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Multiple arterial, venous and ureteric manifestations in horseshoe kidney: Developmental analysis and significance

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Abstract. Horseshoe kidney (HSK), the most common type of congenital renal fusion anomaly, is characterized by ectopia, malrotation, and altered vascular changes. Horseshoe kidney in this case is atypical because of multiple ureters, arteries, and veins, as well as how they originated and formed. During the routine dissection of 83-year-old male donor who died of respiratory failure, we observed the presence of horseshoe kidney in which the lower lobes of the left and right kidneys were connected by an isthmus below the level of inferior mesenteric artery (IMA). Furthermore, the presence of arterial, venous, and ureteric anomalies was also observed; these were sequentially dissected and are described here.

Key words: horseshoe kidney, developmental analysis, multiple vasculatures, multiple ureters, isthmus artery.

INTRODUCTION

Horseshoe kidney (HSK), the most common type of congenital renal fusion anomaly, is characterized by ectopia, malrotation, and altered vascular changes. It consists of two normally functioning kidneys connected at the lower poles by an isthmus of functioning renal parenchyma or fibrous tissue that crosses the midline of the body (Natsis et al., 2014). In 80% of the cases, the isthmus contains renal parenchyma with 20% fibrous tissues (Taghavi et al., 2016). HSKs are found in approximately 1 in 400-600 adults and are more frequently encountered in males (M:F 2:1) (Yoshinaga et al., 2002; O'Brien et al., 2008). HSKs in children are diagnosed as part of a combination of malformations or other urological problems (e.g., in Fanconi anemia in males or in diagnosis of delayed menarche seen in Turner syndrome) (Tischkowitz and Hodgson, 2003; Glodny et al., 2009). Adults are

usually asymptomatic and diagnosis is made incidentally during intravenous pyelography, standard ultrasound, or computed tomography (CT) scan performed for other reasons (Boatman et al., 1971). Anatomically, HSK involves three main anomalies: changes in vascular supply, rotation of the fetal kidneys, and abnormal position (Yoshinaga et al., 2002). The ureteropelvic junction has been reported to be higher in HSK patients and their ureters also enter at a higher level into the renal pelvis, which may result in increased incidence of urinary tract complications (Natsis et al., 2014; Yoshinaga et al., 2002; Tischkowitz and Hodgson 2003; Frego et al., 2007; Ramkumar et al., 2009). We observed other abnormalities in this study, including multiple arteries, ureters, and venous structures.

Embryologically, developing kidneys lie close to each other in the pelvis; they attain their mature position in the lumbar region during the fetal period. This “ascent” results from the growth of the embryo’s body caudal to the kidneys. In the beginning, the hilum of each kidney faces ventrally; however, as the kidneys reposition, the hilum rotates to face medially. As the kidneys migrate, they are sustained sequentially by branches from the common iliac and abdominal aorta. This migration or ascent occasionally causes the kidneys to develop incorrectly. Ectopic kidney occurs when both kidneys fuse and are located in the pelvis (pancake or discoid); kidneys connect on each side at the lower poles (horseshoe kidney); kidneys remain in the pelvis (pelvic kidney); or both kidneys migrate to the same side (crossed renal ectopia) (Moore et al., 2020).

MATERIALS AND METHODS

Case report

For the present study, we utilized a donated cadaver that had been dissected and studied by the medical students at Cooper Medical School of Rowan University. During the dissection of an 83-year-old Caucasian male who died of respiratory distress, we observed the presence of horseshoe kidney; the lower lobes of the left and right kidneys were connected by an isthmus below the level of inferior mesenteric artery (IMA). The right and left renal mass extended approximately between L1 and L3 and the isthmus was at L4 level. The presence of arterial, venous, and ureteric anomalies was also observed; these were sequentially dissected and described.

The authors state that every effort was made to follow all local and international ethical guidelines and laws that pertain to the use of human cadaveric donors in anatomical research.

RESULTS AND OBSERVATIONS

We measured the length of the isthmus, keeping the crossing of ureters anteriorly as a point of reference. The distance between the two ureters was 6.2 cm. The width varied between 2.9 cm and 4.2 cm (in the middle), depending upon where it was measured. The height of the kidneys was measured superiorly from where the suprarenal gland rested on the kidneys and the beginning of the isthmus where the ureter crossed the renal moiety. The right and left kidneys were 11.1 cm and 12.2 cm long respectively. The kidney lobes were difficult to accurately discern. Due to number of vasculatures and ureters entering and leaving the renal moiety, the hilum was inadequately defined. The ill-defined hilum of the kidneys turned anteriorly and a number of arteries branched from the subdiaphragmatic abdominal aorta. To study ureters and vasculatures in detail, some of the renal medullary tissues were removed to expose and define these structures. After careful dissection of the renal tissues, we were able to discern the pattern of veins, arteries and ureters, as described below.

Renal Veins

On the left renal moiety, a major left renal vein [a] from the upper lobe is drained into the inferior vena cava (IVC). Other smaller veins [a1-a3] from the middle and inferior lobes, as well as the isthmus, directly reached the IVC, going posterior to the aorta. Both a well-defined left testicular vein [b] and the left suprarenal vein [c] drained into the left renal vein. The right renal vein from the upper [1] and middle lobe (not labeled) of the kidney and the right suprarenal gland [2] drained directly into the IVC. A noticeably large right renal vein [3] received venous blood from the testicular vein [4] and a large venous return from the lower lobe and isthmus [5] drained into the right renal vein [See Figure 1]. Glodny reported that the incidence of renal vein anomalies in horseshoe kidneys is high (23%) (Glodny et al., 2009). In the present case, the venous system of the HSK showed multiple variations, compared to what has been previously described (Nikumbh et al., 2014).

Renal Arteries

Both the left and right renal moieties, as well as the isthmus, were dissected to demonstrate several renal arteries that were clearly identified; they are listed below and appear in Figure 2. Additionally, the suprarenal artery from the right and left renal artery was dissected

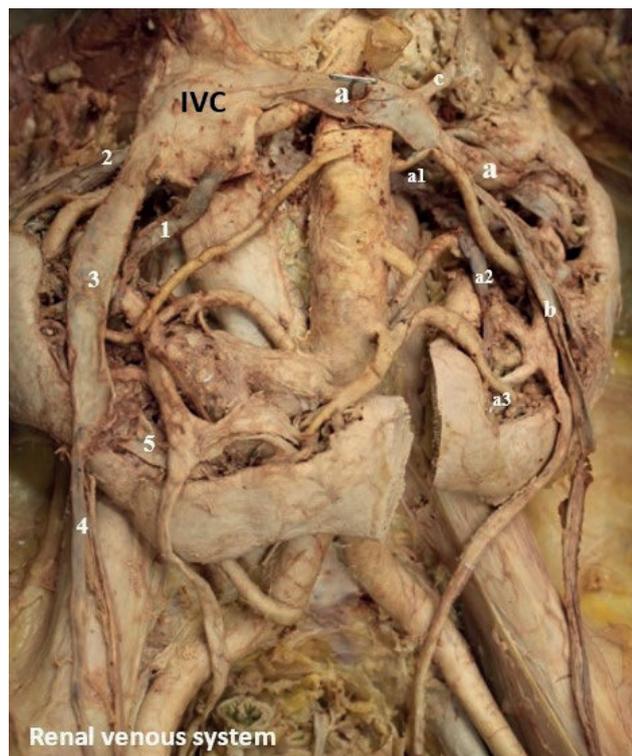


Figure 1. Photograph of a detailed dissection of the venous system of horseshoe kidney studied and presented. IVC. Inferior Vena Cava. The left renal moiety displayed several large and small veins (a, a1-3, b and c) draining into the main left renal vein. The right renal moiety exhibited many large and small veins numbered 1-5.

to show their distributions to the right and left adrenal glands. Unfortunately, the other arteries for the adrenal gland could not be clearly dissected and documented.

Right Renal Arteries

The large right renal artery [1] branched from the lateral aspect of the aorta below the superior mesenteric artery [SMA] and supplied the upper and middle lobe of the right renal moiety. Additionally, a branch from right renal artery also supplied the adrenal gland through a well-defined right suprarenal artery [1a]. The branch [2] that arose from the anterior aspect of the aorta supplied the middle lobe and, through a small branch, the inferior lobe, as well. An arterial branch arose from the lateral aspect of lower part of aorta [3]; it supplied the middle and inferior lobe of the right kidney. A branch [4] arose from the anterior aspect of the lower part of aorta to supply the inferior lobe and isthmus. The branch [5] that originated from the right common iliac [RCI] artery bifurcated behind the isthmus to supply the inferior lobe

and, through an isthmus artery, the isthmus, as well (Killen et al., 1968; Wilder et al., 1963; Cohn et al., 1969) [See Figure 2 - RK].

Left Renal Arteries

A large left renal artery [a] that originated from the lateral aspect of the abdominal aorta below the superior mesenteric artery immediately bifurcated in to a superior and inferior branch. The superior branch supplied primarily the upper lobe and the inferior branch supplied the upper lobe and through a small branch to the middle lobe. Arising from the lateral aspect of the aorta the [b] primarily supplied the middle lobe and through a small branch to the lower lobe. A branch [c] that originated from the aorta inferior to the IMA provided blood supply to the middle lobe and through a small branch the inferior lobe. The large branch [d] began from the anterolateral aspects of the aorta branched to supply the lower lobe and through a well-defined isthmus artery [d1] the isthmus [See Figure 2 - LK].

Ureters

Due to the lack of well-defined hilum, dissection was carried out by removing much of the renal medullary tissues to study the ureters in detail. This exposed the major calyceal system from different lobes of the renal mass which entered the hilum independently and contributed to formation of units of a ureter. Extrarenal calyces, wherein the calyces and renal pelvis lie outside the renal parenchyma, is one of the rare anomalies of the collecting system (Raghunath et al., 2012). There is considerable variation in the number of renal calyces and the shape of the renal pelvis, but there is also a marked variation in the position of the renal pelvis. Thus, a pelvis may lie almost entirely within the sinus (an intrarenal pelvis) or its main portion may be a dilated sac and lie outside the kidney proper (an extrarenal pelvis) (Raghunath et al., 2012). Variations in the major calyces and pelvis are more striking. The major calyces may pass downward for some distance beyond the hilum and end by joining to form the ureter without undergoing any obvious expansion. In such cases, the pelvis is absent; if the calyces dilate, one or two pelvises may be present (Rao et al., 2012) [See Figure 3].

Right Kidney

From the right kidney, the superior lobe calyx formed a large ureter [1] that joined a small ureter [2]

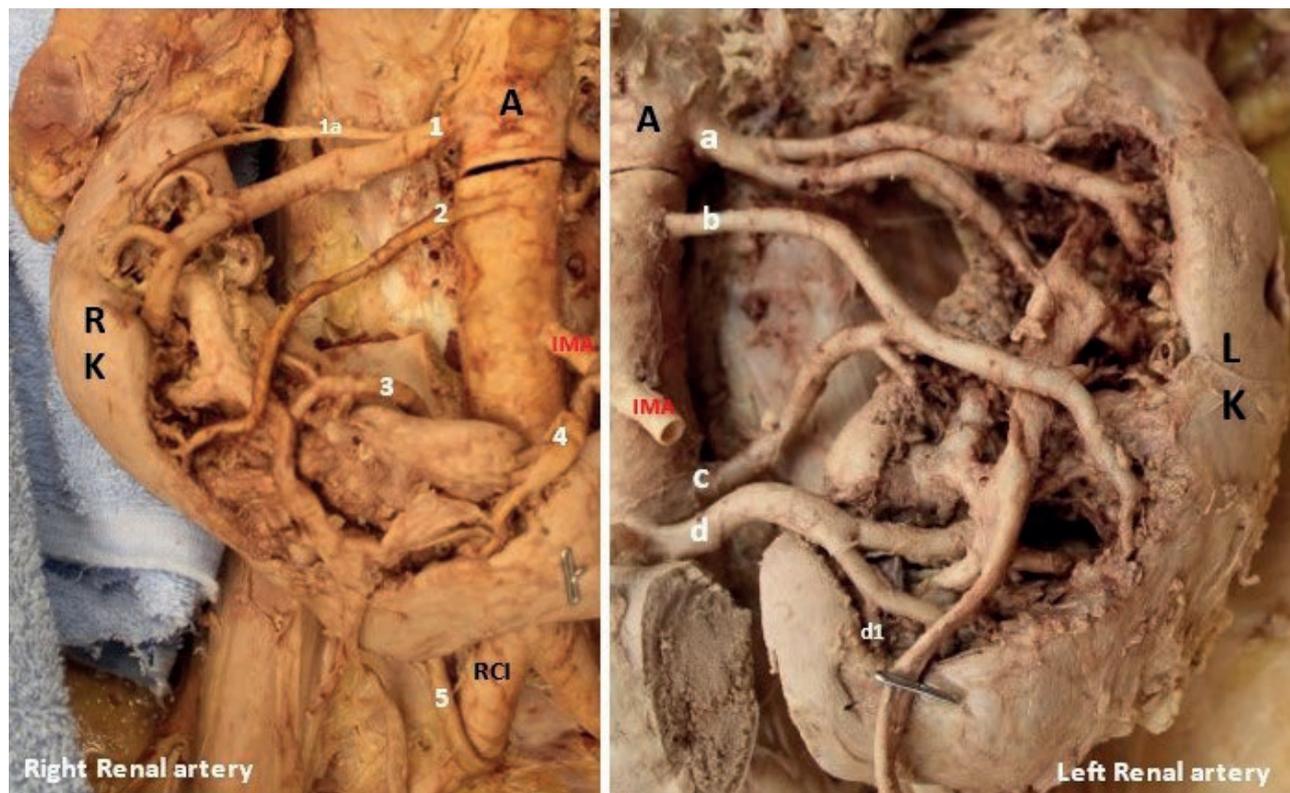


Figure 2. Photograph of a detailed dissection of the horseshoe kidney displaying the heterogeneity of the arterial system of right and left renal moiety and the isthmus studied. RK-Right Kidney, LK-Left Kidney, A-Aorta, IMA- Inferior mesenteric artery, RCI- Right Common Iliac artery. The right renal moiety (RK) is supplied by several large and small arteries labeled [1-4] branching from the aorta, a supra renal artery [1a] branching from artery 1 and a branch 5 from the right common iliac artery [1]. We observed that the isthmus was also supplied by a branch from artery 5 (not displayed in the photograph). The left renal moiety (LK) is also supplied by several arterial branches from the aorta [a-d] and a small ‘isthmus artery’ [d1] branching from d.

from the middle lobe calyx. A small ureter from the calyx of the lower lobe [3] and a large ureter [4] from the isthmus joined the longitudinal ureter. In a real sense, 1 through 4 are tributaries that united to distally form the ureter [Ur] proper. Unlike in a normal kidney, both the ureters in the HSK reported here did not lie on the ventral surface of the psoas muscle, but crossed the common iliac artery distally and entered the urinary bladder posterolaterally [See Figure 3 – RKur].

Left Kidney

From the left kidney, the superior lobe calyx formed a medium sized ureter [a] that joined by a medium sized ureter [b] from the middle lobe calyx. A medium sized ureter from the calyx of the lower lobe [c] and a large sized ureter [d] from the isthmus joined the longitudinal ureter. In a real sense, a through d, are tributaries that united to distally form the ureter [Ur] proper [See Figure 3 – LKur].

DISCUSSION

The development of the kidney begins in the fourth week of gestation by inductive interaction between the ureteric bud and the metanephric blastema. The ureteric bud arising from the mesonephric duct gives rise to the collecting tubules and the pelvicalyceal system; the metanephros develop into an excretory part formed by nephrons. During the sixth to ninth weeks of gestation, the developing kidney ascends due to differential growth of dorsal and caudal regions to reach its mature position in the posterior lumbar region. During ascent, the kidneys sequentially receive arterial supply from iliac arteries and the abdominal aorta. During the ascent, the kidney also undergoes axial rotation, resulting in the hilum which is initially placed anteriorly, but becomes medial. Congenital renal anomalies can occur due to abnormalities of development, migration, and rotation (Moore et al., 2020).

HSK is one of the most common renal anomalies; it occurs approximately 1 in 400-600 individuals and

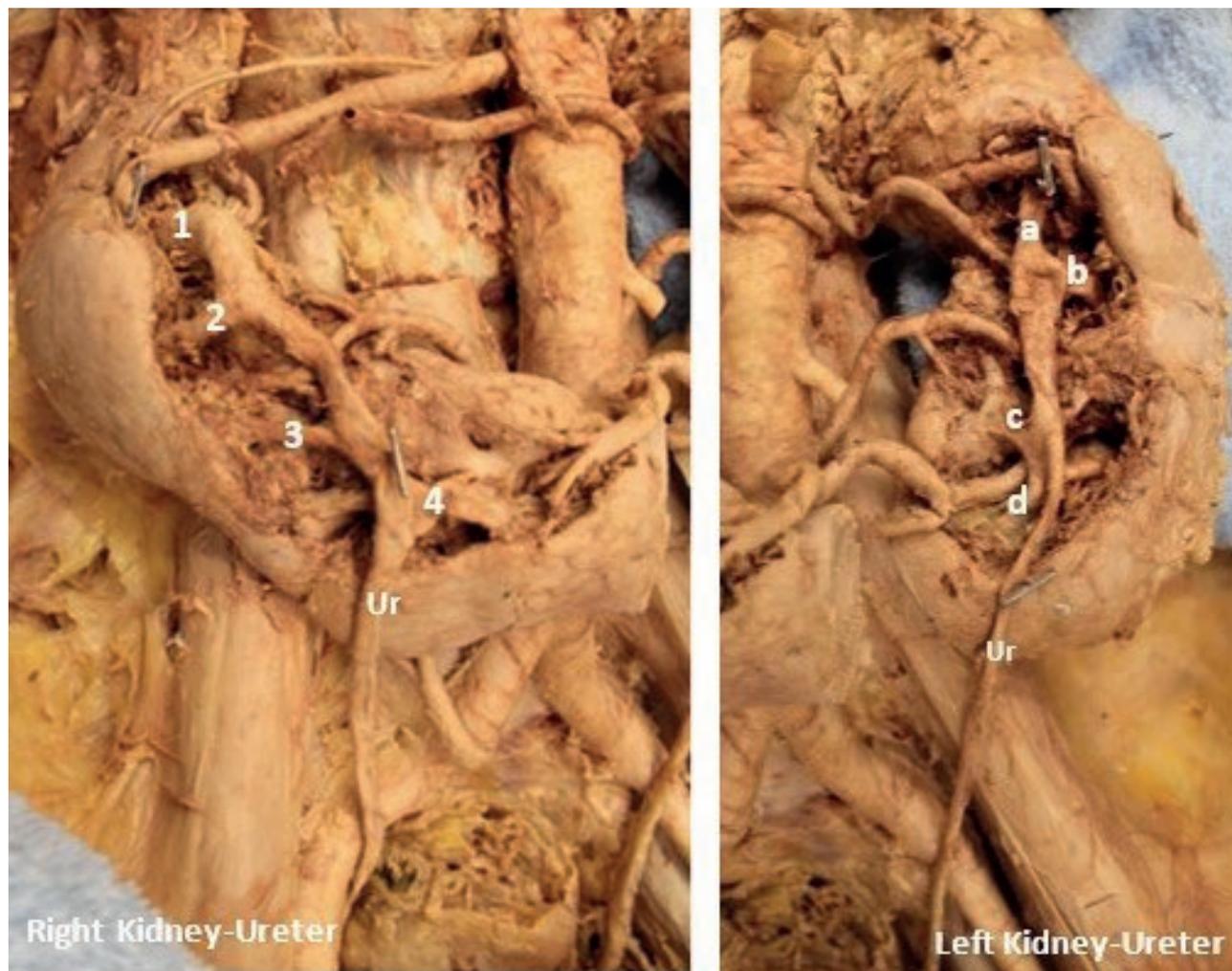


Figure 3. Photograph of a detailed dissection of the horseshoe kidney displaying the heterogeneity of the ureteric system of right and left renal moiety and the isthmus studied. Please note that the position of the kidney facing anteromedially medially with a poorly defined hilum. The right renal moiety [RK] displayed three ureteric components [1-3] and a large ureteric part from the isthmus [4], all joining to form the ureter [Ur]. From the left renal moiety [LK], there are four ureteric structure [a-d] joined to form the ureter [Ur].

is more frequent in men than women (2:1 ratio) (Yoshinaga et al., 2002). No genetic or ethnic association has been linked with HSK, although siblings within the same family have been reported (Yoshinaga et al., 2002). HSK in adults is usually asymptomatic and discovered during routine imaging studies conducted for other reasons. During the early 1900s, embryologists posited a number of theories to explain HSK. Domenech-Mateu and Gonzalez-Compta examined human embryos (crown-rump lengths of 3-19 mm) from the Ballaterra Collection (Domenech-Mateu and Gonzalez-Compta, 1988). They showed that there are two kinds of horseshoe kidneys: one wherein the isthmus is made up of material derived from mesenchyme and the other wherein the isthmus is composed of renal parenchyma. Additionally, they arranged

the HSK malformations into three groups: 1) early fusion due to a converging course taken by the ureteric buds, which may force the metanephric blastemas to become closer and eventually merge (Arey, 1974); 2) as a consequence of the relation between the metanephroi and the umbilical arteries during development (Lewis and Papez (1915); and 3) related to the association of several factors.

MECHANISM OF FUSION ANOMALIES

The exact mechanism of the development of renal fusion anomalies is not completely understood and many theories have been advanced to explain this abnormality (Babu et al., 2015).

1. Mechanical Theory proposes that, during cranial migration, the kidneys pass through the fork between the two umbilical arteries and any positional change in these arteries wedge the kidneys close together, resulting in their fusion and in HSK. Fusion of both nephrogenic blastemas with early arrested migration results in a completely fused pelvic kidney. Abnormal position of an umbilical artery can result in abnormal migration of a renal unit to the contralateral side, following the path of least resistance (crossed renal ectopia).

2. Theory of Abnormal Caudal Rotation suggests that fusion occurs due to lateral flexion and rotation of the caudal end of the embryo, disturbing the relative position of the nephrogenic blastema and ureteric bud (Cook and Stephens, 1977). The distal curled end of the vertebral column permits one ureter to cross the midline and enter the opposite nephrogenic blastema or transplant the kidney and ureter to the opposite side during ascent. Association of scoliosis with crossed renal ectopia supports this theory.

3. Ureteral Theory states that crossover is strictly a ureteral phenomenon with the developing ureteral bud wandering to the opposite side and inducing the differentiation of the contralateral metanephric blastema; it is assumed that the metanephric tissue that does not receive a ureteric bud regresses.

4. Teratogenic Theory posits that HSK results from abnormal migration of posterior nephrogenic cells due to teratogenic insult, forming a parenchymal isthmus (Doménech-Mateu and Gonzalez-Compta 1988; Tijerina de la Garza et al., 2009). The increased incidence of malignancies and other organ system anomalies associated with HSK possibly supports this theory (Nastis et al., 2014).

5. Genetic Theory suggests that genetic influence may play a role because some renal fusion anomalies have been reported to occur in identical twins and siblings within the same family. It is suggested that the sonic hedgehog gene signal is critical for kidney positioning along the mediolateral axis and its disruption will result in renal fusion (Shapiro et al., 2012). McPherson suggested that HSK may occur as a previously undescribed autosomal dominant condition (McPherson, 2007). Analysis of patients with Turner syndrome revealed that 33% of patients studied had some renal malformations, with HSK occurring in 7% of these, rendering support to the genetic theory (Lippe et al., 1988).

The following is intended to highlight the uniqueness of the HSK studied and presented here. These include the veins, arteries, and ureters with what was observed and how they compared and differed from the reports available from other studies.

Veins

In an earlier study, Nikumbh et al. reported that two tributary veins, superior and inferior, that originated from the right hilum and formed the right renal vein drained into the IVC (Nikumbh et al., 2014). The right suprarenal vein directly drained into IVC, but the right gonadal vein drained into right renal vein. The left kidney was drained by the left renal vein, which had four tributaries outside the hilum. Normally, the left suprarenal and gonadal veins drain into the left renal vein. Interestingly, we also observed the presence of an “isthmus” vein that drained into IVC [See Figure 1]. However, Nikumbh et al. and Natsis et al. did not observe an isthmus vein (Nikumbh et al., 2014; Natsis et al., 2014). In the present study, we observed multiple variations of veins, including an isthmus vein, and their drainage pattern [See Figure 1].

Arteries

Because of its anomalous embryologic origin, HSK have multiple renal arteries (Boatman et al., 1971). A systematic study by Graves described six basic patterns of arteries in HSK and, more importantly, that each artery supplies its own area, with no collateral circulation between segments (Graves 1969). In our study, an accurate demonstration and description of the arteries was challenging, due to the lack of a well-defined hilum and the way multiple arteries arose not only from the aorta, but also from the common iliac artery to enter the renal moieties [See Figure 2]. Furthermore, each artery also supplied more than one lobe. While much of the arterial distribution in our case followed Graves's six patterns of arteries, it also differed to some extent in how the arteries branched and distributed (Graves 1969).

Clinical significance

HSK has been reported to have a close relationship with vascular, calyceal, and ureteral abnormalities (Nastis et al., 2014). Upper urinary tracts of HSKs are characterized by the great variation in their number and origin. Typically, calyces are located in the upper two-thirds of each kidney, but an external calyx or an independent ureter may drain the isthmus (Pawar et al., 2018). In HSK, the fusion of the lower poles results in abnormal position of the ureter in the renal pelvis and highly placed ureteropelvic junction. Impaired drainage of the collecting system and associated ureteropelvic obstruction may predispose the patient to kidney stones

and hydronephrosis that is usually the result of a urinary tract obstruction. HSK is also common in some genetic diseases, such as Turner syndrome (Ranke and Saenger, 2001) and Trisomy 18 (Cereda and Caret, 2012). Ribs do not protect HSK well; trauma may cause injury across the lumbar vertebral column (O'Brien et al., 2008).

Clinical manifestation of horseshoe kidney

HSK is usually asymptomatic and often discovered as an incidental finding. When symptoms do occur, it is predominantly due to infection, obstruction, or stones. The most common finding in HSK is ureteropelvic junction (UPJ) obstruction; O'Brien estimates that up to 35% of HSK patients may be affected (O'Brien et al., 2008). UPJ obstruction can occur when a high insertion of ureters into the kidney pelvis causes delayed pelvic emptying. Another rare cause of obstruction can be the crossing of the ureter over the HSK isthmus (Costa et al., 2004). A diagnosis of UPJ obstruction is made based on a CT urography or intravenous pyelography with a typical appearance of a large pelvis with a high-riding ureter in the pelvis.

CONCLUSION

HSK is the most common congenital anomaly of the urinary tract. These kidney fusion anomalies are mostly asymptomatic; however, significant symptoms, especially hydronephrosis, kidney stones, and infections, represent causes of death in HSK patients. An abnormal kidney is usually related to a range of anatomical changes. Vessel relations and supply are highly variable. Furthermore, horseshoe kidneys are characterized by various ureteric patterns. All of these abnormalities have important clinical implications. The vascular and ureteral anomalies seen in the case presented here is especially important when surgery is contemplated.

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