Review

Crossed Renal Ectopia. Embryological Basis of the Rare Entity.

Ashfaq ul Hassan , M. Saleem Wani ,Shomala Jan

Abstract:

The article describes a rare Congenital Anomaly of Kidney Crossed renal ectopia with emphasis on its embryological basis important to neonatologists, paediatric surgeons and paediatric urologists as well as General Surgeons. Abbertions in normal ascent, migration, rotation and vascularization lead to renal ectopia which may present as an isolated entity or as a combination defect with malformations of Renal tract.

Aim: The aim of the article is to provide all updated and renewed information about embryological basis of Crossed renal ectopia and the most possible associations it has been associated till date.

Method: Review of literature from all standard text, latest references from standard indexed journals taken to verify the associations.

Conclusion: The Renal ectopia as a rare entity is now recognized by Embryologists, Paediatricians, Neonatologists and Paediatric surgeons as a clinical entity of immense importance. Although most of the patients with crossed fused renal ectopia are usually asymptomatic, they do present with increased susceptibility to develop complications like urinary infections, urolithiasis, and abdominal mass. Recognition of Renal Ectopia is important.

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Introduction

Crossed fused renal ectopia is a rare congenital malformation, wherein both kidneys are present on one side only usually with the ureter of the crossed kidney opening into the bladder on the opposite side. It may remain silent and can be an incidental finding during a diagnostic work up. There may be varied presentations and the main cause is aberrant embryological development. Such abnormal development poses challenges in the medical as well surgical management. The crossed kidney is fused to the orthotopic kidney in more than 90% of the cases. Crossed renal ectopia is defined as a kidney that is located on the opposite side in relation to its embryologic position. Despite the ectopic renal position, the ureter of an ectopic kidney has normal insertion in the bladder on the normal site. Patients with renal ectopia are more prone to have left-to-right ectopia. It is a rare entity that is seen in almost 7.5 of 10 000 new-borns, with a male-to-female predominance of three to two [1, 2]. It is accompanied by abnormality in vasculature as well [3,4].

Wnt4 and Wnt9b are important in regulating inductive signals [5,6]. The Kidneys develop from mesoderm. The Kidneys develop in the pelvis and ascend upwards. There may be persistence of lower pole arteries in the pelvis initially [7.] This is associated with medial rotation as well. Both Ascent and medial rotation is programmed. During initial stages of embryogenesis in the week 6 to week 9, the metanephric kidneys move and further relocate themselves by following a path on both sides of the dorsal aorta. This relocation process comprises of the ascent, medial rotation, and revascularization. Rotation takes place before vascularization [8]. The kidneys in the early phases of development lie in the sacral region and later move upwards. First, the kidneys ascend from the sacral to the Lumbar region. Second, the hilum of each kidney initially facing ventrally rotates medially to face the

dorsal aorta. This medial rotation ensures the normal anatomical position of kidneys as seen in adults. There may be variants of malrotation but an ectopic kidney is usually malrotated [9,10]. Third, the ascending and medially rotating kidney is progressively vascularized by a series of arterial sprouts from the dorsal aorta. Malrotation can be reverse, excessive , incomplete or transverse [11]. New vessels take up the blood supply of kidneys with regression of the previous vasculature. A permanent renal artery is formed in the lumbar region for each kidney, whereas the original renal arteries in the sacral region and the subsequent ones degenerate. Any defect in thee three well organized process can lead to Ectopic kidney or renal ectopia. There can be arrest of kidney ascent causing kidneys to remain in pelvis or kidneys meeting on one side only followed by fusion.

The important step in normal development of kidney is fusion of the ureteric bud and metanephric blastema. Migration is an important step in nephrogenesis. Abnormal migration of the ureteric bud and metanephric blastema across the midline results in the kidney being located on the opposite side of its normal position. Renal nephrogenesis is a complicated process [12,13] . The role of position of Umblical artery in migration of kidneys has a fundamental role. It is believed that the abnormal position of the umbilical artery influencing the cephalic migration of the kidney, which follows the path of least resistance and, consequently, migrates to the contralateral side. The crossing of ureteric bud is also critical. It is believed that the ureteric bud crosses over because of over bending and rotation of the caudal end of the embryo, preventing the fusion of the ureteric bud with the metanephric blastema. There is a stimulation of the contralateral metanephric blastema while the ipsilateral Metanephros regresses. This can be due to faulty apoptosis. Rescue from apoptosis requires signalling by ureteric bud [14, 15.]The result is a fusion anomaly with ectopic location. From a molecular view point Integrins serve as adhesion receptors for proteins in the extracellular matrix and transduce biochemical signals into the cell. They regulate cell functions including migration, proliferation and apoptosis (programmed cell death). The ILK-PINCH-parvin protein complex (IPP) functions as an intracellular signaling platform for integrins and regulates integrin-mediated signaling pathways. Mutations disrupt the IPP complex to varying

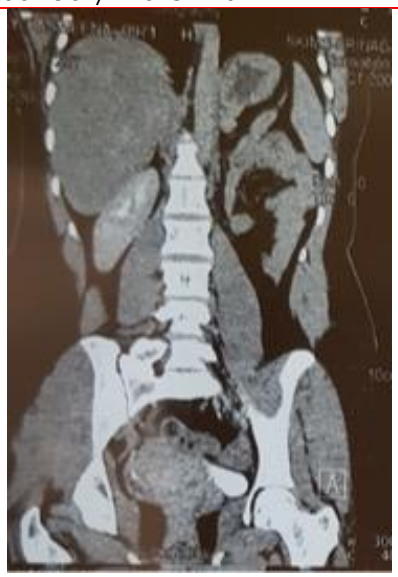

Fig 1: High Resolution image of Renal Ectopia

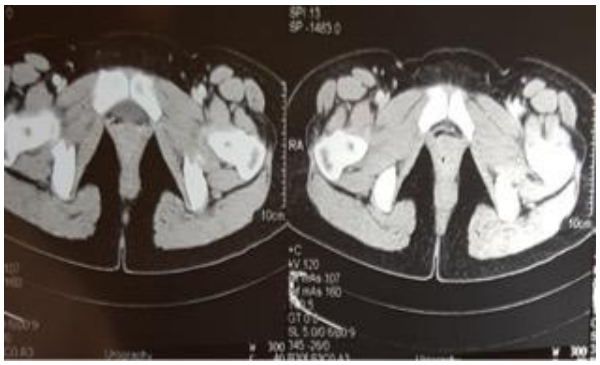

Fig 2: CT Scan image of Renal Ectopia

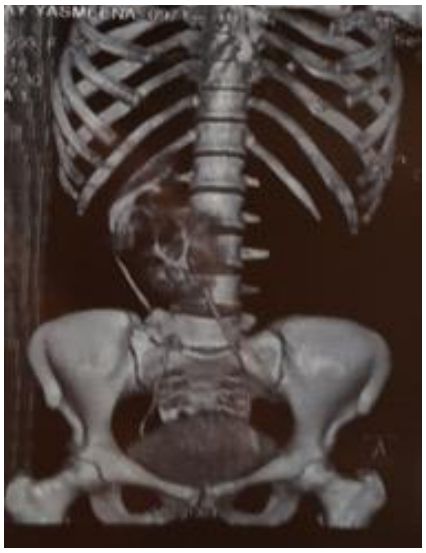

Fig 3: Vertical section showing Renal Ectopia

degrees and caused abnormalities in kidney development. The ILK and its binding partners are involved not only in cancer development but also other pathological processes and differentiation of different cell types [16,-18].

It may remain clinically silent. In symptomatic patients, it can be associated with a wide range of urological problems such as pelviureteric junction obstruction (PUJO), vesicoureteric reflux, ureteric strictures, and renal dysplasia. It is also known to be present along with other congenital malformations affecting the cardiovascular, skeletal, and gastrointestinal systems. Management consists of appropriate imaging and individualized treatment plans with focus on preserving renal function. Crossed Renal ectopia may be present in isolation and may be detected incidentally at autopsy, during surgery or during investigation. Without any association or it may be associated with other abnormalities involving Maldevelopment of the urinary tract such as association with ectopic kidney and consists of reflux, cystic dysplasia, ureteropelvic junction obstruction or carcinoma [19-22]. In all the types of fusion anomalies, the ureteral orifice associated with each kidney is usually orthotopic. Renal stones also accompany renal ectopia [23]. A high incidence of other urological abnormalities has been associated with renal ectopy. Vesicoureteral reflux (VUR) is the most common succeeded by other genitourinary tract aberrations such as undescended testis , hypospadias, multicystic renal dysplasia & hydronephrosis [24]. Most of the renal anomalies are incidental findings and the ectopic kidneys have a high incidence of other urological problems the most prominent being urolithiasis or stone formation. Although most of the patients with crossed fused renal ectopia are usually asymptomatic, they do present with increased susceptibility to develop complications like recurrent urinary infections, stones, and abdominal mass. There are reported cases of renal cell carcinoma and Wilm's tumor associated with crossed fused renal ectopia [25]. The transformation of ectopic renal tissue into malignant tissue warrants a further work up and follow up. There is a reported case of TAR syndrome with renal anomaly that developed Wilm's tumor. Finding of crossed fused renal ectopia warrants complete urologic investigation to rule out surgically correctable pathology in the urinary tract.

In females, agenesis of the uterus and vagina as seen in Mullerian agenesis and Mayer-Rokitansky-Küster-Hauser syndrome and unicornuate uterus have also been reported with cases of renal ectopia. Systemic anomalies include sacral agenesis, imperforate anus, and skeletal deformities like scoliosis, cardiovascular and gastrointestinal abnormalities. We encountered three patients with Pelviureteric junction obstruction, one of which had a crossing vessel across pelvi-ureteric junction.

The extra-urogenital anomaly included the presence of Meckels diverticulum and Hydrocephalous. None of these patients had genital or skeletal anomaly, which by far the most common non-urological anomaly associated with Renal ectopia.

Any diagnostic investigation as simple as plain radiograph can pick up renal ectopia. A clear and good Plain radiograph may show the ectopia by absence of normal kidney shadow and an abdominal mass alongside the normal kidney. The Ectopic mass may be irregular. CT is considered the gold standard in the diagnosis as it offers excellent visualization of the implantation of the ureters and the vascular supply and may differentiate between fused and nonfused variants. It may demonstrate finer details and associated anomalies. Ultrasound is usually helpful and may be the initial investigation done in most cases [26]. It is comparable to CT. MRI may be used in selected cases. Initial diagnosis by USG or later by CT scan or MRI may give additional information about presence of other developmental errors or associated urinary tract pathologies. However anatomic delineation of the CRE with fusion and the functional assessment is best assessed by Intravenous urogram. Additional assessment by nuclear imaging or retrograde pyelogram may be required for better delineation of the anomaly. Absence of kidney in its lumbar position on one side may be confirmatory. CT urography is also used for detecting ectopia [27].

It may be confused with conditions such as horseshoe kidney, transplanted kidney and acquired renal displacement due to hepatomegaly.

The Surgical implications are important because Crossed renal ectopia with fusion is associated with abnormal vascularity. During ascent renal arteries take up the responsibility of blood supply but in case of ectopia aberrant vessels or pelvic vessels may be a source of blood supply to the ectopic renal tissue. Abnormal vasculature predisposes to surgical errors and in case surgery is contemplated, contrast based CT is needed to characterize vascular anatomy, as the vascular supply can be anomalous to both the ectopic & non ectopic kidneys.

Conclusion:

Renal Ectopia is multifactorial and an embryologically significant entity relevant in Paediatric urology,

Embryology, Neonatology and Genetics. Newer facts about Renal Ectopia and associations and embryological and genetic basis of this entity are surfacing. Understanding the basic concept behind renal ectopia is important for Surgeons in view of the fact that it may be associated with other malformations particularly of urogenital system and aberrant vascularization posing serious surgical challenges.

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