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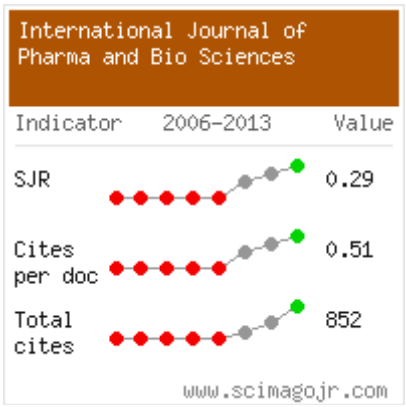

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NON-DIABETIC MATERNAL FACTOR WITH CAUDAL REGRESSION SYNDROME – A NOVEL CASE REPORT

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ABSTRACT

Caudal regression syndrome (CRS) is a rare neural tube defect which impairs thedevelopment of lower (caudal) half of the body. The spectrum of this disease can vary from isolated partialgenesis of the sacrococcygeal spine to complete absence of sacral, lumbar, or lower thoracic vertebrae. Most of the cases which are reported as the causative agent for CRS are mostly due to a diabetic maternal pattern. But there are few cases of CRS which are seen occurring even when there is no maternal diabetes or any genetic pre-disposition or influence from any kind of teratogens. Thus here we are discussing a unique case of a new born deceased infant with CRS with a clear background,that is a non-diabetic mother and no inheritance from the hereditary. We have also done karyotyping from the peripheral blood of the new born infant to identify thechromosomal anomalies which have been allied with this syndrome. Thus these preliminary as well as novel findings are beginning to shed light on this very rare syndrome in which further more researches have to be carried out to uncover the actual pathogenesis linked to this syndrome.

KEYWORDS:Caudal regression syndrome; Non-diabetic; neural tube defect; ambiguous genetalia

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INTRODUCTION

Caudal regression syndrome is a congenital sporadic disorder in which there is an abnormal fetal development in the caudal partition of the spine. CRS was first ascertained by Geoffroy Saint-Hilaire and Hohl during the XIX century and the term "CAUDAL REGRESSION SYNDROME (CRS)" was accustomed by Duhamel in 1961[3, 4, 5]. Other synonyms for this syndrome are caudal regression/dysplasia syndrome, caudal dysplasia sequence, sacral regression syndrome and sacral agenesis [1, 2]. There are two forms of caudal regression syndrome they are type I and type II. Abrupt termination of the cord with sacral deformities with high club-shape is the major hallmark for type I CRS whereas in type II the spinal cord is low-lying and tethered [4, 7].The body parts which can get affected due to this syndrome are lower back andlimbs, the genitourinary tract and the gastrointestinal tract which occurs due to the disruption in the mesoderm formation. Male to female ratio is about 2.7:1[1, 4].The incidence of CRS is 1 - 2.5 per 100,000 live births whereas when the pregnant mother is diabetic then the probabilities of this disease are 1 in 350 live births [7].CRS is caused when the pregnant mother is having an increase in the blood sugar level as well as some other metabolic problems related to diabetes. CRS is associated with both type I and type II forms of diabetes. But in most of the CRS cases it is 200-400 times likely to happen for women who are with insulin dependent diabetes (type 1 form of diabetes)[8,9].However CRS is also seen occurring in non-diabetic mothers due to some sudden genetic mutation or due to any kind of environmental factors. One ofthe environmental agents for causing CRS could be any kind of drug or minoxidil solution for hair loss [2, 6, 9].Some researchers have found that disruption of the pregnancy during the 28thday can also cause CRS [3, 4,9]. There are also some findings which say that CRS can be caused when there is not an ample supply of blood to the caudal portion of the placenta. Genetic factor which plays a vital role in causing this syndrome is the gene VANGL1 located in the chromosome 1p13. Some other genes which are also expressed in CRS syndrome are HLBX9 gene in chromosome 7q36, HOXD13, CYP26A1 [3].Evidence for Mendelian pattern of inheritance is not yet established [3]. Thus in this context we are reporting a case of female with normal medical and non- diabetic condition giving birth to a new born infant with CRS and it's physiological as well as genetic features.

CASE PRESENTATION

A 22 – year – oldshort primivisited first time to SBMCH during her 32weeks of gestation.She had regular menstrual cycles of 3/30 days. She was married for 1 year and it was nonconsanguinous. She had a spontaneous conception which was confirmed by UPT.Her medical and family history was unremarkable. During pregnancy her HbA1C levels were frequently checked which was always in between 4-5.6% only. Even her blood sugar levels were been monitored duly before and after meals which were 4-5.9mm/l and the later reading were under 7.8mm/l only. According to these findings it is very much clear that the mother was non diabetic and her glycemic levels were also under control.Her first trimester report was normal and was just advised to take folic acid tablets. Later at 18th week anomaly scan was been done which was also normal and was been asked to take iron and calcium tablets. During her third trimester i.e. at 32 week an ultrasound was done which showed a single live intrauterine gestation in breech presentation, right kidney was filled with fluid (hydronephrotic)with a thinned out parenchymal narrowing, talipesvarus deformity of one lower limb, skeletal dysplasia in one lower limb, adequate liquor and placenta was in fundal position.Further more study could not be done because of the position of the fetus. Before the day of delivery her health examination done which showed that she was not anemic but was having bilateral pitting pedal edema andrest of the general conditions were normal. The patient underwent lower segment caesarean section (LSCS) in view of short stature, footling presentation and feto pelvic disproportion.She deliveredalive baby weighing 2.6 kgs with multiple congenital anomalies such as 1. Sacral agenesis

2.Ambiguous genitalia 3.Imperforate anus 4.Varus deformity of the foot(Fig 1,2,3,4 and 5).The clinical manifestations which were observed in the new born infant were short intergluteal cleft, flattened buttocks, narrow hips, distal leg atrophy and talipes deformities.The Apgar score was 2 at 1, 5 and 10 minutes for the baby. There was no proper passage of the stool and urine. X-Ray was done after 24hours of the birth which showed sacral agenesis in the pelvis region and the distal lumbar vertebrae region was absent.Meanwhile blood was collected for karyotyping, serum electrolytes and CBC. Until 5days of life of the infant the serum electrolyte and CBC were normal. The results of karyotyping showed a 10q deletion. To check if there is any hereditary chromosomal anomalies in their family the mother's peripheral blood was collected for karyotype analysis. The result of karyotyping for mother was utterly normal. Thus, this proves that there is no hereditary influencebut rather a sudden mutation. The pedigree chart of their family has been shown in figure 6.No gross chromosomal abnormalities were detected for now.The infant deceased within a week after the delivery.Necropsy examination showed that the infant had pulmonary hypoplasia. The anus and rectum were absent and the terminal portion of the colon ended indiscriminately. Infant was having only a single large artery, which diverts blood flow and nutrients from tissues by a typical type of mechanism called as 'steal-effect'; this was the reason for hypoplasia of the vessels and the tissues. A single umbilical artery was seen to be present within the continuity of the abdomen.

Figure 1
Spinal Deformity

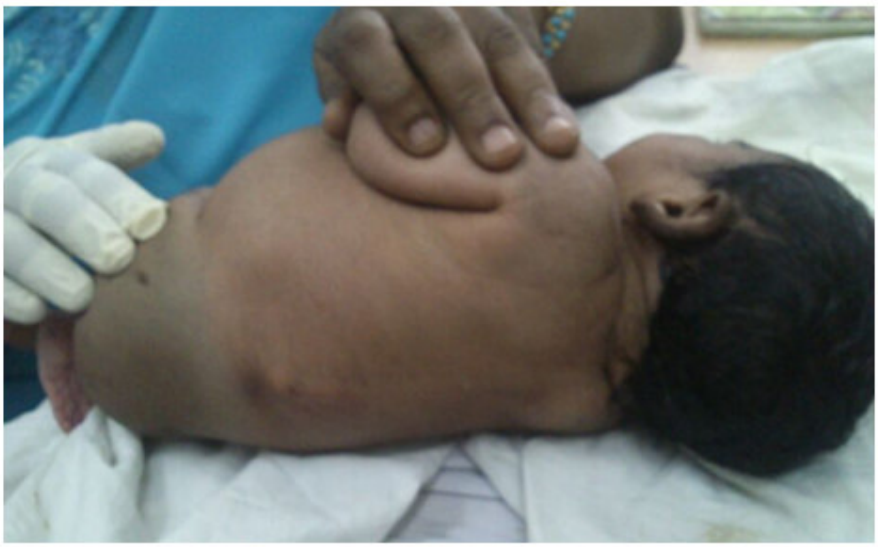


Figure 2
Ambiguous Genitalia

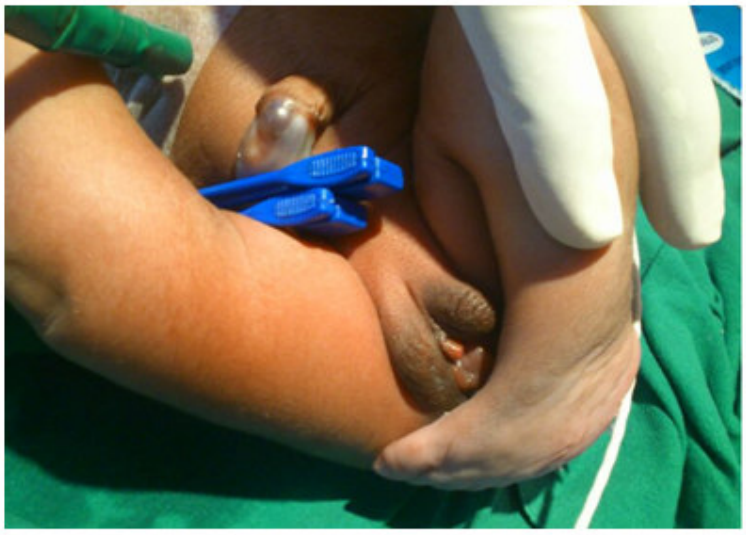


Figure 3
X Ray post delivery

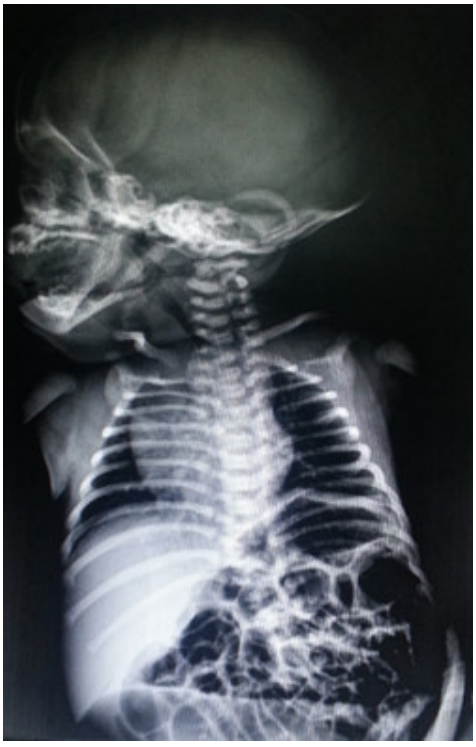


Figure 4
XRAY OF SHOULDER AND ARMS- POST DELIVERY

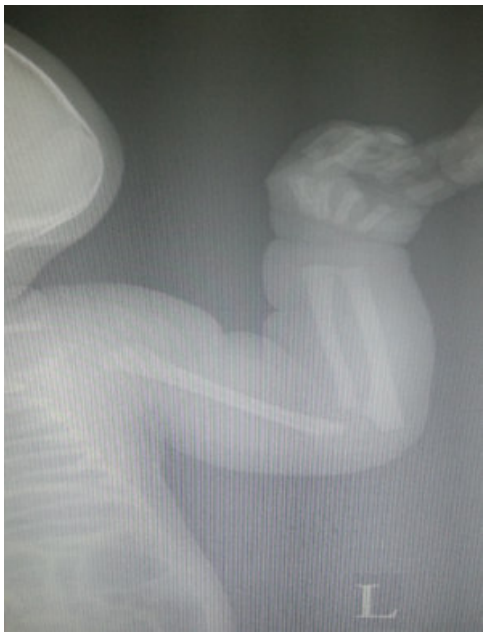


Figure 5
TALIPES DEFORMITY OF FOOT

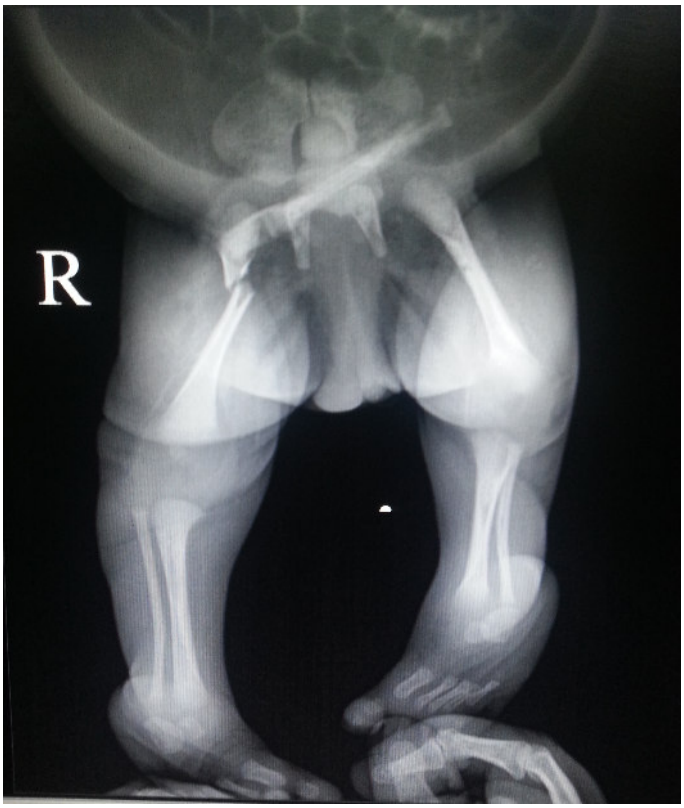


Figure 6
XRAY SPINE- SHOWING DISCONTINUITY OF SPINE

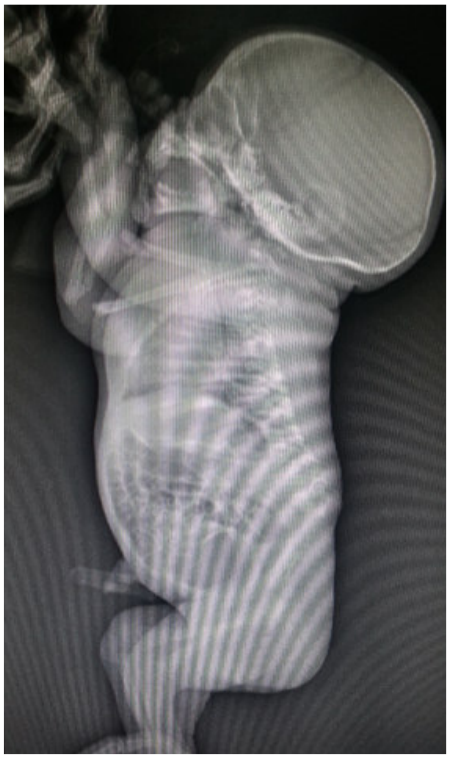
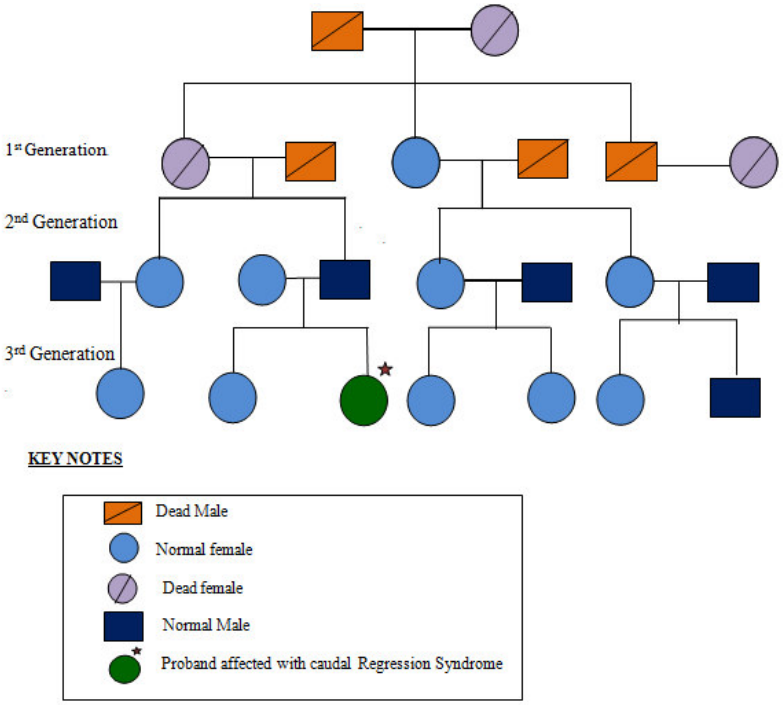


Image 1
Debits the family history of Caudal Regression Syndrome



CONCLUSION

Thus, CRS is an occasional disorder whose pathogenesis is difficult to comment. 70-80% cases of CRS are reported due to maternal diabetes only.Specifically more familiar form of diabetic mothers who are giving birth to CRS infants are with type I form of diabetes [8, 9]. Therefore the major contributing factor for causing this syndrome is the increased level of blood glucose in the mother as well as hyperglycemia which also plays a crucial role as a teratogen in inculcating this syndrome [1, 8, 9]. But few cases of CRS are reported even without maternal diabetes [9]. The precise reasons for such cases of CRS are mysterious. Thus the agent which causes CRS in such normal conditions may be some of the outside teratogens. Drug related etiology has been reported in many CRS cases where the explanation for syndrome is questionable [2]. In the current report we are discussing an out of the ordinarycase of a new born with caudal regression syndrome without any known risk factors such as maternal diabetes or anysort of drug intake by the mother. Clinicians must take extreme effort during the early stages of pregnancy diagnosis. As this syndrome can be diagnosed as early as possible by expert ultrasound antenatally.Using various methods such as X ray,Ultrasound,Myelography, CT scan and myelo CT, MRI- gold standard ,CRS could be confirmed after birth. Furthermore the parents can be given the option whether to go ahead with the baby or to opt for termination if diagnosed at the right time.

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CONFLICT OF INTEREST

The authors declare that there is no Conflict of Interest

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