

Caudal regression sequence:
a forgotten disorder?

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We present a classical case of caudal regression sequence (CRS) in a term newborn of a diabetic mother. This sporadic disorder is more frequent in diabetic mothers but can also be seen in other circumstances. Because of early antenatal diagnosis which is often followed by termination of pregnancy, the clinical syndrome is nowadays rarely seen postnatally.

The mother is a 38-year-old Mauritian G5/P3 who was diagnosed with type I diabetes at the age of 16. She had first been managed by diet and after one year by insulin. Compliance was inconsistent, and, consequently, she developed severe bilateral retinopathy several years later.

Her previous pregnancies resulted in two normal term deliveries in 1998 and 1999, a miscarriage in 2004 and a voluntary interruption of pregnancy in 2005. At 4 weeks of this current pregnancy, there was an episode of severe hyperglycemia (blood glucose 20 mmol/l) without ketoacidosis. At that time, the glycosylated hemoglobin (HbA1C) was normal and, incidentally, the patient was found to be pregnant. Because of poor diabetic control, she was hospitalized at 25 weeks gestation for better diabetic management (HbA1C of 6.2%, normal < 6.0%). Additional risk factors included significant overweight with a BMI of 28, moderate nicotine consumption (<10 cigarettes/day).

Ultrasonography at 22 weeks of gestation at her

gynaecologist's office was difficult to perform because of the patient's overweight but was described as normal. The lower part of the legs were not visible, but the length of the femur was between P25-50 percentile while other parameters were at P50-75. The non-visualization of the lower parts of the legs was ascribed to the fact that the fetus was in a low position. Two further ultrasound examinations were performed with identical findings. The baby was delivered by emergency caesarean section at 38 weeks gestation because of non-reassuring fetal heart rate tracings. No resuscitation was required at birth, Apgar scores were 4, 9, and 9 at 1, 5 and 10 minutes, respectively, her weight was 2970 g (P10-50) with a length of 43.5 cm (< P10) and a head circumference of 35.5 cm (P50-90).

Immediately following delivery, obvious malformations of the lower extremities were noticed: the buttocks and lower limbs appeared atrophic and no bony structures were palpable in the lumbar and sacral regions. The limbs were immobilized in a frog-like position, fixed in flexion with webbing between the thigh and the leg, and a notch on each side was noted anterior to the great trochanters. The feet were also hypotrophic and in equinovarus position (Fig. 1, 2). Otherwise, the exam was normal with a normal female genitalia, an anteposed and patent anus with a weak anal reflex.

Further investigations included a babygram, a MRI, and a voiding cystoureterogram (VCUG). On the babygram,



Fig. 1

Frog-like position of the hypotrophic lower extremities with contractures of hip and knee joints.



Fig. 2

Anteposed anus, small buttocks and dimples in the trochanteric region.

no lumbar or sacral vertebral bodies were visible, and the iliac bone was hypoplastic with fused wings (Fig. 3). The MRI definitely confirmed lumbar and sacral agenesis with the spinal cord fixed at T12 (tethered cord) (Fig. 4). The brain was normal. The abdominal MRI confirmed agenesis of the right kidney. There was no vesicoureteral reflux (Fig. 5). The baby was managed with nasal CPAP for transient tachypnea of the newborn. Feedings were started at 48 hours of life. Because of frequent regurgitation an upper gastrointestinal contrast study was done which confirmed gastroesophageal reflux. The baby was discharged after 10 days with antibiotic prophylaxis to prevent urinary tract infections and metoclopramide and omeprazole for gastroesophageal reflux.

The baby was seen at 2, 4 and 12 months in the outpatient clinic. She is growing between P10-50 for weight and P50-90 for head circumference. She has had no febrile episodes nor urinary tract infections. She has anal incontinence and episodes of constipation have been managed with paraffin oil. She has had persistent moderate gastroesophageal regurgitations without clinical evidence of esophagitis. Cystomanometry performed at one and four months revealed high pressure in the bladder with normal voiding, reduced bladder volume and compliance. The left kidney shows hypertrophic compensation on ultrasonography with compensatory hyperactivity on renal scintigraphy. She is managed by a multidisciplinary team

of pediatric surgeons, orthopedics, occupational therapists, social workers and neurorehabilitation specialists. Except for limitations due to the malformation of her lower extremities, her psychomotor development is normal.



Fig. 3

Babygram with absence of lumbar and sacral vertebral bodies, fused iliac and ischial bones.



Fig. 4

T2-weighted MR image: sagittal view of spine and brain demonstrating an interruption of the spine at the 11th thoracic vertebral body.



Fig. 5

VCUG showing no reflux; note the abnormal pelvic bony structures.

DISCUSSION

The caudal regression sequence (CRS) is a rare malformation with a broad spectrum of manifestations that ranges from sacral agenesis to the most severe form of the sequence as seen in our case. The cause of CRS is unknown, but maternal diabetes, genetic predisposition, and vascular hypoperfusion have been suggested as possible causative factors.

There is a strong association with maternal diabetes, either type 1 or type 2 (1,2). The incidence of CRS is estimated to be 1:60'000 births with a male:female ratio of 2.7:1 (3) and it is 200-250 times higher when the mother is diabetic. A high level of glucose at 6-8 weeks of gestation is known to induce renal defects in mammals (4).

A defect in the induction of caudal elements before the 7th week of gestation leads to the CRS by compromising cellular migration, neurulation and/or differentiation (5). It seems that a faulty gastrulation with subsequent abnormal development of the notochord leads to the CRS (6). The structures that are developmentally separated from these caudal elements are spared. A vascular origin with an anomaly of the unpaired vessels originating from the aorta was described as a possible etiology, operating like in sirenomelia where the persistent vitelline artery "steals" blood from the lower part of the body (7).

The association of CRS with other malformations such as Chiari I malformation and Pierre Robin sequence have been reported (8). CRS is usually a sporadic disorder, but an association with chromosome 18p deletion has been described, with a dysmorphic and hypomimic face, a short neck, hypotonia with motor retardation, and an MRI showing a partial sacral and coccygeal agenesis and non progressive periventricular white matter lesions (9).

The diagnosis can be made antenatally by ultrasonography and fetal MRI. A short crown-rump length on the ultrasound in the first trimester is associated with CRS (10), and the diagnosis is also possible around 22 weeks gestation by demonstrating the frog-like position and immobility of the lower limbs, the interruption of the spine and the defect of vertebrae in typical cases. The clinical spectrum is wide, comprising developmental anomalies of the caudal vertebrae, neural tube, urogenital and digestive organs.

Major complications are the orthopedic deformities related to the syndrome and scoliosis commonly seen in the lumbosacral agenesis. Bladder and bowel incontinence, a subsequent high risk of urinary tract infections and renal impairment are further complications and are associated with high morbidity rates in these patients.

Supportive treatment aims at preservation of renal function by prevention and treatment of urinary infections. Rehabilitative efforts focus on increasing independence and preventing secondary orthopedic complications; they include physiotherapy, occupational therapy and the provision of supportive devices (orthotics, wheelchair). Support of a psychologist and a social worker is also needed.

Because of tight diabetes control prenatally and during pregnancy, CRS is rarely seen nowadays. Abnormal fetal leg position and low position of the fetus specially in a diabetic mother should raise the possibility of a CRS. When suspected antenatally, termination of pregnancy is currently offered.

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