RELATO DE CASO

Sirenomelia: A case report

Sirenomelia: relato de caso

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Abstract Caudal regression syndrome is a congenital malformation described by various degrees of developmental failure, which the most extreme and rare form is known as sirenomelia or mermaid syndrome. The associated malformations comprise anorectal, vertebral, urological, genital, and lower limb anomalies. We reported pathological findings of sirenomelia in a female stillborn with breech presentation that was born by normal vaginal delivery at 35 weeks of pregnancy following an uneventful pregnancy of a 31-year-old woman. Physical examination at birth showed normal facies, fusion of the lower limbs with bilateral presence of hip, knee, and ankle joints, sacral meningocele, omphalocele, agenesia of female external genitalia, of anus, and of cervical vertebrae. The sirenomelia etiology is still unknown but there are suggestions of genetic and teratogenic factors involvement that were not identified in the present case. The association with the agenesis of cervical vertebrae is rare and only one case described previously in the literature was reported.

Keywords Congenital Limb Malformations; Ectromelia; Sacrococcygeal Region; Cervical Vertebrae; Anormalities.

Resumo A síndrome da regressão caudal é uma malformação congênita caracterizada por falhas do desenvolvimento embrionário, da qual a sirenomelia é a forma mais rara. As malformações associadas incluem anomalias anorretais, vertebrais, urológicas, genitais e de membros inferiores. Neste relato são descritos os achados patológicos da sirenomelia em um natimorto do sexo feminino, nascido em apresentação cefálica, de parto normal, de 35 semanas, resultante de uma gestação sem intercorrências, de uma mulher de 31 anos de idade. O exame físico mostrou fusão dos membros inferiores com presença bilateral da articulação do quadril, joelhos e tornozelos, meningocele sacral, onfalocele, agenesia da genitália externa, do ânus e das vértebras cervicais. A etiologia da sirenomelia não está esclarecida, mas há sugestões do envolvimento de fatores teratogênicos e genéticos, que não foram identificados no presente caso. A associação com agenesia de vértebras cervicais é rara e foi relatada em um único caso descrito anteriormente na literatura.

Palavras-chave Malformações Congênitas dos Membros; Ectromelia; Região Sacrococcígea; Vértebras Cervicais; Anormalidades.

Introduction

Caudal regression is a relatively rare congenital anomaly characterized by caudal vertebral agenesis or dysgenesis (including hemisacral anomalies) most often in combination with spinal cord malformations. When associated with several other congenital anomalies, especially of the genitourinary and gastrointestinal systems it is usually called caudal regression syndrome[1,2,3]. The spectrum of involvement is variable and the most severe form is represented by sirenomelia or mermaid fetus, in which there is fusion of the lower limbs[4,5,6]. The defects occur in blastogenesis and represent polytopic field defects[7].

The incidence of the caudal regression syndrome (CRS) is between 0.01 to 0.05 in 1,000 live births[8,9]. Sirenomelia is extremely rare with an incidence of 1.49 in 100,000 live births, occurring more commonly in monozygotic twin pregnancies[10]. A preponderance of males[1,2,8] has been frequently noted and the reason is not completely understood[4,5].

The etiological basis is unclear and few cases of CRS have been diagnosed in the uterus[2,11].

The purpose of this report is to describe a patient who has several features of the caudal regression syndrome, a sirenomelia case, and to describe clinical and pathological findings.

Case report

A 2,070 g stillborn with breech presentation was born by normal vaginal delivery at 35 weeks following an uneventful pregnancy of a non-diabetic, 31-year-old black woman, gravida III, para II. The placenta weighed 200 g (10th percentile). The umbilical cord had a single vein and two arteries. An obstetric ultrasound at 23 weeks of pregnancy revealed severe oligohydramnios and con-

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genital malformations, such as meningocele and omphalocele. Physical examination at birth showed the stillborn with a normal facies. There were fusion of the lower limbs, bilateral presence of hip, knee and ankle joints, meningocele sacral, omphalocele, and absence of female external genitalia and anus (Figures 1 and 2).

An autopsy confirmed the anomalies of the physical examination and revealed a fetus weighting 1,950 g; crown-heel length of 44 cm; head and thoracic circumferences of 29.5 cm and 26.0 cm, respectively. The measurements and organ development were according to the gestational age. An internal examination showed agenesis of cervical vertebrae and a female fetus with normal ovaries, uterine tubes, and uterus. All the other organs were normal. The histological examination showed the meninges with areas of polymorphonuclear inflammatory infiltrate associated with cerebral hemorrhage and vascular congestion. There were also points of alveolar collapse, lung aspiration and thromboembolism, hepatic congestion, hemorrhage of suprarenal gland and renal vascular congestion, cyanotic lips, and fetal maceration.

Discussion

In 1961, Duhamel proposed that a defect in the formation of the caudal region was the origin of a spectrum of malformations including anal imperforation and the mermaid syndrome. Small lesions could cause imperforate anus and mild vertebral anomalies whereas larger lesions could cause urinary or genital anomalies. Extreme lesions could lead to lower limb fusion and sirenomelia. He coined the term "syndrome of caudal regression"[1,5,12,13]. Based on this observation, Smith and Karrer suggested that caudal vertebrae and spinal cord anomalies occur in 40 to 50% of children with anorectal malformations1. Our case presented a fusion of the lower limbs with bilateral presence of hip, knee and ankle joints, myelocele, agenesis of cervical vertebrae, omphalocele, absence of female external genitalia and anus, which was compatible with other cases previously described[1,4]. In the literature, only one paper described the association between sirenomelia and cervical vertebrae anomalies. The patient, a monozygotic twin, presented among other findings, segmentation vertebral anomalies affecting the cervical and the upper thoracic spine[14].

Several mechanisms have been proposed to explain sirenomelia and they included deficiencies in caudal mesoderm and trophic defects due to a deficient blood supply to the distal region.

In 1970, Davies et al. suggested that sirenomelia results from injury to caudal mesoderm between 28 and 32 days of fetal development[5,15]. A wedge-like defect occurs in the primitive streak at the lumbar and sacral areas. Midline structures including cloacal and urogenital derivatives are destroyed, allowing the halves of the hind limb buds to move both medially and dorsally fusing along their postaxial surfaces[5].

In 1980, Gardner and Breuer proposed that neural tube overdistention in the caudal area may lead to roof plate expansion of the tube leading to lateral rotation of the mesoderm by 180º. This rotation would cause fusion of the lower limb buds, closing off the midline primitive gut and urethra[1,5]. Potter described a sequence of anomalies resulting from renal agenesis and oligohydramnios that lead to facial deformities and pulmonary hypoplasia[5]. The current case presented severe oligohydramnios but had normal facies, lungs, and kidneys.

In 1986, Stevenson et al. suggested vascular abnormalities to explain the defects that are usually found in this condition and that sirenomelia arises from failure of the lower limb bud field to be cleaved into two lateral masses by an intervening allantois, caused by insufficiency of nutrient of the distal region of the embryo[16].

However, in 2005, Zaquin et al. report the appearance of the siren phenotype in *Tsg*/*Bmp7* compound mutant mice. They demonstrated that the loss of bone morphogenetic protein 7 (Bmp7) in combination with a half dose or a complete loss of twisted gastrulation (Tsg) causes sirenomelia in the mouse. They also affirm that sirenomelia results from a fusion of the hind limb buds caused by a defect in the formation of ventral mesoderm[17].

The etiology of CRS is still unclear but it has a well-known association with insulin-dependent maternal diabetes mellitus[18,19,20,21]. The only etiologic agents associated with the CRS were reported in mothers that have became pregnant while exposed to organic fat solvents during the first months of their pregnancies[22,23]. Teratogenic agents such as exposure to retinoids, insulin, embryonal trauma, severe fluctuations in temperature, vitamin deficiencies, lithium salts, radiation, stress, alcohol, amphetamines, and trypan blue have all been implicated as causes of caudal agenesis[6,7,8,12]. Furthermore, these vascular disruptions are a well-known factor in the pathogenesis of many structural defects in the fetus[2,5,12]. Our case did not present maternal diabetes or the use of teratogenic substances during the gestation. Familial cases suggest genetic cause with a recurrence risk of 5% in families that already had an affected child. CRS would be transmitted as either dominant or recessive characteristics[6,7,8], but according to Di Lorenzo et al., a genetic mechanism leading to sirenomelia seems unlikely due to the absence of familial cases in the literature[5]. In our case, there was also no familial his-

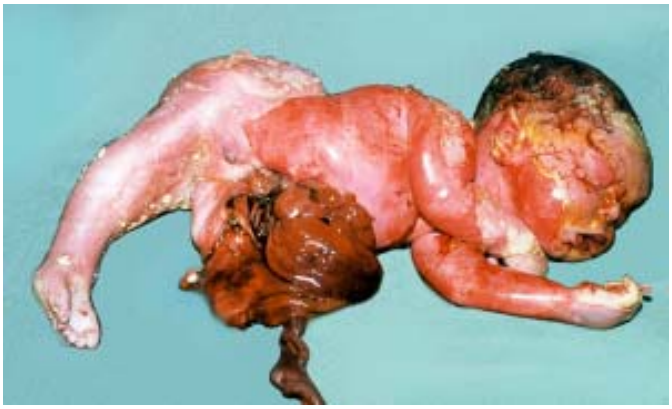

Figure 1 – Frontal view of sirenomelia case.

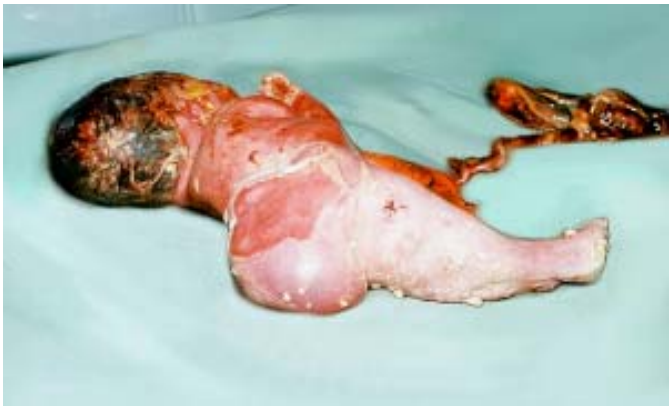

Figure 2 – Posterior view of the case.

tory.

The congenital malformations constitute one of the first causes of death in the perinatal period. Sirenomelia is a condition not compatible with normal life, and only ten patients survived to reconstructive surgery until now[24]. Because of this, countless efforts to carry out prenatal diagnosis must be made in all pregnancies[25]. Detailed observations by ultrasound are important for diagnosis of fetal CRS[26]. Sacral or lumbosacral agenesis in combination with marked hypoplasia of lower extremities is diagnostic of CRS. The measurements of fetal crown-rump length of CRS fetuses in the first trimester reported to be commonly shorter per week than normal fetuses[2]. In our case, the ultrasound showed a gestation of 28 weeks incompatible with a gestational age of 33 weeks. The majority of malformations reported here were compatible with the CRS spectrum previously described.

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