

# Congenital Multicystic Renal Dysplasia as Part of Caudal Regression Syndrome: Complexities and Considerations

Sihem Darouich<sup>1,2\*</sup>, Nadia Boujelbene<sup>2,3</sup> and Aida Masmoudi<sup>2,4</sup>

<sup>1</sup>Fetopathology Unit, University Hospital Habib Bougatfa, Bizerte, Tunisia

<sup>2</sup>Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

<sup>3</sup>Department of Pathology, Salah Azaiez Institute, Tunis, Tunisia

<sup>4</sup>Department of Embryo-Fetopathology, Maternity and Neonatology Center, Tunis, Tunisia

Renal cystic diseases (RCD) are the most common congenital anomalies of the kidney and urinary tract which are almost always detected in the antenatal period [1,2]. They can be encountered both as isolated findings and as part of polymalformative syndromes. They may be inherited, acquired or of unknown etiology [1,3].

The classification of RCD based on the fetopathological findings and genetic studies allow opposing the ease of prenatal ultrasound diagnosis of RCD to its etiopathogenic complexity.

Detailed fetopathological study of RCD, performed on a series of 74 fetuses in the department of Embryo-Fetopathology of Tunis, over a period of 4 years, allowed to ascertain this paradox. In fact, the majority of cases were diagnosed in the second trimester of pregnancy (84%). The common prenatal sonographic features are hyperechogenic kidneys associated with oligohydramnios in the more severe forms. The medical gestation termination was practiced at average of 22-23 SA, with a sex ratio M/F of 1.26. Consanguinity was noted in one third of cases. The RCD was isolated (19%), associated with obstructive uropathy (12%) or polymalformative syndrome (69%). The syndromic forms mainly included renal ciliopathies (23/51), chromosomal aberration (7/51) and unclassified polymalformative syndromes of unknown etiology (18/51). Among the unclassified polymalformative syndromes, the renal dysplasia was as part of caudal regression syndrome (CRS) in 6/18 of fetuses born to non-diabetic mothers. It encompasses single umbilical artery, anal imperforation with frequently colovesical fistula and unilateral renal agenesis (Table 1).

CRS is a spectrum of congenital malformations, due to an embryonic defect in the formation of the caudal region from intermediate mesoderm during gastrulation. It encompasses a wide spectrum of anomalies with varied severity, affecting the anorectal system, urogenital system, lumbosacral spine and the lower limbs. The most severe end of the spectrum is the fusion of the lower limbs with major organ malformations, known as sirenomelia, while the mildest end is imperforate anus. It likely depends on both genetic and environmental factors. Maternal type 1 diabetes is a well-known risk factor for CRS. As I have special interest on renal dysplasia, I would like to invite the scientific communities to share their experiences and their research focused on multicystic renal dysplasia and especially on forms associated with the CRS. Although these conditions are frequently sporadic, it is imperative to be able to provide genetic counseling. Certainly, more work is needed to fully elucidate the underlying embryological and molecular mechanisms. The pilot study of Porsch et al. [4] have recently identified several candidate genes by whole exome sequencing and copy number variation analyses. Interestingly, this study identified 3 genes being known tumor suppressors, *PDZD2*, *GLTSCR2* and *PTEN*. The last have been previously identified in a patient affected with VACTERL association [5]. So, it would be interesting to screen these candidate genes in multicystic renal dysplasia associated with CRS.

In conclusion, the CRD is frequently part of a polymalformative syndrome. The complete fetopathological examination, karyotyping and chromosomal microarray analysis allow to classify some cases

Case	Sex	GA (WG)	Consanguinity/Recurrence	Fetopathological findings
1	M	18	-/-	Hydrops, cystic hygroma, imperforate anus, polysplenia, unilateral renal agenesis, multicystic dysplasia of the left kidney, colovesical fistula, single umbilical artery
2	M	24	-/-	Cranio-facial dysmorphism, camptodactyly, right transverse palmar crease, imperforate anus, horseshoe kidney with bilateral multicystic dysplasia, trilobate left lung, colovesical fistula, single umbilical artery, sacral vertebral anomalies
3	M	21	-/-	Potter's facies, mega-urethra, imperforate anus, rocker-bottom feet, genital hypoplasia, colovesical fistula, agenesis of the left kidney, multicystic dysplasia of the right kidney, single umbilical artery, hydrocephaly
4	F	24	-/-	Sirenomelia, ambiguous genitalia, imperforate anus, bilateral multicystic renal dysplasia, presence of ovaries with agenesis of the internal female genitalia
5	M	16	-/-	Omphalocele, mega-urethra, imperforate anus, blind-ending colon, agenesis of the left kidney, right pelvic multicystic kidney, single umbilical artery
6	M	25	-/-	Potter's facies, Choanal atresia, ambiguous genitalia, imperforate anus, pulmonary hypoplasia, agenesis of the left kidney, right pelvic multicystic kidney with ipsilateral ureteral duplication, colovesicouterine fistula

GA (WG): Gestational Age (Weeks of Gestation); F: Female; M: Male; -/-: Absent

**Table 1:** Congenital renal dysplasia associated with caudal regression syndrome.

according to the available etiopathogenic criteria. However, most cases remain unclassified (accounting for 43% of the cases in our series). Scientific advances in understanding the genetics of CRD involve the fetopathologist and the geneticist. The current use of whole exome sequencing will help to elucidate the underlying molecular mechanisms of CRD of unknown etiology, especially those associated with CRS.

## References

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**\*Corresponding author:** Sihem Darouich, University Hospital Habib Bougatfa, Bizerte, Tunisia, E-mail: [sihem.darouich@free.fr](mailto:sihem.darouich@free.fr)

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