Renal Tubular Dysgenesis

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Renal tubular dysgenesis is a severe kidney disorder characterized by abnormal development of the kidneys before birth.

genetic conditions

1. Introduction

In particular, kidney structures called proximal tubules are absent or underdeveloped. These structures help to reabsorb needed nutrients, water, and other materials into the blood and excrete everything else into the urine. Without functional proximal tubules, the kidneys cannot produce urine (a condition called anuria).

Fetal urine is the major component of the fluid that surrounds the fetus (amniotic fluid), and anuria leads to decreased amniotic fluid levels (oligohydramnios). Amniotic fluid helps cushion and protect the fetus and plays a role in the development of many organs, including the lungs. Oligohydramnios causes a set of abnormalities called the Potter sequence, which includes distinctive facial features such as a flattened nose and large, low-set ears; excess skin; inward- and upward-turning feet (clubfeet); and underdeveloped lungs.

Renal tubular dysgenesis also causes severe low blood pressure (hypotension). In addition, bone development in the skull is abnormal in some affected individuals, causing a large space between the bones of the skull (fontanelles).

As a result of the serious health problems caused by renal tubular dysgenesis, affected individuals usually die before birth, are stillborn, or die soon after birth from respiratory failure. Rarely, with treatment, affected individuals survive into childhood. Their blood pressure usually normalizes, but they quickly develop chronic kidney disease, which is characterized by reduced kidney function that worsens over time.

2. Frequency

Renal tubular dysgenesis is a rare disorder, but its prevalence is unknown.

3. Causes

Mutations in the *ACE*, *AGT*, *AGTR1*, or *REN* gene can cause renal tubular dysgenesis. These genes are involved in the renin-angiotensin system, which regulates blood pressure and the balance of fluids and salts in the body and plays a role in kidney development before birth.

The renin-angiotensin system consists of several proteins that are involved in a series of steps to produce a protein called angiotensin II. In the first step, the renin protein (produced from the *REN* gene) converts a protein called angiotensinogen (produced from the *AGT* gene) to angiotensin I. In the next step, angiotensin-converting enzyme (produced from the *ACE* gene) converts angiotensin I to angiotensin II. Angiotensin II attaches (binds) to the angiotensin II receptor type 1 (AT1 receptor; produced from the *AGTR1* gene), stimulating chemical signaling.

By binding to the AT1 receptor, angiotensin II causes blood vessels to narrow (constrict), which results in increased blood pressure. This protein also stimulates production of the hormone aldosterone, which triggers the absorption of salt and water by the kidneys. The increased amount of fluid in the body also increases blood pressure. Proper blood pressure, which delivers oxygen to the developing tissues during fetal growth, is required for normal development of the kidneys (particularly of the proximal tubules) and other tissues.

Mutations in the *ACE*, *AGT*, *AGTR1*, or *REN* gene impair the production or function of angiotensin II, leading to a nonfunctional renin-angiotensin system. Without this system, the kidneys cannot control blood pressure. Because of low blood pressure, the flow of blood is reduced (hypoperfusion), and the fetal tissues do not get enough oxygen during development. As a result, kidney development is impaired, leading to the features of renal tubular dysgenesis. Hypoperfusion also causes the skull abnormalities found in individuals with this condition.

Medications that block the activity of the angiotensin-converting enzyme or the AT1 receptor are used to treat high blood pressure. Because these drugs impair the renin-angiotensin system, they can cause an acquired (non-inherited) form of renal tubular dysgenesis in fetuses of pregnant women who take them. Acquired renal tubular dysgenesis can also result from other conditions that cause renal hypoperfusion during fetal development. These include heart problems, congenital hemochromatosis, and a complication that can occur in twin pregnancies called twin-to-twin transfusion syndrome.

3.1. The Genes Associated with Renal Tubular Dysgenesis

- ACE
- AGT
- AGTR1
- REN

4. Inheritance

Renal tubular dysgenesis is inherited in an autosomal recessive pattern, which means both copies of the affected gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- Allanson Pantzar McLeod syndrome
- primitive renal tubule syndrome

References

1. Gribouval O, Gonzales M, Neuhaus T, Aziza J, Bieth E, Laurent N, Bouton JM,Feuillet F, Makni S, Ben Amar H, Laube G, Delezoide AL, Bouvier R, Dijoud F,Ollagnon-Roman E, Roume J, Joubert M, Antignac C, Gubler MC. Mutations in genesin the renin-angiotensin system are associated with autosomal recessive renaltubular dysgenesis. Nat Genet. 2005 Sep;37(9):964-8.
2. Gribouval O, Morinière V, Pawtowski A, Arrondel C, Sallinen SL, Saloranta C,Clericuzio C, Viot G, Tantau J, Blesson S, Cloarec S, Machet MC, Chitayat D,Thauvin C, Laurent N, Sampson JR, Bernstein JA, Clemenson A, Prieur F, Daniel L, Levy-Mozziconacci A, Lachlan K, Alessandri JL, Cartault F, Rivière JP, Picard N, Baumann C, Delezoide AL, Belar Ortega M, Chassaing N, Labrune P, Yu S, Firth H,Wellesley D, Bitzan M, Alfares A, Braverman N, Krogh L, Tolmie J, Gaspar H, DorayB, Majore S, Bonneau D, Triau S, Loirat C, David A, Bartholdi D, Peleg A,Brackman D, Stone R, DeBerardinis R, Corvol P, Michaud A, Antignac C, Gubler MC. Spectrum of mutations in the renin-angiotensin system genes in autosomalrecessive renal tubular dysgenesis. Hum Mutat. 2012 Feb;33(2):316-26. doi:10.1002/humu.21661.
3. Gubler MC, Antignac C. Renin-angiotensin system in kidney development: renaltubular dysgenesis. Kidney Int. 2010 Mar;77(5):400-6. doi: 10.1038/ki.2009.423.
4. Moldavsky M. Renal tubular dysgenesis in Israel: pathologist's experience and literature review. Isr Med Assoc J. 2009 Jan;11(1):6-10. Review.
5. Schreiber R, Gubler MC, Gribouval O, Shalev H, Landau D. Inherited renaltubular dysgenesis may not be universally fatal. Pediatr Nephrol. 2010Dec;25(12):2531-4. doi: 10.1007/s00467-010-1584-0.

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