CAKUT

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Congenital anomalies of kidney and urinary tract (CAKUT) is a group of abnormalities affecting the kidneys or other structures of the urinary tract. The additional parts of the urinary tract that may be affected include the bladder, the tubes that carry urine from each kidney to the bladder (the ureters), and the tube that carries urine from the bladder out of the body (the urethra). CAKUT results from abnormal development of the urinary system and is present from birth (congenital), although the abnormality may not become apparent until later in life.

genetic conditions

1. Introduction

Individuals with CAKUT have one or more kidney or urinary tract abnormalities. For paired structures, like the kidneys and ureters, one or both may be affected. Many different developmental abnormalities are classified as CAKUT, including underdevelopment or absence of a kidney (renal hypodysplasia or agenesis), a kidney formed of fluid-filled sacs called cysts (multicystic dysplastic kidney), buildup of urine in the kidneys (hydronephrosis), an extra ureter leading to the kidney (duplex kidney or duplicated collecting system), a blockage in a ureter where it joins the kidney (ureteropelvic junction obstruction), an abnormally wide ureter (megaureter), backflow of urine from the bladder into the ureter (vesicoureteral reflux), and an abnormal membrane in the urethra that blocks the flow of urine out of the bladder (posterior urethral valve).

CAKUT varies in severity. The abnormalities can result in recurrent urinary tract infections or a buildup of urine in the urinary tract, which may damage the kidneys or other structures. Severe CAKUT can result in life-threatening kidney failure and end-stage renal disease.

CAKUT is often one of several features of a condition that affects multiple body systems (syndromic CAKUT). For example, renal coloboma syndrome, 17q12 deletion syndrome, renal cysts and diabetes (RCAD) syndrome, Fraser syndrome, Townes-Brocks syndrome, and branchio-oto-renal syndrome can cause kidney or urinary tract abnormalities in addition to other problems. However, urinary system abnormalities sometimes occur without other signs and symptoms, which is known as nonsyndromic or isolated CAKUT.

2. Frequency

CAKUT is estimated to occur in 1 in 100 to 500 newborns. These abnormalities are the most common cause of end-stage renal disease in children.

3. Causes

The causes of CAKUT are complex. It is likely that a combination of genetic and environmental factors contribute to the formation of kidney and urinary tract abnormalities.

The genetic factors involved in most cases of CAKUT are unknown. Syndromic CAKUT is caused by changes in the genes associated with the particular syndrome. Variations in these same genes can also underlie some cases of isolated CAKUT. The genes most commonly associated with isolated CAKUT are *PAX2*, which is also associated with renal coloboma syndrome, and *HNF1B*, which is involved in 17q12 deletion syndrome and RCAD syndrome. These two genes play critical roles in the formation of the kidneys, urinary tract, and other tissues and organs during embryonic development. Certain mutations in these genes are thought to disrupt development of the kidneys or other parts of the urinary tract before birth, leading to CAKUT. Mutations in many other genes involved in development of the urinary system have also been associated with isolated or syndromic CAKUT.

Research shows that the same genetic mutation can lead to different kidney or urinary tract abnormalities, even among members of the same family. It is likely that additional changes in other genes help determine how the condition develops and how severe it is. In addition, environmental factors may influence development of CAKUT. The risk of CAKUT is higher in babies whose mothers had diabetes; took certain medications that are harmful to the kidneys, such as some anti-seizure drugs; or lacked certain vitamins and minerals, such as folate and iron, during pregnancy.

3.1. The genes associated with Congenital anomalies of kidney and urinary tract

- EYA1
- FRAS1
- FREM1
- FREM2
- GRIP1
- HNF1B
- PAX2
- SALL1
- SIX1
- SIX5
- WNT4

4. Inheritance

Inheritance of CAKUT is complex and not completely understood. About 10 to 20 percent of cases are thought to occur in families. When inherited, CAKUT most commonly follows an autosomal dominant pattern, which means

one copy of the altered gene in each cell is sufficient to cause an abnormality. However, some people who have the altered gene never develop CAKUT, a situation known as reduced penetrance.

Less commonly, CAKUT follows an autosomal recessive pattern, which means both copies of the 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 have signs or symptoms of the condition.

In many cases, the inheritance pattern is unknown or the condition is not inherited. In some of these cases, a new (de novo) mutation in the gene that occurs during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development may underlie the urinary system abnormality. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- CAKUT

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