VERSITA

Cent. Eur. J. Med. • 8(3) • 2013 • 358-361
DOI: 10.2478/s11536-013-0152-y

Central European Journal of **Medicine**

# Unilateral renal agenesis in a neonate with congenital diaphragmatic hernia

**Case Report**

Kyoung Hee Han[1], Kwang Sig Kim[2], Jee Won Chang[3], Young Don Kim[1]

*1 Department of Pediatrics, Jeju National University Hospital, Aran 13gil 15, Jeju city, Jeju Special Self-Governing Province, 690-767, Korea*

*2 Department of Surgery, Jeju National University Hospital, Aran 13gil 15, Jeju city, Jeju Special Self-Governing Province, 690-767, Korea*

*3 Department of Thoracic Surgery, Jeju National University Hospital, Aran 13gil 15, Jeju city, Jeju Special Self-Governing Province, 690-767, Korea*

**Received 6 December 2012; Accepted 31 January 2013**

**Abstract:** Congenital diaphragmatic hernia (CDH) is a rare and severe disorder with a high mortality rate among infants. Unilateral renal agenesis (URA) is a relatively common congenital urinary malformation. Here, we present the case of a newborn infant with left CDH associated with ipsilateral renal agenesis. The male patient was born weighing 3.850 g through normal spontaneous vaginal delivery at 38 weeks and 6 days of gestational age at a maternity hospital. He was transferred to our neonatal intensive care unit due to respiratory distress with tachypnea, grunting and cyanosis after birth. A chest radiography indicated parts of the bowel in the thoracic cavity, consistent with CDH. Renal ultrasonography indicated no kidney structure on the left side and a 5.6 cm right kidney with normal echogenicity. Repair of the diaphragmatic hernia was performed three days after birth. Most of the colon, small bowel, stomach and spleen were located in the left pleural cavity, but the left kidney was not seen. Subsequent dimercaptosuccinic acid scintigraphy indicated non-visualized functional cortical uptake in the left kidney on day 13 after birth. Thus, we report the successful treatment of a patient with CDH accompanied by URA.

**Keywords:** *Congenital diaphragmatic hernia • Bochdalek hernia • Unilateral renal agenesis*



## 1. Introduction

Congenital diaphragmatic hernia (CDH) is a rare and serious disease [1,2]. The incidence of other associated anomalies occurring in CDH patients is approximately 30%, and the mortality rate is high [1-3]. Central nervous system lesions, esophageal atresia, omphalocele and cardiovascular anomalies are commonly associated with CDH [1]. Moreover, CDH is frequently accompanied by genitourinary anomalies (up to 20%), including renal agenesis, dysplasia, hypoplasia, or hydronephrosis [4].

Unilateral renal agenesis (URA) is a relatively common malformation, with an incidence ranging from 1 per 500 to 1 per 3,200 births [5-8]. It is frequently accompanied by genitourinary anomalies or other associated anomalies, some of which can induce irreversible renal function deterioration [9].

Here, we report the survival of a patient where CDH was accompanied by unilateral URA.

## 2. Case report

In January 2012, a 1-day-old boy was transferred with endotracheal intubation from a maternity hospital to our neonatal intensive care unit due to respiratory distress with tachypnea, grunting and cyanosis after birth. He weighed 3.850 g, and was born through normal spontaneous vaginal delivery at 38 weeks and 6 days of gestational age. Physical examination showed no evidence of dysmorphic facies, asymmetric chest expansion with

* *E-mail: cardios@hanmail.net*

intercostal and subcostal retraction, and decreased breath sounds in left thorax. Both hemiscrotums were enlarged and transillumination was observed. Vital signs included: blood pressure, 53/29 mmHg; heart rate, 186/min; respiratory rate, 66/min; and pulse oximeter saturations ($SpO_2$), 75%. His laboratory findings on admission were as follows: white blood cells, $17.2x10^3$/μL; hemoglobin, 13.6 g/dL; hematocrit, 38.9%; platelets, $174x10^9$/L; total protein, 4.1 g/dL; albumin, 3.0 g/dL; total bilirubin, 76 μmol/L; direct bilirubin, 7 μmol/L; glucose, 6.7 mmol/L; alkaline phosphatase, 612 U/L; aspartate aminotransferase, 49 IU/L; alanine aminotrasferase, 12 IU/L; blood urea nitrogen (BUN), 11.1 mg/dL; creatinine (Cr), 115 μmol/L; and C-reactive protein, 0.19 mg/dL. His serum electrolyte data included: sodium, 132 mmol/L; potassium, 4.3 mmol/L; and chloride, 104 mmol/L. Venous blood gas analysis indicated a pH of 7.28, $pCO_2$ of 52.5 mm Hg and bicarbonate 24.9 mmol/L bicarbonate of 24.9 mmol/L.

His chest radiograph (Figure 1) indicated bowel gas in the thoracic cavity, consistent with CDH. The patient was placed on a mechanical ventilator. His preoperative urine output was 0.58 mL/kg/h and the deterioration in renal function (BUN, 29.0 mg/dL; Cr, 124 μmol/L) on day 3 after birth. Renal ultrasonography (US) showed a 5.6 cm right kidney with normal echogenicity but failed to demonstrate a kidney on the left side. Repair of the diaphragmatic hernia was performed on day 3 postpartum revealing a defect in the posterolateral portion of the left diaphragm (Bochdalek hernia). Most of the colon, small bowel, stomach and spleen were located in the left pleural cavity, but the left kidney was not observed. Following surgery, urine output increased up to 3 mL/kg/h, and renal function had recovered completely (BUN, 7.8 mg/dL; Cr, 27 mol/L) by day 3 postoperatively. Extubation was peformed on day 6 postoperatively and the baby's vital signs were as follows: blood pressure, 74/44 mmHg; heart rate, 154/min; respiratory rate, 41/min; and SpO2, 96%. His laboratory findings on day 10 after surgery were as follows: white blood cells, $10.900x10^3$/μL; hemoglobin, 10.1 g/dL; hematocrit, 30.1%; platelets, $294x10^9$/L; pH, 7.42; $pCO_2$, 37.3 mmHg; and $HCO_{3-}$, 24.0 mmol/L. Dimercaptosuccinic acid (DMSA) scintigraphy on postoperative day 10 (Figure 2) indicated a non-visualized functional cortical uptake in the left kidney.

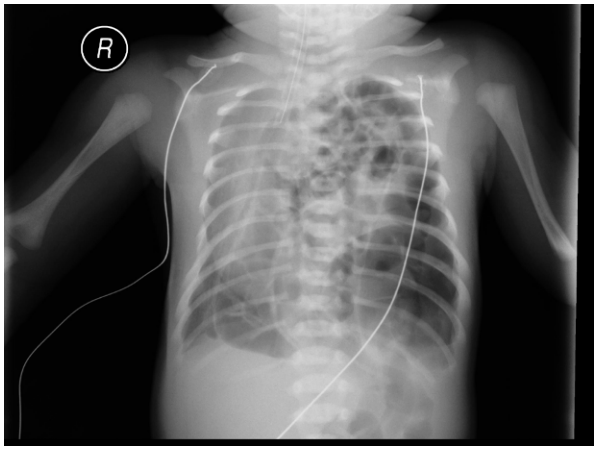


**Figure 1.** Chest radiograph at initial presentation shows extensive bowel gas in the thoracic cavity, consistent with congenital diaphragmatic hernia.

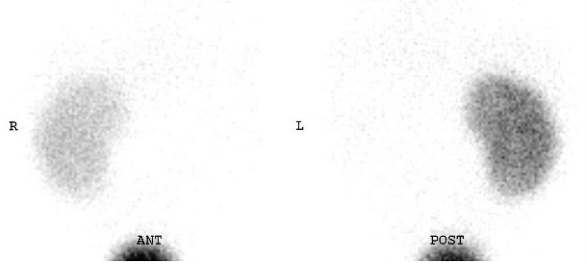


**Figure 2.** Dimercaptosuccinic acid scintigraphy indicates non-visualized functional cortical uptake in the left kidney on day 13 postpartum.

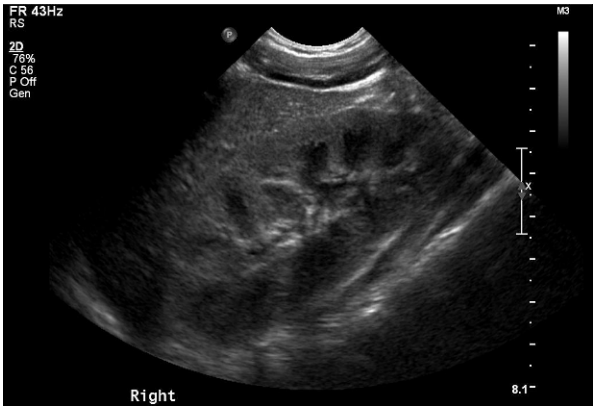


**Figure 3.** Renal ultrasonography indicates a 7.4 cm right kidney with normal parenchymal echogenicity in the patient at 8 months of age.

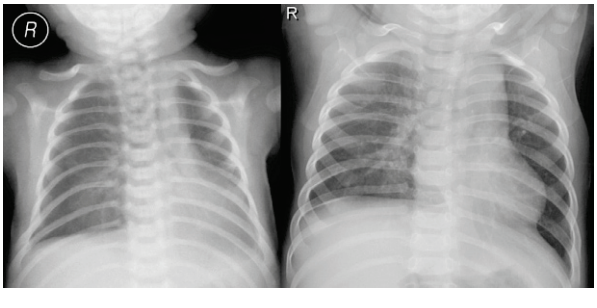


**Figure 4.** Follow-up chest radiographs postoperatively at 2 weeks (left) and at 8 months (right) show normal ventilation of the left lung.

A voiding cystourethrogram showed no vesicoureteral reflux or other urinary anomalies. Mutational analysis of the Wilms' tumor suppressor gene (*WT1*) yielded a normal result.

At present, the 8-month-old patient's laboratory data indicate a serum Cr level of 45 μmol/L and a recent renal US showed a 7.4 cm right kidney with normal parenchymal echogenicity (Figure 3). Normal ventilation of the left lung was also observed on serial follow-up in our outpatient clinic (Figure 4).

## 3. Discussion

This case of CDH had concomitant URA without a major malformation including central nervous system lesions, esophageal atresia, omphalocele or cardiovascular anomalies. Sporadic cases of CDH are commonly observed, but occasionally CDH is accompanied by additional multiple malformations [10]. The frequency of additional major malformations present in newborn infants with CDH has been reported at 39.3%, and malformations of the genitourinary system had a frequency of 23% in one meta-analysis [3,11]. The survival rate of fetuses with CDH and additional major malformations was 7.1% as opposed to 43.7% in those with an isolated CDH [12]. The patient in our case is currently 8 months old and has normal kidney and pulmonary function after intensive management.

According to a recent study of 143 fetuses and newborn infants, a total of 272 malformations were associated with CDH, and genitourinary anomalies, including hydronephrosis, hypospadias, and renal agenesis, were the third most frequent type of anomaly [2]. Losty et al. [13] reported that 33% of cases were found to have associated anomalies following analysis of 301 CDH autopsy records; genitourinary anomalies identified in patients with left-sided CDH included: 21 cases with undescended testes, 1 with hypospadias, 1 with a pelvic kidney, 1 with renal agenesis and 1 with a multicystic kidney. Embryologically, the lateralization of the CDH did not influence the overall incidence of associated anomalies in CDH; however, hypoplastic heart syndrome was found to be developmentally related in some patients with left-sided CDH [13].

URA is a commonly encountered congenital urinary anomaly. The left kidney is involved more often than the right [14-16]. The side involved in URA in our case was the left. URA may be isolated or may be associated with chromosome abnormalities or VACTERL (vertebra, anus, cardiac, trachea, esophagus, renal, limbs) anomalies [8,9]. Vesicoureteral reflux is commonly noted in the contralateral kidney in URA [9,15,17]. We also performed a chromosome study and voiding cystourethrogram, but no abnormal findings were noted.

*WT1* gene mutations have been identified in patients with Denys-Drash, Frasier, and WAGR syndromes and CDH [18-20]. During development, *WT1* is strongly expressed in the mesothelial lining of the abdominal cavity, and this contributes to the development of the diaphragm and epicardium [21]. Abnormalities of *WT1* are reportedly a rare cause of isolated diaphragmatic hernia, as *WT1* mutations were not detected among 21 children with isolated CDH, according to one study [22]. We therefore performed mutational analysis of the *WT1* gene in the present case, but no mutation was noted.

Slit3, one of the Slit family of secreted protein molecules, is known to be expressed in the heart, ovary, intestine, thyroid and developing lung and kidney [23-25]. Slit3-deficient mice were reported to have a defective central tendon of the diaphragm, enlarged right ventricle and unilateral or bilateral agenesis of the kidney [25]. Thus far, the presence of the *SLIT3* mutation in humans has not been reported. However, we did not examine the *SLIT3* gene in the present case.

Fortunately, in the present case, oliguria and azotemia were observed preoperatively. Moreover, we performed a renal US to search for any additional malformation of the urinary system, which failed to demonstrate a kidney on the left side. The surgeons confirmed by inspection that most of the colon, small bowel, stomach and spleen were located in left pleural cavity, but the left kidney was not noted. The associated urinary anomalies in CDH are not as serious as other potential major anomalies; therefore, it would be easy to overlook that fact that CDH might be accompanied by aberrant urinary anatomy. We believe that it is essential to check for the presence of urinary anomalies in a patient with CDH, irrespective of the presence of renal insufficiency. Here, we present a case of an anomaly wherein a rare occurrence of CDH was accompanied by a commonly-associated URA, although the shared pathophysiologic background between the two malformations is still unclear.

## References


[1] Maheshwari A., Carlo W.A., Diaphragmatic hernia, In: Kliegman R.M., Stanton B.F., St.Geme J.W., Schor N.F., Behrman R.E. (Eds.), Nelson textbook of pediatrics, 19th ed., Elsevier, 2011

[2] Zaiss I., Kehl S., Link K., Neff W., Schaible T., Sütterlin M., et al., Associated malformations in congenital diaphragmatic hernia. Am. J. Perinatol., 2011, 28, 211-218

[3] Skari H., Bjornland K., Haugen G., Egeland T., Emblem R., Congenital diaphragmatic hernia: a meta-analysis of mortality factors. J. Pediatr. Surg., 2000, 35, 1187-1197

[4] Siebert J.R., Benjamin D.R., Juul S., Glick P.L., Urinary tract anomalies associated with congenital diaphragmatic defects. Am. J. Med. Genet., 1990, 37, 1-5

[5] Doroshow L.W., Abeshouse B.S., Congenital unilateral solitary kidney: report of 37 cases and a review of the literature. Urol. Surv., 1961, 11, 219-229

[6] Stoll C., Alembik Y., Roth M.P., Dott B., Sauvage P., Risk factors in internal urinary system malformations. Pediatr. Nephrol., 1990, 4, 319-323

[7] Barakat A.J., Drougas J.G., Occurrence of congenital abnormalities of kidney and urinary tract in 13,775 autopsies. Urology, 1991, 38, 347-350

[8] Parikh C.R., McCall D., Engelman C., Schrier R.W., Congenital renal agenesis: case-control analysis of birth characteristics. Am. J. Kidney Dis., 2002, 39, 689-694

[9] Kim J.W., Lee S.E., Jung Y.H., Han K.H., Lee H.K., Kang H.G., et al., Clinical characteristics and associated anomalies in children with solitary kidney. J. Korean Soc. Pediatr. Nephrol., 2010, 14, 42-50

[10] Klaassens M., van Dooren M., Eussen H.J., Douben H., den Dekker A.T., Lee C., et al., Congenital diaphragmatic hernia and chromosome 15q26: determination of a candidate region by use of fluorescent in situ hybridization and array-based comparative genomic hybridization. Am. J. Hum. Genet., 2005, 76, 877-882

[11] Skarsgard E.D., Harrison M.R., Congenital diaphragmatic hernia: the surgeon's perspective. Pediatr. Rev., 1999, 20, e71-78

[12] Bollmann R., Kalache K., Mau H., Chaoui R., Tennstedt C., Associated malformations and chromosomal defects in congenital diaphragmatic hernia. Fetal. Diagn. Ther., 1995, 10, 52-59

[13] Losty P.D., Vanamo K., Rintala R.J., Donahoe P.K., Schnitzer J.J., Lloyd D.A., Congenital diaphragmatic hernia--Does the side of the defect influence the incidence of associated malformations? J. Pediatr. Surg., 1998, 33, 507-510

[14] Campbell M.F., Congenital absence of one kidney: Unilateral renal agenesis. Ann. Surg., 1928, 88, 1039-1044

[15] Cascio S., Paran S., Puri P., Associated urological anomalies in children with unilateral renal agenesis. J. Urol., 1999, 162, 1081-1083

[16] Schreuder M.F., Unilateral anomalies of kidney development: why is left not right? Kidney Int., 2011, 80, 740-745

[17] Robson W., Leung A., Rogers R., Unilateral renal agenesis. Adv. Pediatr., 1995, 42, 575-592

[18] Antonius T., van Bon B., Eggink A., van der Burgt I., Noordam K., van Heijst A., Denys-Drash syndrome and congenital diaphragmatic hernia: another case with the 1097G > A(Arg366His) mutation. Am. J. Med. Genet. A., 2008, 146A, 496-499

[19] Scott D.A., Cooper M.L., Stankiewicz P., Patel A., Potocki L., Cheung S.W., Congenital diaphragmatic hernia in WAGR syndrome. Am. J. Med. Genet. A., 2005, 134, 430-433

[20] Slavotinek A.M., Single gene disorders associated with congenital diaphragmatic hernia. Am. J. Med. Genet. C. Semin. Med. Genet., 2007, 145C, 172-183

[21] Pritchard-Jones K., Fleming S., Davidson D., Bickmore W., Porteous D., Gosden C., et al., The candidate Wilms' tumour gene is involved in genitourinary development. Nature, 1990, 346, 194-197

[22] Nordenskjöld A., Tapper-Persson M., Anvret M., No evidence of WT1 gene mutations in children with congenital diaphragmatic hernia. J. Pediatr. Surg., 1996, 31, 925-927

[23] Itoh A., Miyabayashi T., Ohno M., Sakano S., Cloning and expressions of three mammalian homologues of Drosophila slit suggest possible roles for Slit in the formation and maintenance of the nervous system. Brain Res. Mol. Brain Res., 1998, 62, 175-186

[24] Piper M., Georgas K., Yamada T., Little M., Expression of the vertebrate Slit gene family and their putative receptors, the Robo genes, in the developing murine kidney. Mech. Dev., 2000, 94, 213-217

[25] Liu J., Zhang L., Wang D., Shen H., Jiang M., Mei P., et al., Congenital diaphragmatic hernia, kidney agenesis and cardiac defects associated with Slit3-deficiency in mice. Mech. Dev., 2003, 120, 1059-1070