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Case Report

Caudal regression syndrome: Postnatal radiological diagnosis with literature review of 83 cases ☆,☆☆

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ABSTRACT

Caudal regression syndrome (CRS) is a rare congenital disorder characterized by arrest of caudal spinal growth and associated with wide spectrum multisystemic anomalies. Herein, we presented a case of a newborn baby who did not pass meconium due to imperforated anus and was referred to the pediatric surgeon for urgent diverting loop colostomy. The conventional X-ray, abdominal ultrasound and abdominal pelvic magnetic resonance imaging (1.5 T) at 2-month-old age revealed right kidney agenesis, sacrococcygeal agenesis, vertebral bodies dysraphism and the spinal cord ends at D12-L1 with anterior and posterior bands of the terminating filaments. The diagnosis of CRS was confirmed. Through this case report, we hope to draw attention to this rare syndrome and the wide range of associated anomalies, also to consider this syndrome on the top of differential diagnosis list once the newborn has anorectal malformation mainly imperforated anus.

Introduction

Caudal regression syndrome (CRS) is a rare congenital disorder with incidence around 1-2:100,000 [1]. It was first described by Geoffroy Saint-Hilaire and Hohl in 1852 [1]. It consists of a spectrum of structural defects of the caudal spinal region either closed or open spinal dysraphism [2,3]. CRS includes incomplete development of the sacrum and sometimes involves lumbo-thoracic spine in variable degree [1–6]. Patients with CRS may have also cord tethering [7,8].

Abbreviations: CRS, Caudal regression syndrome; DM, Diabetes mellitus; GIT, Gastrointestinal tract; VACTERL, Vertebral defects, Anal atresia, Cardiac defects, Esophageal atresia with or without tracheoesophageal fistula, Renal and Limb anomalies); NVD, Normal vaginal delivery; ARM, Anorectal malformation; MSK, Musculoskeletal; VCUG, Voiding cysto urethrogram; MRI, Magnetic resonance imaging technique; NA, Not available; Lt, Left.; NICM, Non-iodinated contrast media; Rt, Right; T2 WI's, T2-weighted images; VUR, Vesico ureteral reflux; VSD, Ventricular septal defect; ASD, Atrial septal defect; PDA, Patent ductus arteriousus.

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Variable degree of caudal regression can be associated with other syndromes like; VACTERL (Vertebral defects, Anal atresia, Cardiac defects, Esophageal atresia with or without tracheoesophageal fistula, Renal and Limb anomalies), OIES syndrome, Currarino syndrome, and Mayar Rockitanski Kauser Hauser syndrome MRKHS [9–11]. The clinical presentations of CRS are variable according to the level of spinal lesion and the presence of associated anomalies. Affected infants appear typically to have a small pelvis, small flat buttocks and bilateral buttock dimples with a short intergluteal cleft. Also, patients may have neurogenic bladder and variable degrees of limb deformity [1–5].

Although the mechanism stills unclear, baby born for diabetic mothers has 200-400-fold increased risk of CRS [3]. However, most CRS cases are born for non-diabetic mothers [3,4]. At embryonic level, it is strongly believed that CRS is a result of defects in the development of caudal elements prior to the fourth week of gestation [6–8]. This defect is due to injury in the mesodermal axis leading to variable degree of arrest in the development of the caudal mesoblastic yolk [6–8]. Maternal diabetes, hypoperfusion, toxins and genetic predisposition have been suggested as possible causes for this injury [2,3,6–8].

We present a case of newborn with CRS and VACTERL association that was diagnosed postnatally. A thorough search among the published literature using PubMed search engine was done.

Case presentation

A male newborn weighing 3 kg was referred to the pediatric surgery team with diagnosis of imperforated anus. The full-term newborn was vaginally delivered for primigravida otherwise healthy 22-year-old lady. The pregnancy went uneventfully. He was the offspring of non-consanguineous parents. He was admitted to neonatal intensive care unit, started on intravenous fluid and investigations were done to rule out other anomalies. Clinically he showed no dysmorphic craniofacial features and no abnormalities in both upper and lower limbs with normal heart sounds. His chest X-rays showed normal both lung fields and nasogastric tube in the stomach. Abdomen and pelvis X-rays revealed dilated bowel loops with absence of gas in the pelvis. Multiple vertebral spine anomalies were recognized as hemivertebrae, butterfly vertebrae, spina bifida in the thoraco-lumbo-sacral spine, 13 ribs, scoliosis and partial sacrococcygeal agenesis or dysgenesis (Figs. 1A-C).

Moreover, ultrasonic examination of the abdomen revealed aplastic right kidney, otherwise grossly normal solid organs. Echocardiogram was normal as well. After 24 hours, a diverting loop colostomy in the left upper quadrant was performed. The newborn hospitalized for 11 days then discharged with stable condition. Two months later, MRI abdomen pelvis and lumbar spine was done using SIMENS 1.5 Tesla. Adapted sequences were: Sagittal: T1WI's, T2WI's, STIR/ Axial: T1WI's, T2WI's/ Coronal: T2WI's fat suppression. The findings shown in Figure 2, right kidney agenesis, sacrococcygeal agenesis and the spinal cord ends at D12-L1 with anterior and posterior bands of the terminating filaments.

Discussion

CRS is a rare congenital disorder results from abnormal caudal spinal growth [12,13]. According to OMIM, the inheritance is Autosomal dominant AD on gene VANGL1/ LOCATION 1P13.1. [14].

CRS is defined also in some literatures as "heterogeneous constellation of congenital caudal anomalies affecting the caudal spine, spinal cord, hindgut, urogenital system and lower limbs" [13,14]. The former definition mixed up the CRS with its associated anomalies, therefor the radiological definition of CRS for only "the caudal spinal growth regression" should be used in a separate picture from its associated anomalies [5]. Variable degree of spinal caudal regression can be seen in association with other syndromes [5,9–11]. The followings syndromes are associated with CRS:

1. VACTERL associations: Vertebral defects, Anal atresia, Cardiac defects, Esophageal atresia with or without tracheoesophageal fistula, Renal and Limb anomalies [5].
2. OIES syndrome or cloacal exstrophy is a rare congenital anomaly that affects the lower abdominal wall structures of infant in utero. Four features of OEIS Complex include: Omphalocele, Exstrophy of bladder and rectum, Imperforated anus, and Spinal defect [9].
3. Currarino syndrome: it is a triad of findings that consist of partial sacral dysgenesis, presacral mass (anterior meningocele, enteric cyst, or presacral teratoma) and anorectal malformation [10].
4. Mayar Rockitanski Kauser Hauser Syndrome MRKHS, especially type II, congenital absence of uterus and upper vagina with normal appearing ovaries and fallopian tubes. It may be associated with non-gynecological anomalies as cardiac, urological, skeletal, vertebral systems including sacrococcygeal agenesis [11].

Although, there is an increased risk of CRS among babies born for diabetic mothers, our patient was born for non-diabetic mother.

CRS diagnosis can be confirmed antenatally in the first trimester by noting a short Crown Rumb Length [12]. Sonographic fetal anomalies detailed scan between 18 and 22 weeks of gestation is very helpful in diagnosis of CRS. Scan findings that is suggestive of CRS include sacrococcygeal dysgenesis with blunt end conus medullaris [2]. Also, the scan may reveal other CRS associated anomalies as renal agenesis or limb anomalies [2]. Unfortunately, in our present case, CRS was diagnosed postnatally as the scan was not done antenatally. The postnatal investigations that were done due to the presence of imperforated anus in our present case reveal the diagnosis of CRS/VACTERL association.

The neuroradiological picture of CRS is variable and depends upon the extent of the disease and the site of spinal regression ranging from mild sensory and motoric deficit of the lower limbs to neurogenic bladder and fecal incontinence as well as limb paralysis with fixed abnormal limb position [4,2,13]. Syrinomelia (fused lower limbs) was considered in some literature as severe form presentation of CRS [1,13].

Our present case had CRS with VACTERL association i.e. sacral agenesis with left renal agenesis, imperforated anus

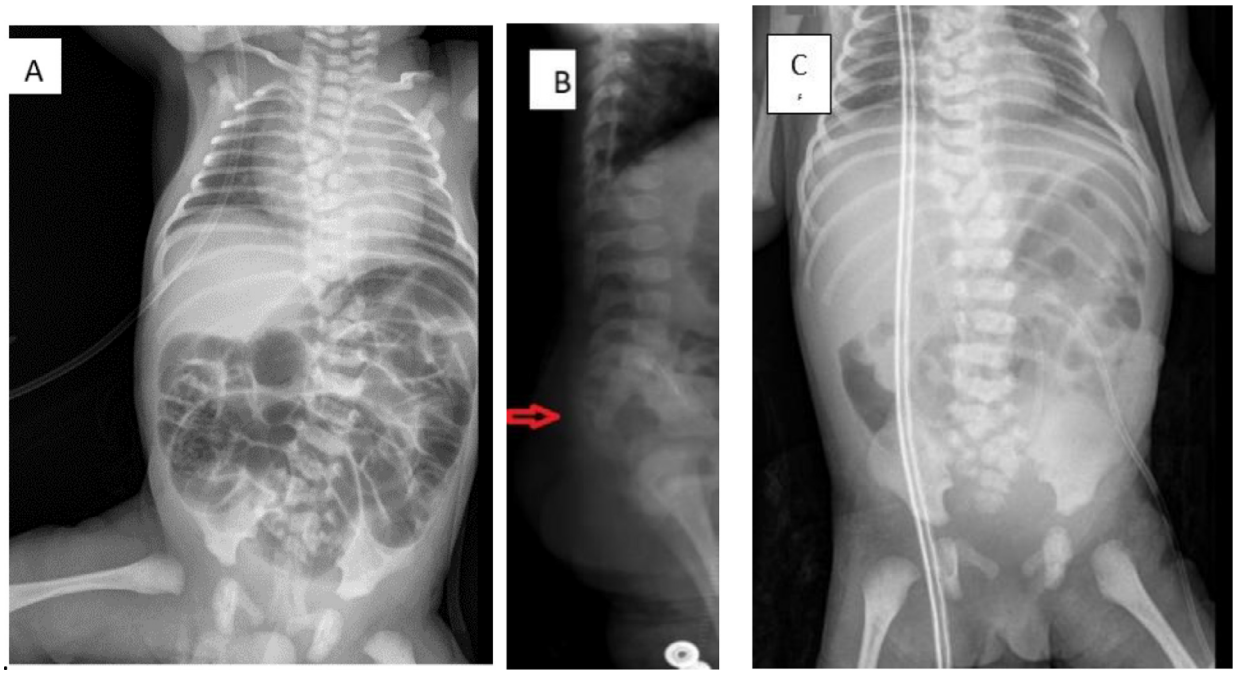

Fig. 1 – (A) Anterior view X-ray at day of birth showed dilated large and small bowel with absence of gas in the pelvis, multiple vertebral spine anomalies (hemi-vertebrae, butterfly vertebrae spina bifida, 13 ribs, scoliosis and sacrococcygeal agenesis or dysgenesis), (B) lateral view X-ray showed caudal regression (red arrow), and (C) 9 days post-diverting colostomy, showed significant reduction of bowel caliber.

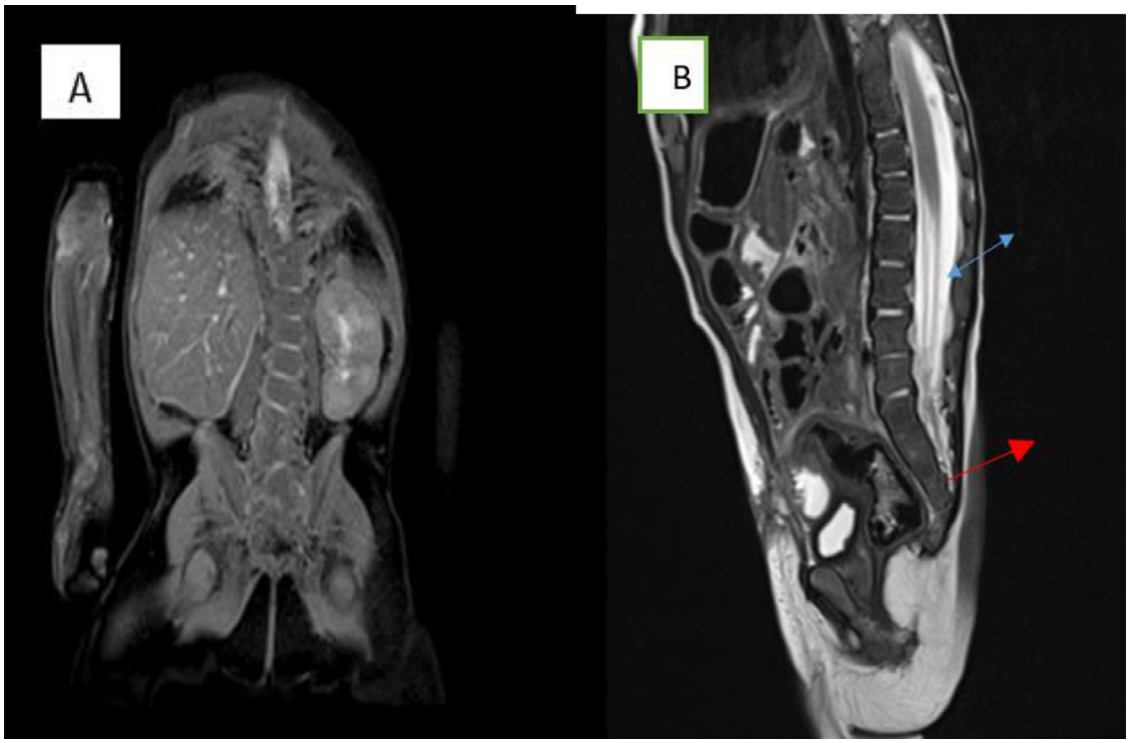

Fig. 2 – (A) MRI coronal T2 WI's fat suppression showed Rt kidney aplasia with spinal scoliosis, (B) sagittal T2WI's the cords end at D12-L1 with anterior and posterior bands inferior to conus medullaris (blue arrow), sacrococcygeal dysgenesis (red arrow) was noted as well.

Table 1 – The presence of different multisystemic CRS-associated anomalies for 83 cases of 46 papers in our literature review.

Author and year	Age	Gender	Maternal DM	Spine and cord anomalies	Limb anomalies	GI anomalies	Cardiorespiratory anomalies	Genitourinary anomalies
(Karthiga et al., 2021)	8 months	Male	Yes	Yes	Yes	No	No	No
(Khushdil et al., 2017a)	Newborn	Female	Yes	Yes	Yes	Yes	No	Yes
(Mehdi et al., 2021a)	Newborn	Male	Yes	Yes	Yes	No	Yes	Yes
(Sharmin et al., 2018)	Newborn	Male	Yes	Yes	Yes	No	No	No
(Aggarwal et al., 2012)	3 years	Male	No	Yes	Yes	No	No	No
(Islam et al., 2017)	Infant	NA	No	Yes	Yes	Yes	No	Yes
(Shojaee et al., 2021)	32 weeks stillbirth	NA	No	Yes	Yes	Yes	No	Yes
(Akhaddar, 2020)	2 years	Male	Yes	Yes	Yes	No	No	No
(Ponde et al., 2021)	14 months	Male	NA	Yes	No	No	No	No
	3 years	Male	NA	Yes	No	No	No	No
	3 days	Male	NA	Yes	No	Yes	No	No
(Bicakci et al., 2014a)	30 months	Female	Yes	Yes	Yes	No	No	Yes
(Puneeth et al., 2014)	10 months	Female	Yes	Yes	No	No	No	No
(Szumera et al., 2018)	6 years	Female	NA	Yes	Yes	No	No	Yes
	6 years	Male	NA	Yes	Yes	No	No	Yes
(Seidahmed et al., 2014)	Newborn	Female	No	Yes	Yes	Yes	Yes	Yes
	Newborn	NA	No	Yes	Yes	Yes	No	Yes
	31-week preterm newborn	NA	No	Yes	Yes	Yes	Yes	Yes
	35 weeks preterm newborn	NA	No	Yes	Yes	Yes	No	Yes
	14 years	Female	Yes	Yes	Yes	No	No	Yes
	4 years	Female	No	Yes	Yes	No	Yes	Yes
(Zaw & Stone, 2002)	Newborn	NA	Yes	Yes	Yes	No	No	No
(Bicakci et al., 2014b)	30 months	Female	Yes	Yes	Yes	No	No	Yes
(Duesterhoeft et al., 2007)	Infant	Male	NA	Yes	Yes	Yes	Yes	Yes
	20 weeks gestation	NA	NA	Yes	Yes	Yes	Yes	Yes
	stillborn at 23 weeks	NA	NA	Yes	Yes	No	Yes	Yes
	Infant	Female	NA	Yes	No	Yes	No	Yes
	Infant	Male	NA	Yes	Yes	No	No	Yes
(Fukada et al., 1999)	6 weeks	Female	NA	Yes	Yes	No	No	No
(Gedikbasi et al., 2009)	Stillbirth	NA	NA	Yes	Yes	Yes	No	No
(Griffet et al., 2011)	1 year	Male	No	Yes	Yes	No	No	Yes
(Das et al., 2002)	Newborn	Male	No	Yes	Yes	Yes	Yes	Yes
(Duh et al., 2007)	10 days	Male	No	Yes	Yes	Yes	No	Yes
(Lorenzo et al., 1991)	Newborn	Male	No	Yes	Yes	Yes	No	Yes
(Miller, 1972)	Newborn	Male	No	Yes	No	No	No	Yes
(Romeo et al., 2000)	Newborn	Female	No	Yes	Yes	Yes	No	No
(Mihmanli et al., 2001)	3 months	Female	Yes	Yes	Yes	No	No	Yes
(Bouchahda et al., 2017)	Newborn	Male	Yes	Yes	Yes	No	Yes	No
(Martucciello et al., 2004)	Newborn	Female	NA	Yes	No	Yes	No	Yes
	Newborn	Female	NA	Yes	No	Yes	No	No
	Newborn	Female	NA	Yes	No	Yes	No	Yes
	Newborn	Female	NA	Yes	No	Yes	No	Yes
	Newborn	Female	NA	Yes	No	Yes	No	Yes
	Newborn	Male	NA	Yes	No	Yes	No	No
(Shah et al., 2006)	3 years	NA	No	Yes	No	No	No	No
(Pappas et al., 1989)	Newborn	Male	NA	Yes	Yes	No	No	Yes
(Guirgis et al., 2003)	10 weeks	Female	No	Yes	Yes	Yes	No	Yes
(Turnock & Brereton, 1991)	2 days	Male	NA	Yes	No	No	No	Yes
(Tsugu et al., 1999)	6 months	Female	NA	Yes	Yes	Yes	No	Yes
(Singer et al., 2005)	Newborn	NA	NA	Yes	Yes	No	Yes	Yes
(Rubenstein & Bucy, 1975)	15 months	Male	NA	Yes	Yes	No	No	Yes
	Newborn	Female	NA	Yes	Yes	No	No	Yes
	5 years	NA	NA	Yes	No	No	No	Yes
(Bohring et al., 1999).	20 weeks	Female	No	Yes	Yes	Yes	No	No
	Infant	Male	No	Yes	Yes	No	Yes	Yes
	Infant	NA	Yes	Yes	Yes	No	No	Yes
	Infant	Female	NA	Ye	Yes	Yes	No	Yes
	Newborn	Male	Yes	Yes	Yes	Yes	Yes	Yes
	Newborn	Male	No	Yes	Yes	No	No	Yes
	Infant	Female	No	Yes	Yes	No	Yes	No
	Newborn	Female	No	Yes	Yes	Yes	No	Yes
	Stillborn 22 weeks	Male	No	Yes	Yes	No	No	Yes
	Stillborn	NA	No	Yes	Yes	No	No	No
	Stillborn	Male	No	Yes	Yes	No	No	No
	Infant	Male	No	Yes	No	No	Yes	No
	Infant	NA	Yes	Yes	Yes	Yes	No	Yes
	Infant	Female	No	Yes	Yes	IA	Yes	Yes
	Infant	Female	No	Yes	Yes	No	Yes	No

(*continued on next page*)

Table 1 (*continued*)

Author and year	Age	Gender	Maternal DM	Spine and cord anomalies	Limb anomalies	GI anomalies	Cardiorespiratory anomalies	Genitourinary anomalies
(Khushdil et al., 2017)	Newborn	Female	No	Yes	No	No	No	Yes
(Tubbs & Oakes, 2006)	Newborn	Male	Yes	Yes	Yes	No	Yes	Yes
(Yegin et al., 2005)	9 days	Male	Yes	Yes	Yes	No	Yes	Yes
(Toguri et al., 1981)	4 years	Female	NA	Yes	Yes	Yes	No	Yes
(Hentschel et al., 2006)	Newborn	Male	No	Yes	Yes	No	Yes	Yes
(Krenova et al., 2010)	Infant	Female	Yes	Yes	Yes	No	No	Yes
(Hirano et al., 1998)	Infant	Female	No	Yes	Yes	Yes	No	Yes
	34 months	Female	NA	Yes	Yes	Yes	Yes	Yes
(Towfighi & Housman, 1991)	Newborn	NA	No	Yes	Yes	Yes	No	Yes
	Newborn	NA	No	Yes	Yes	Yes	Yes	Yes
	Newborn	NA	No	Yes	Yes	Yes	Yes	Yes
	Newborn	NA	Yes	Yes	Yes	Yes	No	Yes
(Kokrdova, 2013)	18-week gestational age	NA	Yes	Yes	Yes	No	No	Yes
	20-week gestational age	Female	Yes	Yes	Yes	No	Yes	Yes
(Gonzalez et al., 1985)	Newborn	Male	Yes	Yes	Yes	Yes	No	Yes
(Mehdi et al., 2021)	Newborn	Male	Yes	Yes	Yes	No	Yes	Yes

and multilevel vertebral anomalies (dysraphism). The low level spinal regression in our cases with absence of dysmorphic facial gluteal and limb clinical features, the presence of 3 components of VACTERL association, the presence of thirteen ribs and vertebral dysraphism characterize our present case.

Literature review

A thorough search among the published literature using PubMed search engine using "caudal regression syndrome" keywords with human and English language filters results in about 46 applicable articles present 83cases of postnatal diagnosis of CRS. The following data were collected for each patient: age, gender, maternal diabetes, and the presence of associated congenital anomalies namely; spine and cord anomalies, limb anomalies, gastroenterology anomalies, genitourinary anomalies and cardiorespiratory anomalies (Table 1). About 65% of cases were diagnosed within the first month postnatally, while 85% were diagnosed within the first year, less than 1% diagnosis delayed to the puberty age. Almost all patients who were diagnosed within the first month of life, had either imperforated anus or apparent limb anomalies. Additionally, there was no gender predilection. Only one third of cases delivered for diabetic mother. All reviewed patients had partial or complete sacral agenesis (The main criteria for CRS diagnosis) which was diagnosed either antenally by ultrasound or postnatally by conventional X-ray and MRI; however, associated higher level of spinal agenesis was not rare.

The most common spine and CNS anomalies which were identified in our review includes: bony vertebral dysraphism (hypoplastic vertebrae, vertebral fusion, hemi vertebra and butterfly vertebrae), tethered cord, and high abrupt termination of the spinal cord at various levels and spinal column malalignment (scoliosis and kyphosis).

About 81% of patients had limbs and other bones anomalies (excluding the spine anomalies), the lower limb was involved primarily in all these patients. Short limb, talipes equinovarus, popliteal webbing and abnormal posture were frequent limb findings. The incidence of genito-urinary anomalies was 72%, the most common is renal agenesis followed by neurogenic bladder, variable degree of hypoplastic /dysplastic urinary system and external genatalia agenesis/dysgenesis. About 42% of patients had gastroenterology anomalies, the most common is ano-rectal malformation, and imperforated anus was the most encountered gastrointestinal anomaly.

Rectal fistula and esophageal atresia were not uncommon.

The cardiovascular and respiratory anomalies were seen in 24% of patients. The most common associated cardiac anomalies were: patent ductus arteriousus, ventricular septal defect, arterial septal defect, pulmonary hypoplasia/dysplasia and the vascular anomalies which involved the pulmonary artery, and aorta with its branches.

Dysmorphic facial features like Potter face, abnormal gluteal contour, shallow natal cleft and posterior dimple was seen in less than13%.

This literature review showed the wide variation of patients radiological and clinical presentation of congenital anomalies associated with CRS.

Conclusion

CRS is a rare congenital anomaly that may be associated with wide spectrum of multisystem anomalies. It should be considered in patient with imperforated anus. CRS assessment can be done by X-rays, ultrasound and MRI. X-rays is more informative for vertebral dysraphism and bony anomalies in newborn compared to MRI (1.5 Tesla).

Ethics approval

Our research was approved by institutional ethics committee.

Consent for publication

Our research does not contain any personal data, photos or clinical trial for medication or radiation or any hazard; however, written consent form was signed by both parents, moreover agreement of institutional ethics committee.

Availability of data and material

The data that support the findings of this study are available from the computerized patient medical archived file in the hospital, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [M.O.H hospitals].

Authors' contributions

All authors have made substantial contributions to the conception, design of the work; acquisition, interpretation of data, they have drafted and revised it, and they have approved the submitted version and the modified version.

Patient consent

The parents of the newborn patient agreed (without any financial compensation/award) to use and publish the radiological images as well as the clinical data of their son without mention any personal data like patient name, family name, date of birth or hospital also no personal photo were allowed to be published.

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