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"CONGENITAL ANOMALIES OF THE KIDNEY" EMBRYOLOGICAL BASIS AND ITS CLINICAL IMPORTANCE

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ABSTRACT

The development of the kidney begins on the 4th week with three slightly overlapping kidney systems during intrauterine life in humans. The series are pronephros, mesonephros, and metanephros. During day 22 of human gestation, there is the formation of pronephros in the cervical region of the embryo. The mesonephros is developed after the pronephros is developed. Mesonephric duct develops an out pouching, the ureteric bud near its attachment to the cloaca during the fifth week of gestation. Congenital anomalies may arise from the failure of the ureteric bud to develop or malrotation.

Introduction

The development of the kidney begins on the 4th week with three slightly overlapping kidney systems during intrauterine life in humans. The series are pronephros, mesonephros, and metanephros. During day 22 of human gestation, there is the formation of pronephros in the cervical region of the embryo. The mesonephros is developed after the pronephros is developed. Mesonephric duct develops an out pouching, the ureteric bud near its attachment to the cloaca during the fifth week of gestation. The metanephros arises caudal to the mesonephros at 5 weeks of development. It derives from mesoderm, the metanephrogenic blastema; lateral to the developing urogenital sinus and lateral to the mesonephric duct. Congenital anomalies of the kidney and urinary tract (CAKUT) account for more than 50% of cases of abdominal mass found in neonates and involve some 0.5% of all pregnancies (Scott et al. 1988). Despite recent advancements in prenatal diagnosis and early surgical intervention, these anomalies still remain the primary cause of kidney failure in infants. Notably, the therapeutic interventions that are available to adults and older children, such as kidney transplantation, are often not feasible in infants. This is the migration of nephric duct download and connects with the bladder to form the ureters. The ureters will carry urine from the kidneys to the bladder for excretion from the fetus to the amniotic sac. The torso elongates as the fetus develops and the kidneys rotate and migrate upwards within the abdomen which causes the length of ureters to increase.

Congenital abnormalities of the kidney can be grouped based on abnormalities during development, abnormalities in shape and position and abnormalities of the collecting systems. Most often, congenital anomalies of the kidney and urinary tract (CAKUT) are put together since the abnormalities of the kidney will eventually affect the urinary tract.

Incidence

Congenital anomalies of the kidney and urinary tract (CAKUT) represent 20% to 30% of all antenatally diagnosed fetal congenital anomalies in developed countries. [Queisser-Luft A et al. 1998]. The North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS)' report indicated that 30% to 50% of cases of end-stage renal disease are related to congenital anomalies of the kidney and the urinary tract; [Seikaly MG et al. 2003] therefore, it is crucial to have early diagnosis and management, whether medical or surgical, to minimize renal damage and to avoid or delay end-stage renal damage.

Ontogenesis of normal development of Kidney

The kidney systems are formed in a craniocaudal sequence in intrauterine life, there are three phases which slightly overlaps the formation of the kidney; these are pronephros, mesonephros, and metanephros. Pronephros starts development at the beginning of the fourth week and it is represented by 7 to 10 cell groups in the cervical region which form vestigial excretory units. By the end of the fourth week, the pronephric system disappears. Mesonephros and mesonephric ducts are derivatives of intermediate mesoderm. During regression of the pronephros in the fourth week, excretory tubules of the mesonephros emerge. These tubules lengthen and form an S-shaped loop and acquire a tuft of capillaries to form the glomerulus. The tubule forms the Bowman's capsule around the glomerulus. The mesonephros functions as the kidney for a short period during the fourth to eighth weeks of intrauterine life. Metanephros is the permanent kidney which develops in the fifth week. Its excretory unit is developed from metanephric mesoderm in the same way as the mesonephric system. The formation of duct system differs from that of other kidney systems. Ureteric bud an outgrowth of mesonephric duct close to the cloaca gives rise to the collecting ducts of the permanent kidney.

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The bud penetrates the metanephric tissue and subsequently dilating to form the primitive renal pelvis and split to form future major calyces. Each calyx forms two new buds while penetrating the metanephric tissue. The buds subdivide into 12 or more generations which form the minor calyces of the renal pelvis. Collecting tubules of the fifth successive generations elongates and converge on the minor, forming the renal pyramid. The ureteric bud gives rise to the ureter, renal pelvis, major and minor calyces and over 3million collecting tubules.Incidence

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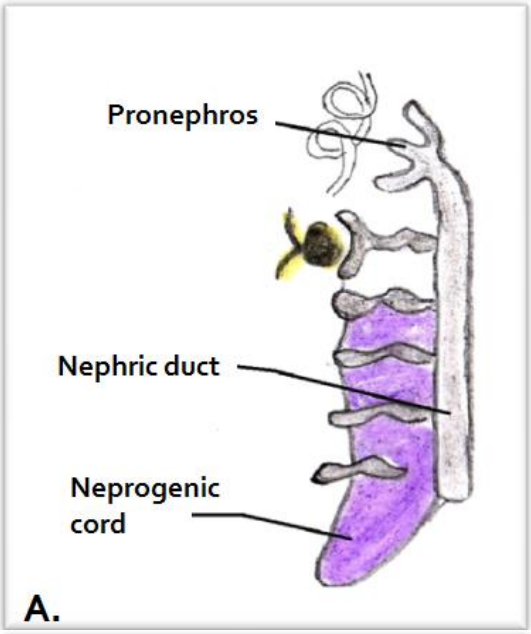

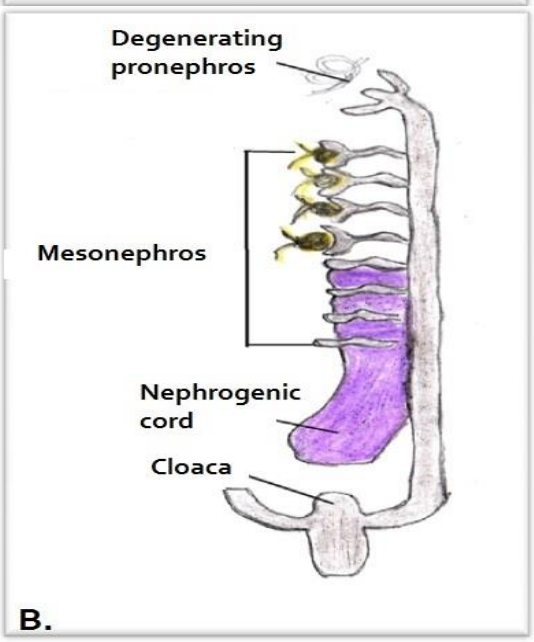

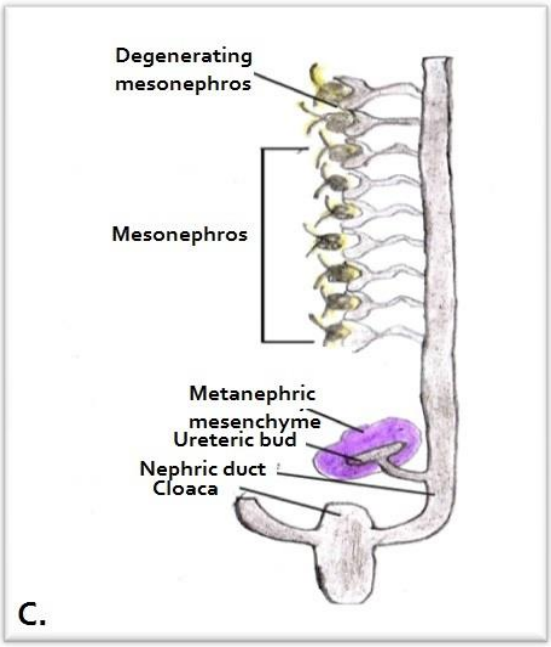

Fig 1. A. Diagram showing developmental stages of kidney with the onset of the pronephros. B. Degenerating pronephros and the formation of mesonephros. C. Outgrowth of ureteric bud and metanephric mesenchyme forming the metanephros which eventually becomes the permanent kidney.

Ontogenesis of abnormal development of kidney

The abnormal development of the kidney can be categorized into two stages;

A. Abnormalities during development: Dysgenesis of the kidney

a) Renal agenesis (absent kidney): This will arise if the ureteric bud fails to interact with the metanephric mesoderm. The Glial-derived neurotrophic factor (GDNF) produced by the metanephric mesoderm produces branching and growth of ureteric bud. Failure to produce GDNF may result in renal agenesis. This can be grouped into two;

Unilateral renal agenesis where there is the absent of one kidney and Bilateral renal agenesis which is the absent of both kidneys. Bilateral agenesis leads to Potter's syndrome.

B. Abnormalities in shape and position

a) Ectopic kidney or renal ectopia is defined as an atypically placed kidney due to faulty migration from the fetal pelvis during embryologic development (Meizner I, Yitzhak M, Levi A, et al. 1995). Ectopic kidney may be abdominal, lumbar or pelvic, based on its position in the retroperitoneum (Bauer SB. 1998). It can be placed either ipsilaterally or contralaterally, when it is called crossed renal ectopia.

The incidence of ectopic kidneys is 1:12,000 clinical and 1:900 post-mortem cases (Meizner I, Yitzhak M, Levi A, et al. 1995), indicating clinically benign significance of this usually asymptomatic aberration. A simple ectopic kidney is usually asymptomatic. However, if malrotated, there is a risk of calculus formation with consequent hydronephrosis which may present as colicky pain and hematuria

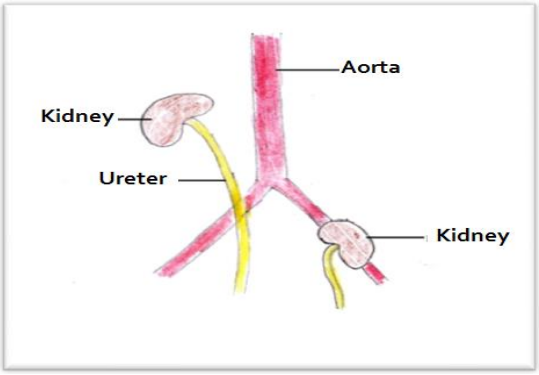

Fig 2. Diagram showing an ectopic kidney with one kidney in the pelvis which is abnormal position kidney.

b)Fusion Anomalies

i) *Horseshoe kidney:* is formed during organogenesis, when the inferior poles of the early kidneys touch, fusing in the lower midline or it can be as the result of a teratogenic event involving the abnormal migration of posterior nephrogenic cells, which then combine to form the isthmus. The fusing causes the kidney to take the shape of horseshoe or "U" (Bauer SB, et al. 1992).

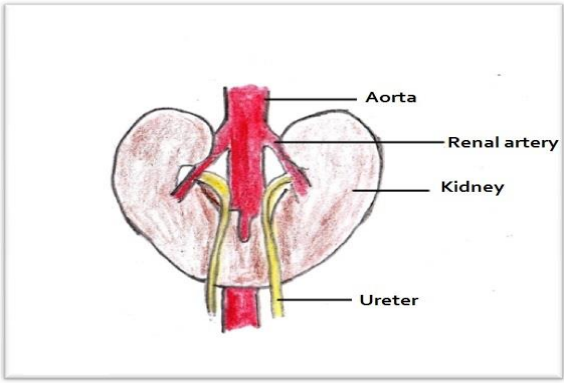

Fig 3.Diagram showing horseshoe kidney with the inferior poles touching and fusing together.

ii)Cross fused ectopia: is a markedly rare congenital malformation of the urinary system where one of the kidneys crosses the midline to become located on the opposite side of its ureter entrance to the bladder and the parenchyma of the two kidneys fuse. Cross fused ectopia has a reported autopsy incidence of around 1: 2000 and is the second most frequently observed fusion anomaly of the kidneys following the horseshoe kidney. Resulting from aberrant migration and crossing of the midline of the metanephric blastema and the ureteral bud, cross fused ectopia is thought to develop during the fourth to eight weeks of gestation.

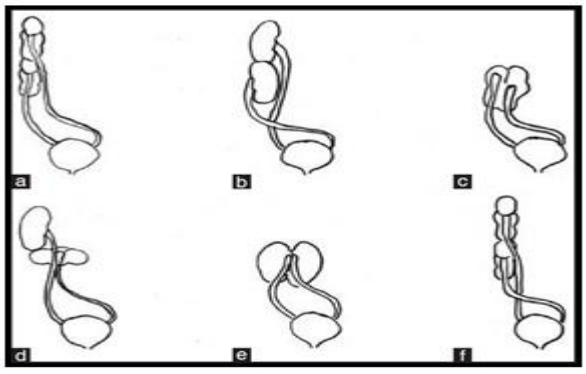

Fig 4.Diagram showing cross fused ectopia: (a) Inferior crossed fusion, (b) sigmoid kidney, (c) Lump kidney, (d) L-shaped kidney, (e) Disc kidney and, (f) Superiorly crossed fused.

Mostly remaining asymptomatic and detected as an incidental finding during imaging studies, six well-defined anatomical variations of CFRE have been reported (Bauer SB, et al. 2002, T. V. Patel and A. K. Singh, 2008).

Discussion

Congenital anomalies of the kidney constitute approximately 20 to 30 percent of all anomalies identified in the prenatal period.

The reported incidence of kidney anomalies in live and stillborn infants is 0.3 to 1.6 per 1000. Kidney anomalies are found in more than 200 described syndromes.

Kidney anomalies represent a broad range of disorders that result from abnormal embryogenic renal development due to renal parenchymal malformations, abnormalities in renal migration, or abnormalities in the developing collecting system (Sadler T. 2015).

Malformations of the renal parenchyma result in failure of normal nephron development as seen in renal dysplasia, renal agenesis, renal tubular dysgenesis, and polycystic renal diseases. The pathogenesis of renal parenchymal malformations is multifactorial involving genetic and environmental factors.

Disruption of the normal embryologic migration of the kidneys results in renal ectopia (eg, pelvic kidney) and fusion anomalies (eg, horseshoe kidney).Ultrasound examinations are often done as part of prenatal care. This is to examine the baby before birth. It can be detected if there is an abnormality and treatment determined if necessary. In many cases, these abnormalities do not havce major impact on the child's overall health (Sadler T. 2015).

The development of the kidney and ureters are essential in the formation of the urinary system. In all the anomalies of the kidney, patients may not show symptoms except for bilateral agenesis which the child will be born with the Potter syndrome as a result of renal failure. This is characterised by anuria, oligohydramnios (decreased volume of amniotic fluid) and hypoplastic lungs secondary to oligohydramnios. Kidney anomalies are linked with WT1, a transcription factor that initiates the induction of the ureteric bud. It also regulates the production of Glial-derived neurotrophic factor (GDNF) which stimulates the branching and growth of the ureteric bud (Sadler T. 2015).

Conclusion

The development of the mesonephros and mesonepheric duct is very important in the development of the kidney. It is when the mesonephric duct develops that there is an outgrowth of the ureteric bud.

Renal anomalies may be due to known causes like failure of Glial-derived neuronephric factor (GDNF) to be produced by metanephric mesoderm, faulty and abnormal migration of the kidneys to their normal position.By the end of the fifth week, a CT scan can show whether there is an abnormal development or not.

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