Case Report and Review of Literature

Caudal regression syndrome

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ABSTRACT

A case of caudal regression syndrome was reported in 20 wks foetus during routine foetal autopsy at GMCH, Chandigarh. The external examination showed 2 vessels in umbilicus. There was anteroposterior lengthening of skull. The anal opening was absent. The lower limbs were fused in thigh region with a small appendages attached to this on left side which also terminated in foot. The right foot had 5 toes and left foot had 3 toes. No external genitalia were seen. On internal examination, the gut was opening in a dilated cloaca like blind chamber. Kidneys were absent on both sides.X ray examination revealed small sacrum, femur, tibia in both the legs. Fibula was absent bilaterally. Caudal dysgenesis syndrome and caudal regression syndrome are broad terms that refer to a constellation of caudal congenital anomalies affecting caudal spine and spinal cord, hind gut, urogenital system, and the lower limbs. The etiology, incidence, causative factors of this case will be discussed in light of available literature.

Key words: *Sacral agenesis, presacral mass, anorectal malformation*

Introduction

Sacral agenesis is defined as the congenital absence of the whole or part of the sacrum. It has a heterogeneous aetiology. In its classical form, often described as the caudal regression syndrome, there are malformations of structures derived from the caudal region of the embryo, that is, the urogenital system, the hindgut, caudal spine and spinal cord, and the lower limbs. [1]

Case report

A case of caudal regression syndrome was reported in 20 wks foetus during routine foetal autopsy at GMCH, Chandigarh. Obstetric history: Mother was 24 year old second gravida. The first pregnancy terminated in spontaneous abortion one year back at home. The cause of abortion and sex of the fetus was not known to the parents. Present pregnancy also resulted in spontaneous abortion. Medical history of the mother revealed that she was suffering from hypothyroidism for which she was on medication during the pregnancy also. Not suffering from diabetes. Antenatal history showed regular intake of iron folic acid and vaccination. Past history and family history was not suggestive of any etiological factor of the disease.

The external examination showed 2 vessels in umbilicus (Fig.1). There was

anteroposterior lengthening of skull. The anal opening was absent (Fig.2). The lower limbs were fused in thigh region with a small appendages attached to this on left side which also terminated in foot. The right foot had 5 toes and left foot had 3 toes. No external genitalia were seen (Fig.3). On internal examination; the gut was opening in a dilated cloaca like blind chamber (Fig.4). Kidneys were absent on both sides (Fig.5). X ray examination revealed small sacrum, femur, tibia in both the legs. Fibula was absent bilaterally (Fig.6). Caudal dysgenesis syndrome and caudal regression syndrome are broad terms that refer to a constellation of caudal congenital anomalies affecting caudal spine and spinal cord, hind gut, urogenital system, and the lower limbs

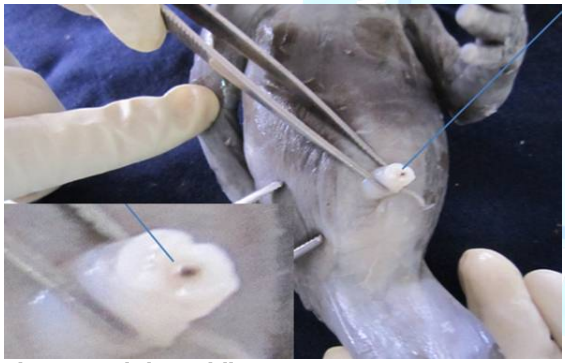

Fig.1 Vessels in umblicus

Fig.2 Absence of anal opening

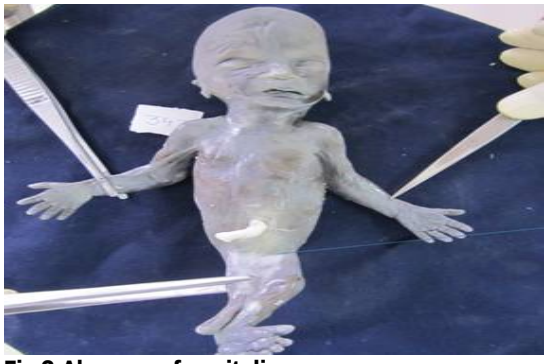

Fig.3 Absence of genitalia

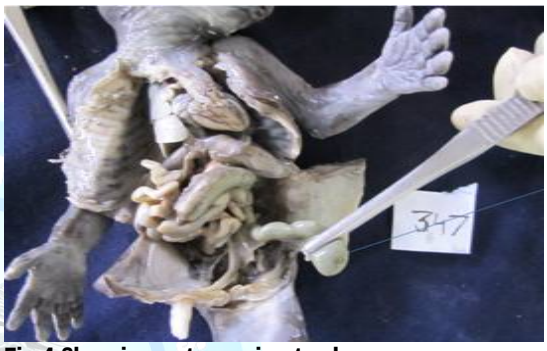

Fig.4 Showing gut opening to cloaca

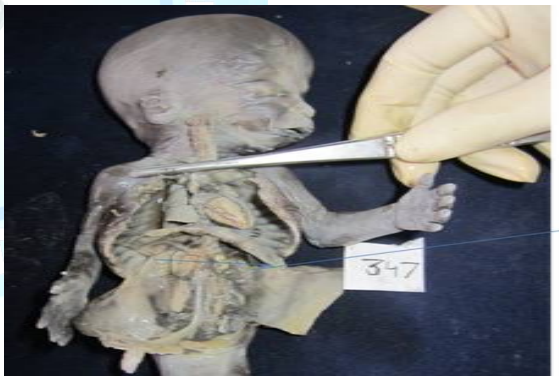

Fig.5 Showing bilateral absence of kidney

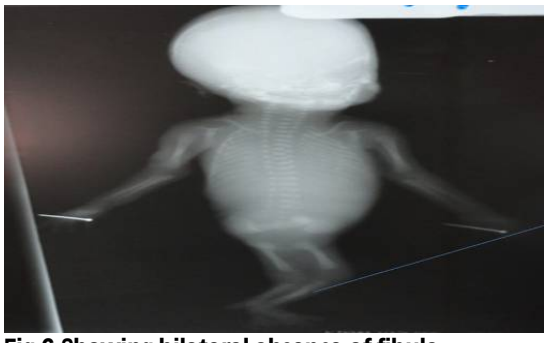

Fig.6 Showing bilateral absence of fibula

Discussion

Caudal regression syndrome was first proposed by Duhamel, based on his observation that sirenoid monsters have a number of abnormalities in addition to characteristic synmelia or fusion of the lower limbs. [2]Sacral agenesis (sacral hypoplasia) can occur in isolation or as a part of caudal regression syndrome and involves abnormal fetal development of vertebral column and spinal cord. [3] It is a rare anomaly with a very low incidence (approximately 1 per 25,000 live births). By 4th week of gestation formation of the sacrum/lower back and corresponding nervous system is usually nearing completion. According to some studies perturbations of mesoderm specification, epithelial-mesenchymal transition, and mesodermal cell migration can lead to such structural birth defects. [4] Caudal regression syndrome occurs in about one in 350 infants of diabetic mothers, representing an increase of about 200-fold over the rate seen in the general population. [5] Sacral agenesis is listed as a rare disease by the office of rare disease (ORD) of National institute of health. It is usually sporadic. It occurs at 3rd-7th week of embryonic development during gastrulation. [6]

Though the aetiology is not known various hypotheses have been suggested like interaction of multiple genetic & environmental factors. Apart from these 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. [7] It is suggested that an abnormal artery in the abdomen diverts the blood flow away from the lower areas which may be the primary cause or this artery itself may be secondary to abnormal mesoderm**.** [8] Rumplessness, a condition similar to sacral agenesis, has been noted in animals, particularly chickens. [9] Duraiswami demonstrated that insulin injected into chick embryos could cause rumplessness. [10] Detailed evaluation of the foetal spine and lower extremities is an important aspect of every prenatal ultrasound examination. Sacral agenesis is a less severe variant of caudal regression syndrome and in the presence of normal amniotic fluid; the diagnosis can be made by demonstrating the termination of lumbar spine and small and abnormal lower extremities**.** [11] Segmental spinal dysgenesis (SSD) is a rare congenital abnormality in which a segment of the spine and spinal cord fails to develop properly. SSD and caudal regression syndrome probably represent two faces of a single spectrum of segmental malformations of the spine and spinal cord. [12] Sirenomelia is a common differential diagnosis, which was initially considered to be a severe variant of caudal regression syndrome. Sirenomelia is characterized by fused lower limbs, severe renal anomalies with oligohydramnios and is now considered to be a separate entity. It is frequently associated with VACTERL syndrome. [6]

Renshaw classified sacral agenesis into four types:

- Type I: Total or partial unilateral sacral agenesis.
- Type II: Partial sacral agenesis but bilaterally symmetrical defect and a stable articulation between the ilia and a normal or hypo plastic first sacral vertebra (most common).

- Type III: Variable lumbar and total sacral agenesis with the ilia articulating with the sides of the lowest vertebra present.
- Type IV: Variable lumbar and a total sacral agenesis, the caudal end-plate of the lowest vertebra resting above either fused ilia or an iliac amphiarthrosis. [13]

Welch and Alterman classified congenital sacral anomalies into 4 distinct clinical types:

- Non familial type associated with maternal diabetes showing complete absence of sacrum and lower vertebrae and lower congenital anomalies
- Agenesis of the distal sacral and coccygeal segments
- Hemisacral agenesis with presacral teratoma
- Hemisacral dysgenesis with anterior meningocele. [14]

A few instances of caudal regression have been reported in siblings Finer NN. [15]

The diagnosis is often made late in pregnancy. In this case, detection of the abnormality at 22 weeks allowed termination of pregnancy. Early detection of caudal regression syndrome at 11 weeks of gestational age by transvaginal ultrasound scanning was reported. In the first trimester crown-rump length was found to be smaller than expected in caudal regression using abdominal ultrasound. [16] Incidence of major foetal malformations is 5-10% among women with pregestational diabetes. Severe malformations result from poor peri conceptional control of blood sugars. [17] A part from caudal regression syndrome, there seems to be an increase incidence of other malformation complex such as visceral anomalies in connection with maternal diabetes. Slavotinek et al., reported three babies with situs ambiguous born to mothers with insulin-dependent diabetes mellitus. [18]

Table 1- Congenital anomalies associated with partial or complete sacral agenesis

Orthopaedic	Congenital hip or knee dislocation Talipes equinovarus and calcaneovalgus Absent or atrophic extremities Myelomeningocele Absent, dysplastic or fused vertebra All variants of anorectal malformations
Gastro intestinal	Inguinal and umbilical hernias Duodenal atresia Malrotations and situs inversus Vesico-ureteral reflux
Urological	Congenital hydronephrosis Hypospadias Cryptorchidism Duplication of collecting system Renal agenesis
Miscellaneous	Tracheo-oesophageal fistula Hydrocephalus Strabismus Congenital heart disease

Conclusion

In our case, there was no history of maternal diabetes or teratogenic substance intake during gestation with negative familial history. Hypothyroidism in mother was also corrected at the time of pregnancy. So there was no etiological factor for production of this syndrome in this case. Our case falls into type 2 of both Renshaw and Welch and Alterman classification. The diagnosis of sacral agenesis is often overlooked as happened in our case. Prenatal ultrasonographic diagnosis of caudal regression syndrome is possible at 22 weeks' of gestation. Hence, we suggest that presence of any associated anomalies and urinary dysfunction should attract our attention to underlying possibility of sacral agenesis.

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