CASE REPORT

Cloacal dysgenesis sequence with bilateral renal agenesis and normal pulmonary development in twin pregnancy

Sundram Jegadeesh, Jai Kumar Mahajan

Department of Pediatric Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Correspondence to
Dr Jai Kumar Mahajan,
jkmahajan@gmail.com

Accepted 6 January 2016

SUMMARY

Cloacal dysgenesis sequence (CDS) is a rare congenital anomaly. It is characterised by a smooth perineum with absence of anal and genitourinary orifices, with reported incidence of 1:50 000–250 000 births. Association with bilateral renal agenesis is still rarer and resultant severe oligohydramnios is associated with pulmonary hypoplasia. Only a few cases of CDS with bilateral renal agenesis have been reported in the English language literature, with associated pulmonary hypoplasia as a default phenomenon. We report a case of CDS and bilateral renal agenesis without associated pulmonary hypoplasia in a twin pregnancy, which, to the best of our knowledge, is the second reported case of this amalgamation.

CASE PRESENTATION

A 10 h-old new-born, one of twins, born to a primigravida mother at 35 weeks gestation, presented with a smooth perineum showing absence of anal, genital and urinary orifices.^{1 2} Level-1 antenatal ultrasonography (USG) at 22 weeks of gestation had revealed a monoamniotic twin pregnancy with adequate liquor without any associated anomalies. There was no history of consanguinity. The baby was pink, haemodynamically stable and breathing well. On examination, there was no formation of female or male genitalia and the anal orifice was also absent. Only a small nubbin of tissue was present in the perineum (figure 1). The other twin was a girl with a normal perineum and no obvious congenital anomaly.

Abdominal USG showed absence of both kidneys and a dilated bowel loop on the left side of the abdomen. A radionuclide ethylene di-cysteine scan

was performed to confirm the findings of USG. It also showed a complete absence of renal uptake of radionuclide on both sides (figure 2). Other associated anomalies included fifth lumbar hemivertebra and sacral hypoplasia (figure 3). Biochemical renal function tests of the affected baby were normal on the first day of life, probably because of a placental filtration effect. The parents were advised on the severity of the defect and they opted to discontinue the treatment. The child died at home on day 13 of life. The parents were recommended autopsy but did not agree to it.

GLOBAL HEALTH PROBLEM LIST

- Complex embryological development
- Rare presentation
- Association with renal agenesis
- Antenatal diagnosis and intervention
- Long term outlook
- Cumulative information in the literature

GLOBAL HEALTH PROBLEM ANALYSIS

Cloacal dysgenesis sequence (CDS) is characterised by a smooth perineum with absence of anal, genital and urinary orifices, with non-development of labioscrotal structures; the colon, bladder and vagina end blindly. The defect has also been described as full urorectal septum malformation sequence (URSMS) by Escobar *et al*,² who hypothesised that the cause of this septum malformation is failure of the urorectal septum to migrate downwards and fuse with the cloacal membrane. However, the new theory of differential mesenchymal growth is now widely accepted, hence the condition is better known as CDS rather than URSMS sequence.³ The defect probably arises due to disturbance of the structures derived from the caudal mesodermal axis of embryo or mesodermal

Figure 1 Perineum showing only a nubbin of tissue, with no urogenital and anal openings.

Figure 2 Ethylene cysteine renal scan showing absence of renal tissue on both sides.

To cite: Jegadeesh S, Mahajan JK. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-214130

Figure 3 X-ray of the affected baby showing normal lung fields, lumbar hemivertebra and sacral hypoplasia.

disturbance early in gestation.⁴ The caudal mesodermal defects give rise to anal, genital and spinal disturbances.^{5 6} Renal agenesis is the consequence of failure of differentiation of the metanephric blastema during the 25–28th day of development, and both the ureters, kidneys and renal arteries are absent. Genetic

Figure 4 Line diagram depicting monoamnioticity and sharing of amniotic fluid by the affected twin.

or environmental teratogens may affect pathways that are critical to both renal and extrarenal development. Some groups proposed that CDS might result from twinning, possibly due to an

Table 1 CDS and multiple gestations

Authors	Status of index case	Status of other fetus/es
Koffler <i>et al</i> ⁴ (monoamniotic)	<ul style="list-style-type: none"> ▶ Right renal hypoplasia ▶ Polycystic left kidney ▶ No lung hypoplasia 	Normal
Sinniah and Manuel ¹⁴	<ul style="list-style-type: none"> ▶ Renal status not known ▶ Persistent urachus ▶ No lung hypoplasia 	Normal
Berry <i>et al</i> ¹⁰ (mono amniotic)	<ul style="list-style-type: none"> ▶ Bilateral renal agenesis ▶ No lung hypoplasia 	Normal
Wheeler <i>et al</i> ⁷ Case 1 (triplet)	<ul style="list-style-type: none"> ▶ Bilateral MCDK ▶ Lungs hypoplastic 	<ul style="list-style-type: none"> ▶ One normal ▶ The other with meningocele + cardiac anomalies
Wheeler <i>et al</i> ⁷ Case 2 (twin)	<ul style="list-style-type: none"> ▶ Right renal agenesis ▶ Left MCDK ▶ Lungs hypoplastic 	<ul style="list-style-type: none"> ▶ Stillborn ▶ No CDS
Qureshi <i>et al</i> ¹³ (monoamniotic)	<ul style="list-style-type: none"> ▶ Cystic dysplasia with hydronephrosis ▶ Lungs hypoplastic ▶ Limb anomalies 	<ul style="list-style-type: none"> ▶ Also CDS ▶ Cystic dysplasia with hydronephrosis ▶ Normal lungs ▶ Limb anomalies
Jain <i>et al</i> ⁹	<ul style="list-style-type: none"> ▶ Bilateral renal agenesis ▶ Lungs hypoplastic 	Normal
Gupta <i>et al</i> ³	<ul style="list-style-type: none"> ▶ Bilateral ectopic dysplastic kidney ▶ Lungs hypoplastic 	<ul style="list-style-type: none"> ▶ Bilateral MCDK ▶ Lungs hypoplastic
Mukhtar <i>et al</i> ¹¹	<ul style="list-style-type: none"> ▶ Bilateral MCDK (renal transplantation done) ▶ Pulmonary hypoplasia (improved) ▶ Survival until 25 months 	Normal
Our case (mono amniotic)	<ul style="list-style-type: none"> ▶ Bilateral renal agenesis ▶ No pulmonary hypoplasia 	Normal

CDS, cloacal dysgenesis sequence; MCDK, multicystic dysplastic kidney.

insufficient number of cells in the gastrulation stage to populate two separate embryos.

About 100 cases with morphological abnormalities have been reported in the English language literature.^{3–9} These fetuses usually have renal insufficiency leading to oligohydramnios and pulmonary hypoplasia. Wheeler *et al*⁷ reported 80% incidence of pulmonary hypoplasia in CDS. Despite lacking renal function, our patient did not have pulmonary hypoplasia, as the amniotic fluid production by the normal fetus in this case compensated for deficiency of amniotic fluid for the fetus with CDS (figure 4), similar to the cases reported by Koffler *et al*⁴ and Berry *et al*.¹⁰ The different points from these cases were that those twins were of a diamniotic type. As mentioned by Mukhtar *et al*,¹¹ there are about 22 reported cases of CDS or related anomalies in twins. But CDS or complete URSMS in twins has been reported to be very rare.

Renal agenesis is associated in 50% of cases of CDS.¹² Eighteen cases of bilateral renal agenesis associated with CDS have been reported, of which only one was a twin pregnancy.^{7–9} Our patient had bilateral renal agenesis in addition to a smooth perineum and absent perineal openings.

On antenatal USG, distended bowel loops, over-distended urinary bladder with absence of keyhole sign or non-visualisation of bladder and external genitalia in the presence of oligohydramnios should alert the physician to the possibility of CDS. However, visualisation of the external genitalia may be difficult in the presence of a severe oligohydramnios.⁸ Fetal MRI is better than USG in delineating anatomical details, associated anomalies and pulmonary hypoplasia. Prenatal diagnosis of this condition is essential as it is usually lethal; parents should be advised regarding the poor prognosis and counselled for termination of pregnancy. CDS should be suspected in a karyotypically male fetus with antenatal imaging features of obstructive uropathy without normal demonstration of phallus.¹³ After birth, the child should undergo ultrasound of the abdomen, radionuclide scan and radiographs, to know the status of the kidneys, skeletal anomalies and bowel distension. Chromosomal analysis will help in gender assignment early in life. The child with bilateral renal agenesis would need renal transplantation to survive. Although CDS is fatal, patients with patent urachus or other means of draining urine may be spared of the lethal secondary effects when underlying kidneys are

normal.¹⁴ Survival beyond 1 year of age was reported only in five cases up to 2012, when Yanai *et al*¹⁵ reported a 12-year-old female survivor of CDS undergoing antenatal intervention in the form of a vesicoamniotic shunt followed by postnatal staged surgical procedures.^{8–11} The literature review regarding association of CDS with multiple gestations is presented in table 1.

In summary, CDS with bilateral renal agenesis is a lethal combination. If suspected on antenatal USG, termination of pregnancy is advisable.¹⁶ If these babies are born alive, presence of renal tissue should be confirmed before subjecting them to surgical interventions for CDS. The role of early antenatal intervention in CDS without renal agenesis to preserve renal function and prevent pulmonary hypoplasia needs to be evaluated in view of few reported survivals.

Contributors JKM cared for the patient and planned investigation, and drafted the manuscript; SJ performed the literature search and drafted the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Blott M, Greenough A, Nicolaides KH, *et al*. Fetal breathing movements as predictor of favourable pregnancy outcome after oligo-hydramnios due to membrane rupture in second trimester. *Lancet* 1987;2:129–31.
- 2 Escobar LF, Weaver DD, Bixler D, *et al*. Urorectal septum malformation sequence. Report of six cases and embryological analysis. *Am J Dis Child* 1987;141:1021–4.
- 3 Gupta R, Parekar SV, Oak S, *et al*. Cloacal dysgenesis sequence in a set of twins: new insights into embryology and a review of the literature. *Eur J Pediatr Surg* 2010;20:355–7.
- 4 Koffler H, Aase JM, Papile LA, *et al*. Persistent cloaca with absent penis and anal atresia in one of identical twins. *J Pediatr* 1978;93:821–3.
- 5 Källén B, Winberg J. Caudal mesodermal pattern of anomalies: from renal agenesis to sirenomelia. *Teratology* 1974;9:99–111.
- 6 Wheeler PG, Weaver DD. Partial urorectal septum malformation sequence: a report of 25 cases. *Am J Med Genet* 2001;103:99–105.
- 7 Wheeler PG, Weaver DD, Obeime MO, *et al*. Urorectal septum malformation sequence: report of thirteen additional cases and review of the literature. *Am J Med Genet* 1997;73:456–62.
- 8 Patil SJ, Phadke SR. Urorectal septum malformation sequence: ultrasound correlation with fetal examination. *Indian J Pediatr* 2006;73:287–93.
- 9 Jain D, Sharma MC, Kulkarni KK, *et al*. Urorectal septum malformation sequence: a report of seven cases. *Congenit Anom* 2008;48:174–9.
- 10 Berry SA, Johnson DE, Thompson TR. Agenesis of the penis, scrotal raphe, and anus in one of monoamniotic twins. *Teratology* 1984;29:173–6.
- 11 Mukhtar RA, Baskin LS, Stock PG, *et al*. Long-term survival and renal transplantation in a monozygotic twin with cloacal dysgenesis sequence. *J Pediatr Surg* 2009;44:E31–3.
- 12 Chien JC, Chen SJ, Tiu CM, *et al*. Is urorectal septum malformation sequence a variant of the vertebral defects, anal atresia, tracheo-oesophageal fistula, renal defects and radial dysplasia association? Report of a case and a review of the literature. *Eur J Pediatr* 2005;164:350–4.
- 13 Qureshi F, Jacques SM, Yaron Y, *et al*. Prenatal diagnosis of cloacal dysgenesis sequence: differential diagnosis from other forms of fetal obstructive uropathy. *Fetal Diagn Ther* 1998;13:69–74.
- 14 Sinniah D, Manuel JK. A syndrome of multiple congenital malformations with absent external genitalia, urethral and anal openings in one of twins. *Singapore Med J* 1980;21:534–6.
- 15 Yanai T, Urita Y, Amagai T, *et al*. Long-term survival with cloacal dysgenesis sequence. *Pediatr Surg Int* 2012;28:107–10.
- 16 Sahinoglu Z, Mulayim B, Ozden S, *et al*. The prenatal diagnosis of cloacal dysgenesis sequence in six cases: can the termination of pregnancy always be the first choice? *Prenat Diagn* 2004;24:10–16.

Learning points

- Cloacal dysgenesis sequence (CDS) is a rare anomaly that, in combination with bilateral renal agenesis, is lethal.
- Pulmonary hypoplasia is a norm in the presence of bilateral renal agenesis, except in cases with monoamniotic twins, where the normal twin prevents oligohydramnios.
- Active treatment is recommended in cases of CDS with normal renal development, at least on one side.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow