

Case Study

FAMILIAL EXPRESSION OF DUPLEX KIDNEY AND BIFID URETERS: IMPLICATIONS IN PATIENT CARE

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ABSTRACT

Background: A duplex kidney or bifid ureteric collecting system is one of the common congenital urinary tract abnormalities but familial occurrence is much less frequent. While considered an anatomical variant, duplex-collecting systems may be complicated by vesicoureteric reflux, obstruction or ureterocoele. Furthermore, accessory renal arteries, while frequently encountered, might cause hydronephrosis.

Materials and Methods: We report here a case of 77- and 82-years male siblings who donated their body to a willed body program with unilateral double and bifid ureter and accessory renal arteries. The siblings died approximately 15 months apart; the 77-year old sibling (donor 1) was the first to die of lung cancer. The 82-year older sibling (donor 2) died later from a cerebrovascular incident.

Results and Observations: During dissection of the 77-year-old donor, (donor 1) we observed that the right kidney had two ureters, one emerging from the upper pole and the other from the lower pole. Probing the ureters revealed that the lower pole ureter entered the bladder via a superior orifice while the upper pole ureter opened into an inferior orifice. In the dissection of the 82-year older sibling (donor 2), we observed that the left kidney had two ureters emerging one each from the upper and lower poles. The two ureters on the left kidney fused caudally and opened into the bladder via a single orifice. Both donors had accessory renal arteries.

Conclusions: Familial nature of the variance in the renal system is uncommon and only a few reports have been described. In the absence of the medical history of the donors we are unable to comment on whether their conditions caused any kidney problems. Additionally, in the absence of family history we are unable to expand the study to include other members of the donor's family; however early recognition of this condition is vital in patient care.

KEY WORDS: Familial Double and Bifid Ureter, Congenital Anomaly, Accessory Renal Artery, Clinical Significance, Patient Care.

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BACKGROUND

A duplex kidney is a kidney with two-pyelocaliceal systems, that either have a single or bifid ureter (partial duplication) or a double ureter draining separately into the urinary bladder

(complete duplication), encapsulated in a common renal capsule that is drained by the two pyelocaliceal systems [1]. While this may be a common condition that remains asymptomatic, there is potential for complications such as

pelviureteric junction obstruction and vesico-ureteral reflux [2]. In the case of bifid ureter system the two-pyelocaliceal systems join at the pelviureteric junction or the two ureters (bifid ureters) join before entering the bladder.

Development of kidney and ureters: Metanephroi, or the primordia of the permanent kidneys, begins to develop in the fifth week and becomes functional approximately 4 weeks later. The ureteric bud (aka metanephric diverticulum) is an outgrowth from the mesonephric duct near its entrance into the cloaca. The metanephric blastema is derived from the caudal part of the nephrogenic cord. As the ureteric bud elongates, it penetrates the blastema, a mass of metanephric mesenchyme. The stalk of the ureteric bud becomes the ureter [3]. As with most organs, differentiation of the kidney involves epithelial mesenchymal interactions. That is epithelium of the ureteric bud, from the mesonephric duct, interacts with mesenchyme of the metanephric blastema. Development of the permanent kidney depends upon the branching of the ureteric bud and its reciprocal inductive interactions with the metanephric blastema. The cranial part of the ureteric bud, through a series of divisions gives rise to the collecting tubules, calyces, renal pelvis and ureter (collecting system) [4].

Duplication of collecting (ureter) system: Embryologically, double ureter occurs when two separate ureteric buds arise from a single mesonephric duct. Two ureteral buds result in two separate ureters and a duplex pyelocaliceal systems in a common renal capsule. Duplication of the ureter and the kidney itself can be variable [3]. Double ureter may be unilateral or bilateral and can be associated with a variety of other congenital abnormalities of the urinary tract [5]. Ureteral duplication is either partial in that the two ureters drain into the bladder through a single common ureter (bifid ureter) or complete in which the two ureters drain separately (double ureter) either into the bladder and or ectopically.

Ascension of kidney and formation of accessory renal arteries: Initially, the primordial permanent kidneys lie close to each other in the pelvis, ventral to the sacrum. As the abdomen

and pelvis grow, the kidneys gradually relocate to the abdomen and move farther apart. During the changes in the kidneys' positions, the kidneys receive their blood supply from vessels that are close to them. Initially, they receive blood supply from the renal arteries that are branches of the common iliac arteries. Later, the kidneys receive their blood supply from the distal end of the abdominal aorta and when the kidneys ascend to a higher level, they receive new arterial branches from the aorta. Normally, the caudal branches of the renal vessels undergo involution and disappear [3]. Accessory (supernumerary) renal arteries usually arise from the aorta superior or inferior to the main renal artery and follow them to the hilum of the kidney or may enter the kidneys directly, usually via the superior or inferior pole. Accessory renal arteries are the end arteries [3].

MATERIALS AND METHODS

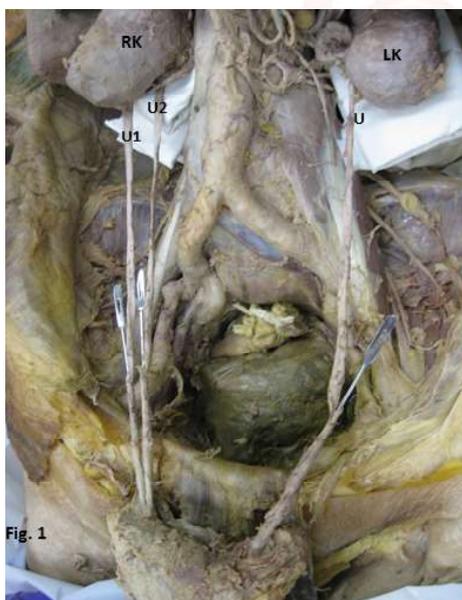
The following are the observations made during the dissection of male Caucasian sibling 77-years and 82-years of age who donated their body to a willed body program. The siblings died approximately 15 months apart; the 77-year-old younger sibling died first from lung cancer (donor 1). The 82-year older sibling died later from a cerebrovascular incident (donor 2).

During the dissection of donor 1, we observed that the right kidney had two ureters, one emerging from the upper pole and the other from the lower pole (figure 1). On the contra lateral side there was only a single ureter, which arose from the hilum and entered the bladder (Figure 1). Longitudinal section of the right kidney further showed that one ureter was connected to the upper pole and the second to the lower pole (Figure 2). Both ureters were the same size as the contralateral left side. Probing the ureters revealed that the lower pole ureter entered the bladder through a superior orifice while the upper pole ureter opened into an inferior orifice. The ureters descended vertically lying on the psoas muscle. Detailed dissection also demonstrated that on the right side the presence of an accessory renal artery, arising from the aorta inferior to the main renal artery, which entered the lower pole. Additionally, an accessory renal artery also arose from the main renal artery and

entered the lower pole. Both accessory renal arteries coursed anterior to both of the ureters. The vasculature supply of the left kidney was normal and left renal vein received the testicular vein (Figure 3).

During the dissection of donor 2, we observed that the left kidney had two ureters emerging from it, one from the upper pole and another from the lower pole (figure 4). On the contralateral side there was only one ureter arose from the hilum that entered the bladder (Figure 4). The ureters on the left kidney fused caudally and-

Fig. 1: Specimen showing double ureter on the right kidney of donor.



1. The ureter 1 (U1) leaving the lower pole and ureter 2 (U2) the hilum. The left side one ureter (U) leaving the hilum of the kidney. RK-Right kidney; LK-left kidney.

Fig. 2: Longitudinal section of the kidney showing that ureter 1 (U1) and ureter 2 (U2) arising from two different calyces.



Fig. 3. Shows the accessory renal artery (ARA) for the left kidney also arising from the abdominal aorta.



Fig. 4: Specimen showing double ureter on the left kidney of donor 2.



The ureter 1 (U1) leaving the lower pole and ureter 2 (U2) the hilum join together before entering the bladder. On the right side one ureter (U) leaving the hilum of the kidney. RK-Right kidney; LK-left kidney.

Fig. 5: A detailed view of the kidneys showing multiple renal arteries arising from the aorta supplying the kidneys. The accessory renal arteries arising from the abdominal aorta (AA) to each kidney supply the lower pole and courses anterior to the ureters. Renal vein is marked as RV draining into the inferior vena cava (IVC). The supra renal artery (SRA) branching off the aorta on the left side is also indicated.



opened into the bladder in one orifice (Figure 4). Further dissection also demonstrated that both the kidneys received multiple accessory renal arteries arising from the aorta entering the upper and lower poles independently. The accessory renal arteries coursed anterior to the ureters on both sides. (Figure 5).

RESULTS AND DISCUSSION

What induces the formation of the ureteric bud and stipulates its location along the mesonephric duct? The induction and location of the ureteric bud largely depends on the metanephric mesenchyme. Formation of the ureteric bud from the mesonephric duct is induced by signals coming from the metanephric mesenchyme and involves the Ret receptor expressed within the mesonephric duct, and the ligand, a Glial-derived neurotrophic factor (*Gdnf*) that is expressed within the metanephric mesenchyme. The *WT1*, expressed by the mesenchyme, enables the metanephric mesenchyme to respond to induction by the ureteric bud. The *Gdnf* and hepatocyte growth factor (HGF), also produced by the mesenchyme, interact through their receptors, RET and MET, respectively, in the ureteric bud epithelium, to stimulate growth of the bud and maintain the interactions. The growth factors, fibroblast growth factor 2 (FGF2) and bone morphogenetic protein 7 (*BMP7*), stimulate proliferation of the mesenchyme and maintain *WT1* expression [4,6].

The ureteric bud normally does not bifurcate until it enters the substance of the metanephric mesenchyme. However, it occasionally bifurcates prematurely, resulting in two ureteric buds forming two separate ureters and a duplex kidney (bifid pyelocaliceal systems) encapsulated in a common renal capsule [1] as observed in the dissection of donor 1 (Figures 1-3). At this stage we can only speculate that the mesonephric duct responded to misexpression of *Gdnf* elsewhere within the metanephric mesenchyme resulting in ectopic ureteric buds prior to entering the substance of the mesenchyme. Subsequent ureteric bud mesenchyme interactions resulted in the bifid pyelocaliceal systems.

In bifid ureter, two ureteric buds sprout from the mesonephric duct and the more cranial bud induces formation of the cranial pole of the kidney

and the caudal bud induces formation of the caudal pole. In this bifid ureter (arising from two separate ureteric buds) the two ureters from the renal pelvis join extravascular (Y-junction) to enter the bladder by a common ureter and ureteric orifice [7]. On a detailed dissection of donor 2, we observed a Y-shaped bifid ureter (Figure 4). Although the two branches of the Y arise from the same ureteric bud, the contractions of their muscular walls seem to be asynchronous. Therefore, urine may reflux from one branch into the other, resulting in stagnation of urine and predisposing the individual to infections of the ureter [6].

In the case of a double ureter, the ureters remain completely separate to the point where they enter the bladder. The upper pole ureter drains into the bladder infero-medial to the lower pole ureter thus maintaining the original embryological relationship (8). This relation is classically called 'Weigert-Meyer rule' [9,10]. In the detailed dissection of donor 1, we observed that the two renal pelvises, which are drained by two ureters and at the same time the upper pole ureter drains caudal to the lower pole ureter. This is also described in the literature as 'double' ureter or duplicated ureters in that the two ureters drain separately [11].

A duplex collecting system is one of the most common congenital urinary tract abnormalities. While considered an anatomical variant, duplex collecting systems may be complicated by vesicoureteric reflux, obstruction or ureterocolic. Duplex collecting systems are seen in 0.7% -1% of the healthy adult population and 2-4% of patients investigated for urinary tract symptoms [12]. Unilateral duplication is six times more frequent than bilateral. Right and left sides appear to be affected similarly with unilateral duplication [13]. A demographic study indicated that double kidney is more common in female and Caucasians [14]. Ureters can be duplicated completely or partially, and occasionally terminate ectopically affecting the urine flow and urine reflex due to lack of an adequate valve. Such an event will result in urine stagnation, infection, a distended ureter and eventually hydronephrosis [8]. The lower renal moiety has orthotopic insertion laterally and superior to the ureter draining the upper pole and reflux

typically occurs. Kidneys drained by double ureters, the lower pole system is dominant in majority of the individuals; and hence the lower moiety is more frequently affected in pelvic-ureteric junction obstruction as compared to the upper moiety [15].

The familial nature of the duplex kidney and bifid ureter raises the likelihood of inheritance of this condition. Since our findings were seen in anonymously donated body we have no family history to further explore. The possibilities of a familial nature were suggested in earlier reports [2,16]. Atwell et al [16] in their study of 101 relatives, found that 21 relatives had bifid pyelocaliceal and 11 had double and/or bifid ureters. Some families had more than one affected relative. The authors thus suggested an autosomal dominant type of inheritance and that the inheritance is by a dominant gene, which fails to manifest in some patients, i.e. is of low penetrance [17]. In trisomy 18 there is a high incidence of renal malformation [18], and ureteric bud anomalies also occur in association with Fanconi's anemia a condition inherited by an autosomal recessive gene [19]. In Nailpatella syndrome (NPS), a rare genetic disorder [20-22] and hereditary osteo-onychodysplasia [23] patients exhibited congenital renal disease. However, given the normal physical stature of the donors NPS can be ruled out.

The common variations, in the blood supply to the kidneys reflect the manner in which the blood supply continually changes during embryonic and early fetal life. Approximately 25% of adult kidneys have 2 to 4 renal arteries. Accessory (supernumerary) renal arteries usually arise from the aorta, superior or inferior to the main renal artery. Accessory renal arteries are end arteries; consequently, if an accessory artery is damaged or ligated, the part of the kidney supplied by it will become ischemic [3].

In the cases presented here, we observed accessory renal arteries. In donor 1, on the left side, the accessory renal artery arose directly from the aorta and coursed anterior to both ureters to reach the inferior pole of the kidney. Additionally, the main renal artery also provided a branch to the lower pole (Figure 3). However, the arterial pattern on the contralateral side was normal. Interestingly, in dissection of donor 2,

we observed on both sides that multiple arteries arose directly from the aorta and coursed anterior to the ureter. There was no one large single renal artery but multiple same size small arteries (Figure 4,5). An accessory artery to the inferior pole (polar renal artery) may cross anterior to the ureter and obstruct it urine out flow, causing hydronephrosis.

Clinically, knowledge of renal artery variation is important for radiologists and surgeons. It is important to be aware that accessory renal arteries are end arteries and ligation or damage will result in ischemia to the part of the kidney supplied by it. The harvesting of kidneys with multiple renal arteries from living donors has been discouraged, because of increased risk to the donor while obtaining the specimen, technical difficulty of completing multiple arterial anastomosis resulting prolonged ischemia time. A longer ischemia time increases the incidence of acute tubular necrosis rejection episodes, and decreased graft function [24].

CONCLUSION

The familial nature of variance in the renal system is uncommon and only a few reports have been described in the literature. In the absence of medical history of the donors, we are unable to comment on whether their variations caused any kidney problem. In addition, in the absence of family medical history we are unable to expand the study to include other members of the donor's family.

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Conflicts of Interests: None

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