Case Report

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A congenital renal anomaly concomitant with a vascular emergency: a case of an ectopic pelvic kidney accompanied by aortoiliac aneurysms

Mudar Aljadaan, MD[a], Omar Al Laham, MBBS[a,*], Louay Khaled, MD[a], Joudy Eljerdie, MD[a], Mohammad Ghannam, MD[a,b], Ammar Mohammad, MD[a,b]

Introduction and importance: Ectopic pelvic kidneys are an extremely rare congenital renal system anomaly. This embryological occurrence transpires between the 4th and 8th gestational weeks, and is seen in 1 in every 2100–3000 births. Moreover, research articles indicate an incidence of ectopic pelvic kidneys ranging from 0.033 to 0.047%. The co-occurrence of this anomaly with an abdominal aortic aneurysm is an even rarer finding.

Case presentation: We report a rare case involving a 62-year-old Middle Eastern male with a right ectopic pelvic kidney. The condition initially manifested as vague abdominal discomfort in the periumbilical region. The pain evolved into a continuous, localized, and insidious sensation. This was escorted by the perception of a pulsatile abdominal mass. Preoperative radiology illustrated a right ectopic pelvic kidney with concomitant aortoiliac aneurysms.

Clinical discussion: Via a successful surgical intervention, the abdominal aortic aneurysms were repaired via synthetic Dacron grafts and the renal perfusion to the ectopic pelvic kidney was secured. Moreover, the aneurysmal wall underwent a full histopathological analysis, and the results of which indicated an atherosclerotic cause.

Conclusion: Ectopic pelvic kidneys are an exceptionally rare congenital anomaly, especially when coupled with life-threatening co-occurrences like an abdominal aortic aneurysm. The need for timely surgical interventions is critical, and this topic requires comprehensive documentation as a guide for surgical professionals. This unique case is the first documented instance in the country. It emphasizes the fundamental role of proper intraoperative techniques in repairing aneurysmal conditions while preserving the function of the ectopic kidney.

Keywords: aortoiliac aneurysm, case report, congenital anomaly, ectopic pelvic kidney, vascular emergency, vascular surgery

Introduction

Congenital abnormalities affecting the renal system manifest in a noteworthy percentage of the populace. This ranges from 3.3 to 11%[1]. Furthermore, this encompasses variations in the morphology, number, and/or anatomical location of the organ[2]. The congenital pelvic kidney represents a tremendously rare abnormality arising as a direct result of the embryological kidney's lack of success to correctly ascend to its natural anatomical location. This results in its anomalous positioning within the lumbar region in the retroperitoneal space. To further mark its origins and rarity, this atypical embryological occurrence was found to transpire between the 4th and 8th gestational weeks, afflicting ~1 in every 2100–3000 births[3]. Moreover, statistics designate an incidence of ectopic pelvic kidneys to range from 0.033 to 0.047%[4], with the prevailing presentation being

HIGHLIGHTS

- The congenital pelvic kidney represents an exceedingly rare anomaly originating as a consequence of the embryological kidney's failure to properly ascend to its natural anatomical site.
- A pelvic kidney arises from a failure of kidney migration, particularly between the 4th and 8th gestational weeks. The overall incidence of pelvic kidney ranges from 1 in 2100 to 1 in 3000.
- The relationship of this congenital anomaly with an abdominal aortic aneurysm is rare, with a profound scarcity of literature articles addressing this co-occurrence.
- Aberrant renal vasculature is an issue in ectopic kidneys. The blood supply may originate from multiple distinct locations. This needs meticulous attention intraoperatively.
- Surgical repair of the ensuing aneurysms is crucial to be successfully carried out while maintaining adequate renal perfusion throughout the operation. This intricate balance spares patients the possibility of any potential renal ischemia.

[a]Faculty of Medicine and [b]Department of Vascular and Endovascular Surgery, Al Assad University Hospital, Damascus University, Damascus, (The) Syrian Arab Republic

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*Corresponding author. Address: Faculty of Medicine, Damascus University, Damascus, (The) Syrian Arab Republic. E-mail: 3omar92@gmail.com (O. Al Laham).

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unilateral rather than bilateral. Nevertheless, instances of bilateral ectopic occurrence have been documented in the literature[5]. The confluence of this congenital anomaly with an abdominal aortic aneurysm is seldom seen. This is marked by the scarcity of literature addressing this association. Besides, reports suggest the occasional presence of one or two anomalous renal arteries related to the ectopic kidney. They could emanate from diverse arterial anatomical segments[6]. Opting for surgical intervention as the most viable recourse mandates careful consideration and contemplating that preserving optimal renal perfusion constitutes a pivotal determinant for the success of the surgical procedure. Furthermore, special attention must be directed toward the identification and management of aberrant ectopic renal arteries to ensure a successful surgical outcome. Additionally, meticulous timing of cross-clamping assumes paramount importance during the concurrent repair of the accompanying aneurysms. After conducting a broad review of the existing literature, we can firmly state that our case of a congenital ectopic pelvic kidney (CEPK) concomitant with aortoiliac aneurysms is unprecedented in our country. This further highlights the groundbreaking merits of our findings. The work has been reported in line with the SCARE criteria and the revised 2023 SCARE guidelines[7].

Presentation of case

Patient information

We herewith present the rare case of a 62-year-old Middle Eastern male who is a known case of a congenital right ectopic kidney situated in the pelvis and discovered 25 years prior. The patient's chief complaint was pain located in the periumbilical area, which originally began as a vague abdominal discomfort that progressively morphed into pain. It was described as insidious, localized, and did not radiate to any region, dull in nature, and continuous. Furthermore, the pain scored 03/10 on the numerical pain scale. Initially responding partially to over-the-counter analgesic medications, it later became unresponsive to them. In addition, the pain was associated with the feeling of a pulsatile periumbilical abdominal mass. Noteworthy is that these complaints were not intercalated with any intermittent claudication, limb swelling, cyanosis, or impotence. Additionally, no alterations in the color of his stool or urine were reported. Also, the patient denied any emesis or hematemesis. Further diving into his clinical history, he denied having any genitourinary, gastrointestinal, or respiratory symptoms. Furthermore, no notable local inflammatory signs were reported (i.e. Edema, redness, hotness, or loss of function). The patient denied any immune disorders, physical trauma, recent infections, or previous similar episodes. His medical history included an ectopic right pelvic kidney discovered 25 years ago and hyperlipidemia, whereas his surgical history only involved an umbilical hernial open repair surgery 15 years prior. Remarkably, his family history was overall unremarkable and negative for a similar congenital anomaly. Furthermore, his drug history included prophylactic Aspirin 81 mg and Rosuvastatin 20 mg for the management of his hyperlipidemia. The patient's psychosocial history only encompassed tobacco smoking for 70 pack-years with no reported alcohol consumption. Lastly, his allergic history revealed nothing noteworthy, and his BMI was 27 kg/m^2.

Clinical findings

The patient's physical examination commenced with the recording of vital signs, whereby all of which fell within normal ranges. Initiating the structured examination with inspection, the findings solely included a conspicuous transverse surgical scar from a previous umbilical hernial repair surgery. Superficial palpation of the abdomen revealed no significant findings except for mild periumbilical pain and tenderness. However, deep palpation uncovered heightened sensations of pain and tenderness, along with the presence of a pulsatile infraumbilical mass. Despite these findings, arterial pulses in both lower limbs were palpable throughout. Abdominal percussion produced a tympanic sound overall but induced pain over the periumbilical region. Auscultation detected an audible bruit over the infraumbilical area where the pulsatile umbilical mass was identified.

Diagnostic assessment

Initially, a *transabdominal ultrasound* was conducted to assess the situation. The patient had a total of two kidneys, a normal left one and an ectopic right kidney. It was situated in the pelvis concurrent with aortoiliac aneurysms. The aortic aneurysm had a maximal diameter that approximately measured 8 cm, whereas the right common iliac artery aneurysm had a maximal diameter of 7.5 cm. Both aneurysms were fusiform. However, the arterial axes in both lower limbs displayed normal three-dimensional signals along their entire course, and the remainder of the examination yielded unremarkable results. Subsequently, a *duplex ultrasound* corroborated the previous findings. It highlighted the thrombotic nature of the infrarenal abdominal aortic aneurysm. This aneurysm extended across the iliac bifurcation and along the course of the right common iliac artery and the initial segment of the right external iliac artery. The remainder of the examination of the arterial trees in both lower limbs revealed no anomalies. In light of these discoveries, a comprehensive high-resolution contrast-enhanced *Multi-Slice Computed Tomography Angiography (MS-CTA)* with three-dimensional reconstruction was done (Fig. 1A, B, C, D). This imaging modality precisely depicted the previously identified infrarenal abdominal aortic aneurysm. It confirmed its extension as revealed by the duplex ultrasound. Furthermore, it outlined thrombosis within its wall that extended along the course of the aneurysm and identified another thrombus along the extension of the right common iliac artery. Markedly, a single right aberrant renal artery was observed arising from the right common iliac artery close to the abdominal aortic bifurcation. It measured 5 mm. The remainder of the examination disclosed no other noteworthy findings. A comprehensive laboratory panel was checked for anomalies. His creatinine level was 1.1 mg/dl, whereas his urea level was mildly elevated (33 mg/dl). Yet, no other abnormal values were detected. Given these findings, the rationale was directed toward performing a surgical intervention. Prior to the procedure, requisite cardiovascular, respiratory, and anesthetic consultations were conducted. All of which cleared the patient for surgery. Furthermore, blood samples were drawn for blood grouping and crossmatch, and the patient's nutritional status was designated as NPO (nil per os – nothing by mouth). Additionally, two large-bore intravenous cannulas were established to facilitate the administration of fluid infusions, blood, or antibiotics. In terms of challenges, no obstacles or limitations were reported during any of the perioperative phases.

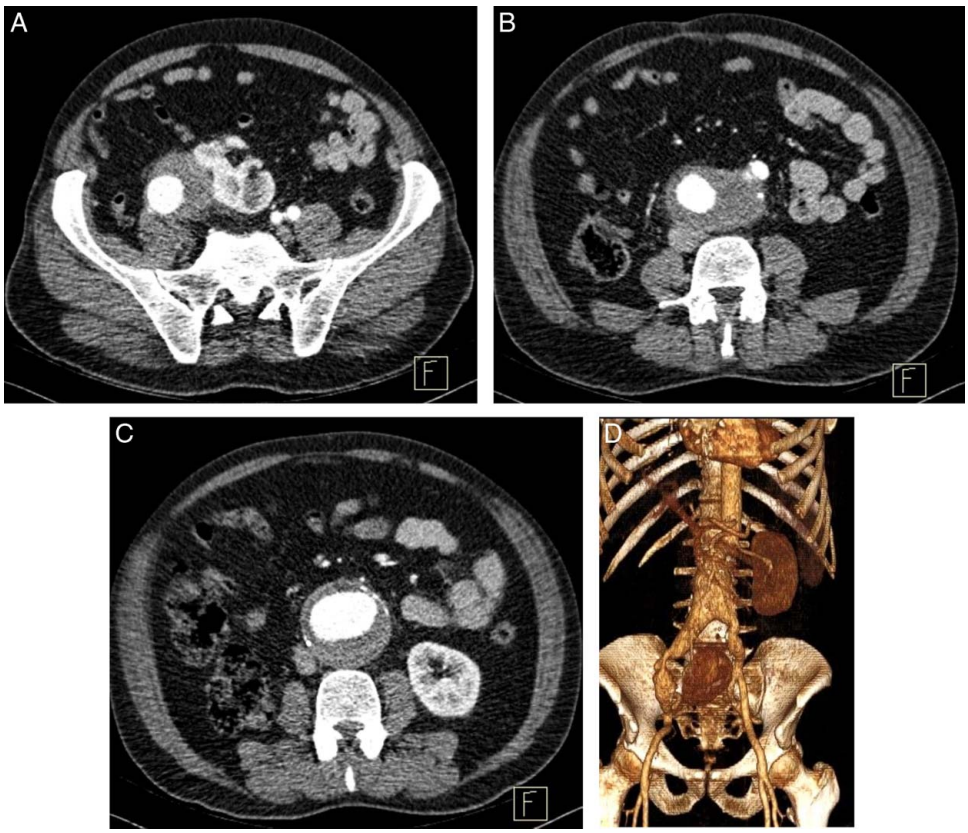

Figure 1. (A) Preoperative high-resolution Multi-Slice Computed Tomography Angiography (MS-CTA) image with an axial view. It shows the ectopic pelvic kidney and its anatomical position at the level of the abdominal aortic bifurcation. (B) Preoperative high-resolution MS-CTA image with an axial view. It shows the abdominal aortic aneurysm at the level of iliac bifurcation. (C) Preoperative high-resolution MS-CTA image with an axial view. It shows the largest diameter of the abdominal aortic aneurysm while demonstrating the normal anatomical location of the left kidney. (D) Preoperative high-resolution MS-CTA image with three-dimensional reconstruction in coronal view. It clearly shows the ectopic pelvic kidney with the subsequent arterial aneurysms.

Therapeutic intervention

Our patient underwent surgery at our tertiary university hospital. The operation was conducted under the expert guidance of general anesthesia and devoid of any perioperative complications. The surgery was impeccably executed by two specialists in vascular surgery, each seasoned with 17 years of invaluable experience. Additionally, they were primarily assisted by a senior resident in vascular surgery who had 6 years of surgical expertise. The optimal choice for our patient was an open surgical approach. Through a supraumbilical and infraumbilical abdominal incision, full exposure of the surgical area was achieved (Fig. 2A). The respective layers of the abdominal wall were carefully dissected to access the abdominal aorta through the posterior peritoneum, where we subsequently isolated and controlled at the level of the left renal artery. Afterward, the common iliac arteries were adeptly isolated and controlled, followed by the complete isolation and control of the aberrant renal artery supplying the aforementioned ectopic pelvic kidney. The ensuing step involved bilateral inguinal incisions, facilitating the thorough dissection of underlying layers to properly expose the common femoral artery on both sides, which were then isolated and controlled along with their respective branches. A meticulously prepared bifurcated synthetic Dacron graft measuring 16×8 mm was employed, and another tube synthetic Dacron graft measuring 6 mm, was neatly anastomosed to the initial graft's main body. Following this, the infrarenal aortic segment, the right renal artery, and the bilateral common iliac arteries were precisely clamped, and anastomosis with the main body of the first synthetic Dacron graft was conducted using 3/0 Prolene sutures. The ensuing step involved establishing an anastomosis between the renal artery of the ectopic kidney and a synthetic Dacron graft measuring 6 mm. Subsequently, a clamp was applied to the right renal artery for 30 min, accompanied by the appropriate cooling of the ectopic kidney using hypothermic perfusion of Ringer's lactate solution at 4°C. Mannitol and heparinized saline were administered during this phase. The aortic clamps were then released, maintaining control over the common iliac arteries until the subsequent end-to-side aorto-bi-femoral bypassing was accomplished via bifurcated synthetic Dacron grafts using 5/0 Prolene sutures (Fig. 2B). Finally, bilateral drainage systems were adeptly placed, and meticulous suturing of the wounds was successfully executed. The excised aneurysmal sac underwent histopathological analysis. It grossly depicted the aneurysm with a 1 cm thick wall and an inner hemorrhagic surface. Microscopically, hematoxylin and eosin staining revealed chronic inflammatory infiltrations, hyalinization fibrosis, cholesterol crystals, and calcifications. However, no granulomas or evidence of malignancy were observed. Postoperatively, the patient was transferred from the operating room to the surgical ICU with stable vital signs and mechanical

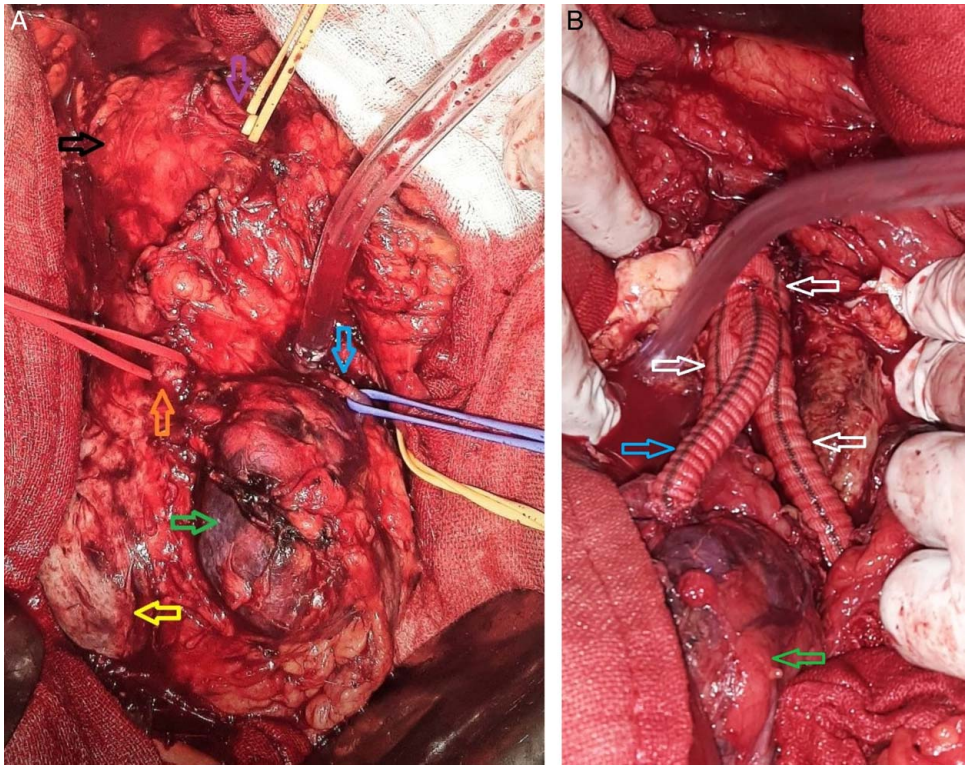

Figure 2. (A) Intraoperative image showing the surgical field prior to the surgical repair of the corresponding aneurysms. The *black arrow* identifies the infrarenal abdominal aortic aneurysm. The *yellow arrow* identifies the arterial aneurysm of the right common iliac artery and its external iliac artery. The *green arrow* identifies the ectopic pelvic kidney. The *purple arrow* identifies the inferior mesenteric artery. The *blue arrow* identifies the renal vein of the pelvic kidney. The *orange arrow* identifies the renal artery of the pelvic kidney. (B) Intraoperative image showing the surgical field after surgical repair of the corresponding aneurysms. The *green arrow* identifies the ectopic pelvic kidney. The *blue arrow* identifies the tube synthetic Dacron anastomosis supplying the ectopic pelvic kidney and connecting it to the body of the main bifurcated synthetic Dacron graft. The *white arrows* identify the bifurcated synthetic Dacron aorto-bi-femoral bypass grafts.

ventilation. He remained there for 2 days before transitioning to the ward. On the day of surgery, the patient's creatinine levels gradually rose from 1.2 to 2.5 mg/dl, subsequently decreasing to 1.5 mg/dl the following day. Moreover, his urea level decreased from its preoperative value to 27 mg/dl. Before the patient's discharge to the ward, a comprehensive evaluation ensured the patient's overall well-being, stable vital signs, and normal vascular examination of both lower limbs. During the postoperative period, the patient's fluid and food intake increased gradually without reported discomfort or pain. His urea level returned to normal (23 mg/dl). Furthermore, he stayed in the ward for 3 days until creatinine values normalized to 0.96 mg/dl. Throughout this time, the patient received necessary fluid infusions, analgesics, antibiotics, aspirin and clopidogrel as anti-thrombotic medications, and apixaban as an anticoagulant. Moreover, regular changes to wound dressings were carried out by medical professionals. Notably, the patient reported complete relief of symptoms after surgery and was discharged to outpatient settings on the 5th postoperative day. Subsequent follow-ups in our outpatient vascular surgery clinic spanned 2 months thus far. Follow-up incorporated comprehensive clinical and radiological examinations. Analysis via high-resolution contrast-enhanced MS-CTA with three-dimensional reconstruction (Fig. 3A, B) demonstrated adequate blood perfusion to the ectopic kidney and confirmed the patency and normal functioning of the synthetic grafts. Doppler ultrasonography was performed 2 months postoperatively. It affirmed normal blood perfusion (Fig. 4A, B). No anomalies with the anastomotic grafts were reported in any of the previous imaging results. Also, no anomalous laboratory findings were present, and no wound-healing defects were observed. In parallel, the patient received education on essential lifestyle modifications to avoid further vascular complications. This included smoking cessation, body weight reduction, adopting a healthy diet, and incorporating proper physical activity.

Discussion

Addressing genitourinary anomalies poses an obstacle that vascular surgeons should overcome when they face abdominal aortic aneurysms. On this note, we should mention that the most prevalent anomaly linked to such aneurysms of the abdominal aorta is the congenital abnormality termed '*Horseshoe kidney*'[8–12]. In terms of rarity, there are six congenital kidney anomalies in terms of anatomical location (lumbar, pelvic, crossed, thoracic, cephalic, and abdominal). Of those, the congenital pelvic kidney stands out as the rarest[13]. In terms of embryological development, CEPKs arise in the pelvis during the early period of fetal development. The kidney gradually ascends to its normal anatomical site. During the embryogenic ascent, each of the two kidneys secures its adequate perfusion from the neighboring vessels (initially from the internal and external iliac arteries and directly from the aorta at the 8th week of embryologic formation)[14]. Diving deeper into the origins of this developmental anomaly, a pelvic kidney arises from a failure of kidney migration, particularly between the 4th and 8th gestational

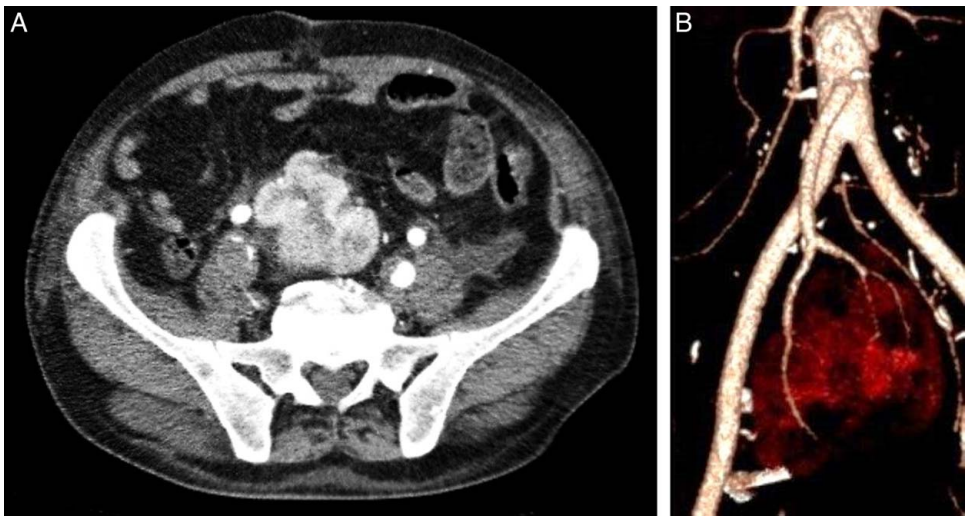

Figure 3. (A) Postoperative high-resolution Multi-Slice Computed Tomography Angiography (MS-CTA) image with an axial view two weeks after surgery. It shows the ectopic pelvic kidney after implanting the synthetic anastomotic graft that connects it to the synthetic abdominal aortic graft. (B) Postoperative high-resolution MS-CTA image with three-dimensional reconstruction two weeks after surgery. It demonstrates the patency of the synthetic grafts and the adequate blood supply and perfusion of the ectopic pelvic kidney.

weeks. The overall incidence of pelvic kidney ranges from 1 in 2100 to 1 in 3000. Moreover, its co-occurrence with aneurysms of the abdominal aorta is exceedingly rare[15,16]. To further depict the rarity of this abnormality, statistics reveal an incidence of ectopic pelvic kidneys ranging from 0.033 to 0.047%[4], with the predominant presentation being unilateral, although documented instances of bilateral ectopic occurrences exist[5]. By taking a glimpse at the historical precedence of this pathological co-occurrence, we can mark that while cases of ectopic kidneys that co-occur with aortoiliac aneurysms have been documented in the published literature, the precise prevalence rate and many epidemiological parameters remain vague due to its extreme rarity. In 1977, Ezzet *et al.*[17] pioneered depicting the case of a patient who has CEPK concomitant with an aneurysm of the abdominal aorta. Approximately 0.18% of patients undergoing major operations on the aorta were found to have a CEPK[18]. Consequently, the correlation between CEPKs and aneurysms of the abdominal aorta is exceptionally rare. Another vital aspect of CEPK is the resultant aberrant blood vasculature. Moreover, the renal anatomic distortion during embryogenic tissue formation introduces variability in the corresponding blood supply, as vasculature of the fetus may persist, resulting in several blood vessels providing perfusion for a single kidney. The blood supply may originate from multiple distinct locations like the hypogastric, iliac, abdominal aorta, and or mid-sacral[6,19,20]. CEPK exhibits, in the majority of cases, no symptoms and operates as normal kidneys do. Yet, potential disease complications in patients with CEPK come in the form of infection, obstruction, or renal stones[6,21–23]. Despite the asymptomatic nature of the majority of cases, ectopic renal anomalies can lead to renal malfunction, prompting patients to endure urinary tract diseases such as urinary tract infections, vesicoureteral reflux, renal calculi, and urinary obstruction[19,20]. In terms of preoperative and intraoperative diagnostic, therapeutic, and preventative measures, a twofold approach is imperative to mitigate potential renal injury: detailed preoperative assessment of the anatomy of the vasculature and intraoperative protection, factoring in the expected duration of cross-clamping. Preoperative evaluation is,

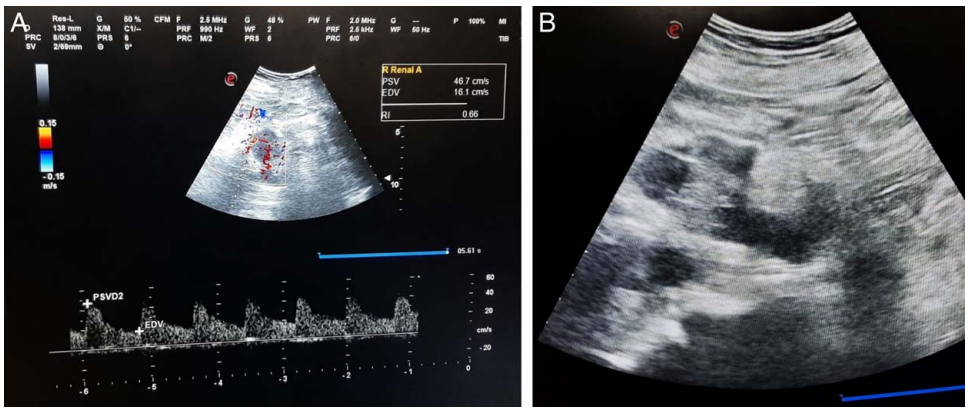

Figure 4. (A, B) Postoperative Doppler ultrasonography images of the right ectopic pelvic kidney two months after surgery. The images demonstrate its adequate blood flow and blood perfusion, which confirms the success of the surgery and the patency of the synthetic anastomotic grafts.

therefore, facilitated by contrast-enhanced computed tomography imaging[24]. Three-dimensional reconstruction of computed tomography angiography, in addition to magnetic resonance angiography utilizing gadolinium contrast material, exhibit sensitivities of 100 and 97%, respectively, in delineating accessory and/or aberrant renal arteries, surpassing arteriography and even removing the need to perform it[25–27]. When assessing the risks of CEPK, we must denote that unilateral pelvic kidneys are chiefly concurrent with a contralateral kidney that works normally. In turn, this will greatly diminish the intraoperative perils of renal failure and ischemia[6]. In terms of surgical treatment, various strategies for open surgery are delineated in the published literature. Their selection is primarily influenced by considerations related to the anatomy of the surgical field and, to a degree, the surgeon's expertise and choice[28]. Overall, these surgical methods typically involve the use of a synthetic graft for aneurysmal repair and anastomoses (Dacron or ePTFE in bifurcated or tubal configurations)[6,29]. The documented results discussing distinct techniques used in open surgical repair consistently highlight impeccable success, with minimal impact on renal function[30]. To further dive into the details of the surgical treatment of a CEPK, we must keep in mind that while alternative modalities like medial visceral rotation are outlined for specific cases, the predominant surgical modality of choice is the anterior transperitoneal one. This facilitates ideal conception and handling of corresponding ectopic renal vasculature that often originates from the iliac arteries. Key considerations in these surgical operations involve safeguarding renal tissue from ischemia during aortic cross-clamping and soundly determining the positioning of the arterial grafts used for the repair. Moreover, various surgical techniques have been proposed to achieve these goals. One straightforward approach amongst these techniques involves the utilization of mannitol or furosemide prior to performing the step of cross-clamping of the suprarenal aorta, followed by reconstruction of the aortic segments without additional protective measures. Nevertheless, we must denote that this method is predominantly viable in cases where aortic reconstruction is uncomplicated, given the limited allowable time for aortic reconstruction (30–40 min) to prevent prolonged renal ischemia[31]. Using a hypothermic solution secures renal perfusion, and this gives surgeons additional necessary time during cross-clamping. In turn, this significantly diminishes the potential subsequent renal injury. In their article, Murakami *et al*.[4] reported an incidence of an abdominal aortic aneurysm concomitant with a CEPK. That kidney was perfused via two aberrant renal arteries arising from the left common iliac artery and the bifurcation of the aorta. They utilized hypothermic Ringer's lactate solution and slushes of ice for topical cooling to maintain kidney perfusion and secure the viability of the parenchyma[4]. To further highlight the importance of this technique, we must also report that it has been considered the most appropriate one overall in situations anticipating cross-clamping durations exceeding 60 min. Furthermore, this cold perfusion is either established through constant or bolus administrations at regular time intervals (each 20–30 min)[15]. Other intraoperative techniques encompass the utilization of a Gott-type shunt to maintain renal perfusion during the period of cross-clamping of the aortic segments. To clarify what a Gott shunt is, it is a heparin-bonded shunt that is utilized to bypass segments of the aorta that are being operated on. Nevertheless, complications such as iatrogenic injury or embolization during the placement or extraction of the shunt have been documented[32,33]. Alternatively, another intraoperative technique entails establishing a provisional axillofemoral bypass. This maintains the retrograde perfusion of the kidney during the period of aortic cross-clamping. The primary disadvantage of this approach is that, while it's effective in renal protection, this technique prolongs the surgical time so that axillary and inguinal exposures are set up[34,35]. Therefore, the implementation of this surgical technique and the one entailing the usage of extracorporeal circulation remain less popular within the Vascular Surgery community[36]. Reimplantation of renal arteries that arise from the aortic aneurysm is essential to safeguard renal perfusion and prevent ischemic renal injury[23]. According to the Society of Vascular Surgery Consensus guidelines on the management of aneurysms of the abdominal aorta, the advocated approach during open aneurysmal repair entails safeguarding and reimplanting any key aberrant renal artery measuring more than 3 mm or any arteries providing at least 33% of the kidney[37]. Despite this, O'Hara *et al*.[11] have documented instances where grafting of renal vessels becomes a must due to insufficient arterial length after aneurysm repair had been achieved.

Conclusion

Ectopic kidneys represent a rare congenital anomaly. When coupled with an abdominal artery aneurysm, this event stands out as the most uncommon variant. The ensuing vascular complications pose life-threatening risks. This underscores the decisive importance of timely and impeccably executed surgical interventions. Such cases necessitate thorough examination and inclusion in the existing literature. This fosters the foundation for pertinent research studies that contribute to the establishment of effective preoperative diagnostic and postoperative follow-up protocols. Meticulous intraoperative surgical techniques address two critical objectives: resolving the aneurysmal condition and salvaging the kidney while restoring/maintaining its essential perfusion. Upon a comprehensive review of the literature, we can say that our case stands as the first documented instance from our country of an ectopic pelvic kidney concomitant with abdominal aortic aneurysms.

Ethics approval

Institutional review board approval is not required for deidentified single case reports or histories based on institutional policies.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

O.A.: Conceptualization, resources, methodology, data curation, investigation, who wrote, original drafted, edited, visualized, validated, literature reviewed the manuscript, and the corresponding author who submitted the paper for publication.

M.A.: First assistant during the surgical operation, in addition to validation, visualization, data curation, resources, and review of the manuscript.

L.K., J.E.: Data curation, resources, visualization, validation, and review of the manuscript.

M.G., A.M.: Vascular Surgery specialists who performed and supervised the operation, in addition to validation, supervision, project administration, resources, and review of the manuscript.

All authors read and approved the final manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Omar Al Laham.

Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available because the data were obtained from the hospital's computer-based in-house system. Data are available from the corresponding author upon reasonable request.

Provenance and peer review

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Department of Pathology, Al Assad University Hospital, Damascus University, Damascus, (The) Syrian Arab Republic; Department of Radiology, Al Assad University Hospital, Damascus University, Damascus, (The) Syrian Arab Republic.

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