposis, such as congenital heart diseases (patent foramen ovale) and neurological disorders (seizures), findings highlighted in the second case patient, besides the characteristic arthrogryposis contractures[5,10,12].

AMC can also cause dysphagia and difficulty in swallowing in patients with sequelae such as micrognathia[13]. Temporomandibular joint contraction is also a common aggravating factor[14]. When associated with these oropharyngeal dysfunctions they can prevent safe oral feeding due to the risk of aspiration, indicating the opening of an alternative route[13-14]. In case 2, gastrostomy was prescribed in order to provide an adequate long-term enteral nutrition route to the patient[14]. Moreover, in the follow-up of these patients, it is necessary to investigate other problems, such as respiratory, aesthetic and speech problems, common in people with micrognathism, to increase the quality of life, and their survival[10,15].

The diagnosis of arthrogryposis is complex and essentially clinical, due to the great variety of syndromes that can be studied with joint contractures[12]. About 75% of the time the diagnosis is made late (after birth), as found in case 1, possibly due to the lack of research on fetal movement during prenatal care, which delays the early onset of treatment and impairs prognosis[7,12]. For a complete evaluation, it is necessary to investigate pregnancy, birth route, family history, and a thorough physical examination, mainly to classify which types of contractures, limbs involved, flexion or extension posture, presence of altered musculature and neurological alterations[4,9,12].

The range of differential diagnoses for arthrogryposis is extensive, and exams such as radiographs, genetic tests, muscle biopsies, and blood tests can exclude other causes when the only clinical diagnosis is difficult to conclude[15.] Among these differential pathologies are Larsen syndrome, Escobar syndrome, osteogenesis imperfecta, fetal alcohol syndrome, myelomeningocele, Turner syndrome, trisomy 21, among others[9]. The exclusion of diagnoses is made by exams and clinical details characteristic of each disease. In cases of doubt, AMC should be evaluated as a diagnosis of exclusion, ruling out other causes. To exclude Escobar syndrome, for example, in addition to contractures, we should evidence the presence of syndactilias, cleft lip or palate and, more classically, cervical pterygium[9,15].

Described in both cases, early diagnosis and conduct, via a multidisciplinary team, is of singular importance, especially during the first year of life, when the child is adapting to start walking, minimizing the sequelae and the impairment of autonomy of the infant[9,12].

The follow-up and treatment of arthrogryposis must occur carefully, due to the various manifestations that the disease can present, the multiple joints that can be affected, and the characteristic of recurrence over the years, because the contractures and stiffness of periarticular tissues prevent a definitive osteoarticular remodeling, making it necessary a prolonged follow-up with the assistance of a multiprofessional team[1,7,9].

In cases of more severe or neglected AMC, besides physiotherapy sessions, the use of orthoses, immobilization with plaster and handling of deformities, surgery to correct osteoarticular deformities in hands, wrists, spine, hips, knees or feet is necessary, seeking independence of socialization and walking by allowing limb mobility[9,12].

The best conduct for the AMC includes, in all phases of life, the education of parents regarding the nature of the disease and a multidisciplinary care with professionals from various areas - pediatrician, orthopedist, neurologist, geneticist, physiotherapist, psychologist, nutritionist, social worker, among others[5,10].

Thus, the integrality of care associated with equity is a principle of the Unified Health System (SUS) fundamental to the follow-up of care for patients with AMC. Since it contemplates all actions of promotion, treatment and rehabilitation, and ensures access to all levels of care, through the integration of services, as described in the reports that needed to be forwarded via MACC. Thus, it is possible to evidence how important and necessary the SUS is for the diagnosis and management of patients with the challenging AMC syndrome, aiming at a coordinated and resolutive care[16].

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