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Post-Renal Biopsy Acute Kidney Injury and Page Kidney from Intra-Renal Hematoma Aggravated by Reversible Contrast-Induced Nephropathy **Following Renal Arterial Embolization**

Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G

ABCDEF Macaulay A. Chukwukadibia Onuigbo

BCDEF Vivek Sharma

DF Omotola O. Balogun BCEF Allina Ghimire

Division of Nephrology, Department of Medicine, The Robert Larner, M.D. College of Medicine, University of Vermont, Burlington, VT, U.S.A.

Corresponding Author: Conflict of interest: Macaulay Amechi Chukwukadibia Onuigbo, e-mail: macaulay.onuigbo@uvmhealth.org

None declared

Patient:

Male, 73-year-old

Final Diagnosis:

Page kidney from intra-renal hematoma aggravated by reversible contrast-induced nephropathy fol-

lowing renal arterial embolization

Symptoms:

Flank pain • nausea • vomiting

Medication:

Apixaban

Clinical Procedure:

Kidney biopsy and subsequent renal arterial embolization

Specialty:

Objective:

Rare co-existance of disease or pathology

Background:

Page kidney was described by Dr. Irving Page in animal kidneys in 1939 with renal failure and persistent arterial hypertension from "cellophane perinephritis". By 2009, about 100 cases of Page kidney had been reported. Bleeding complications after percutaneous kidney biopsy has, however, been well described. Moreover, the perioperative management of the recently introduced non-vitamin K antagonist anticoagulants (NOACs) remains uncertain due to inadequate evidence.

Current guidelines to determine the appropriate duration of withholding NOACs before a surgical procedure, and when to restart NOACs safely after a procedure, however, cognizant of the implications of renal dysfunction, and levels of risk of the procedure are still unclear and sometimes conflicted.

Case Report:

We describe a case of Page kidney from an intrarenal hematoma complicating ultrasound-guided percutaneous right native kidney biopsy with acute kidney injury after withholding apixaban, a NOAC, for 3 days. Computed tomography evidence of continuing intrarenal bleeding from a renal pseudoaneurysm was treated with super-selective renal artery embolization; the case was further complicated by superimposed acute kidney injury from contrast-induced nephropathy.

Conclusions:

We reviewed the vagaries of Page kidney with respect to the presence, or otherwise, of hypertension and how to explain worsening renal failure despite only unilateral involvement of a single kidney in a patient with 2 kidneys. Furthermore, we revisit the risks of contrast-induced nephropathy following iodinated contrast exposure. We explored the alternative management options for a post-biopsy renal pseudoaneurysm, that would avoid the use of iodinated contrast that could have potentially mitigated, if not fully prevented, the ensuing contrast-induced acute kidney injury.

MeSH Keywords:

Acute Kidney Injury • Contrast Media • Hematoma • Pneumoradiography

Full-text PDF:

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Background

Page kidney was described by Dr. Irving Page following his very elaborate experiments with animal kidneys in 1939 with the production of persistent arterial hypertension from "cellophane perinephritis" [1]. By 2009, about 100 cases of Page kidney had been reported [2]. Earlier on, most cases of Page kidney were related causatively to extrarenal compression following post-traumatic episodes from blunt abdominal trauma [2-4]. Nevertheless, more recent reports of Page kidney resulting from intrarenal pathology, such as cysts, tumors, and hematomas, have been described [2,5,6]. Bleeding complications after percutaneous kidney biopsy, albeit low, has been well described [7-12]. More recently, there has been an increasing use of super-selective renal artery embolization for the management of post-biopsy renal bleeding [13]. Furthermore, contrast-induced acute kidney injury complicating extrarenal coil embolization procedures has been reported [14]. We recently encountered a case of Page kidney with acute kidney injury resulting from a right lower pole hematoma complicating an ultrasound-guided right native kidney biopsy. Subsequently, on admission and following a super-selective right renal angiography procedure to stop the active intrarenal bleeding from a renal pseudoaneurysm, our patient developed reversible contrast-induced acute kidney injury. This raised the question of the most appropriate alternative management option for post-biopsy renal pseudoaneurysm that could have mitigated, if not fully prevented, the ensuing contrast-induced acute kidney injury.

Case Report

A 73-year-old white male was evaluated in our Emergency Department (ED) following a transfer from a peripheral medical center with 2 hours of excruciating, mostly non-radiating, acute onset right flank pain. There was no trauma. He reported some nausea with minimal vomiting up to 3 times but denied fever, chills, chest pain, dyspnea, abdominal pain, dysuria, hematuria, testicular pain, leg pain or tingling. He vaguely noted that since the kidney biopsy 26 days earlier, he had experienced mild discomfort in the same area. Tylenol, 1000 mg, was without effect. He had a history of hypertension, heart failure, and atrial fibrillation and had been taking apixaban 5 mg twice daily for about 2 years; he also had a history of Raynaud's disease, previous laparoscopic cholecystectomy, tonsillectomy, vasectomy, and ablation for atrial fibrillation 2 years earlier. He had an uneventful ultrasound-guided right native kidney biopsy 26 days before presentation at our ED. His vital signs were stable: temperature was 35.7°C, pulse as 63 beats per minute, respiratory rate was 12 breathes per minute; blood pressure was 136/78 mm Hg, pulse oximetry was 100% on room air. Physical examination was unremarkable with the abdomen

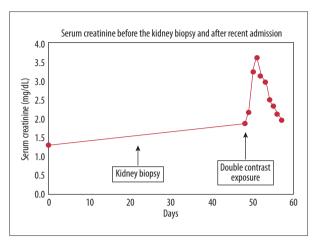


Figure 1. Serum creatinine trajectory before the native kidney biopsy and following recent hospital admission for selective renal arterial embolization.

soft, not distended, non-tender, and was without costovertebral area tenderness. He was not dehydrated, appeared euvolemic, and was not orthostatic. Intravenous (IV) morphine sulfate was administered for pain control, together with some IV fluids. He also received 2106 units of prothrombin complex concentrate infused over 20 minutes.

The right kidney biopsy was carried out for increased baseline serum creatinine 3 years earlier, together with a new diagnosis of uveitis in the last year. Nonetheless, serum creatinine had been stable at about 1.30 mg/dL in the past 2 years before the kidney biopsy. Apixaban was withheld for 3 days before the right kidney biopsy. Protime international normalized ratio (INR) was 1.1 and partial thromboplastin time (PTT) was 13.2 seconds on the day of the kidney biopsy. Under ultrasound guidance, a 17-gauge coaxial needle was advanced into the lower pole of the right kidney. Through the coaxial needle, multiple 18-gauge core biopsy samples were obtained. The coaxial needle was removed, and a sterile dressing was applied. The procedure was well tolerated and there were no immediate complications. Indeed, the post-biopsy renal ultrasound was normal. Apixaban was resumed 3 days after the kidney biopsy. The kidney biopsy demonstrated hypertensive nephrosclerosis, moderate interstitial fibrosis, and mild interstitial chronic inflammation; no further interventions were planned.

Urinalysis was significant for trace ketones, 2+ blood, and 2+ protein. Serum creatinine was higher at 1.86 mg/dL; it was 1.31 mg/dL in May 2019, a month before the kidney biopsy (Figure 1). Serum electrolytes were normal. WBC was 12 000/mm³, platelet count 234 000/mm³, and hemoglobin 11.7 g/dL, just slightly lower than a level of 12.0 g/dL, 8 months earlier. Admission Protime INR was 1.3 (range 0.9–1.1) and PTT was 15.5 seconds (range 10.3–13.4 seconds).



Figure 2. Computed tomography scan of the abdomen with contrast showing a right kidney lower pole hematoma measuring up to 5.9 cm with active bleeding before the coil embolization.

A computed tomography (CT) scan examination of the abdomen and pelvis, with and without contrast (100 cc), demonstrated a right lower pole intra-parenchymal renal hematoma measuring up to 5.9 cm together with evidence of active intrarenal bleeding (Figure 2). Our Interventional Radiology Department was consulted, and the patient quickly underwent a selective renal angiography with coil embolization of a ruptured pseudoaneurysm (Figure 3). The small bleeding pseudoaneurysm in the lower pole of the right kidney was successfully embolized. The remainder of the right kidney perfusion remained patent although antegrade arterial perfusion was noted to be sluggish.

The patient received empiric antibiotics for leukocytosis and suspected pneumonia. Serum creatinine progressively increased, peaking at 3.60 mg/dL on hospital day 3. However, thereafter, serum creatinine started to improve and was 1.96 mg/dL on discharge, hospital day 9 (Figure 1). Additionally, within 24 hours of the coil embolization, the patient developed persistent frequent hiccups. Radiological evaluation with chest radiographs and a follow-up right abdominal upper quadrant ultrasound failed to reveal any new lesions including the absence of any sub-diaphragmatic abnormalities. He required combination oral metoclopramide 5 mg at 3 times per day, gabapentin 100 mg per day and baclofen 2.5 mg every 6 hours to control the hiccups. On discharge, the patient was feeling much better, with no flank pain and reduced frequency of the hiccups.

Discussion

Page kidney from the intrarenal hematoma complicating the kidney biopsy would explain the initial increase in serum



Figure 3. Super-selective renal embolization of a right renal pseudoaneurysm.

creatinine from 1.31 mg/dL to 1.86 mg/dL on admission [1,5] (Figure 1). The classic features of Page kidney include new-on-set hypertension, in patients who are normotensive previously, with or without renal impairment [15–17].

Our patient was clearly unusual since he had been a known hypertensive patient for many years and at the time of the index admission was on 3 antihypertensive agents: metoprolol 100 mg daily, spironolactone 25 mg daily, and torsemide 10 mg daily. Arguably, therefore, the continued administration of all 3 antihypertensive agents could have masked the appearance of new hypertension in the Emergency Department.

Moreover, between 1999 and 2017, the patient had a baseline serum creatinine of about 0.7 gm/dL: eGFR (estimated glomerular filtration rate) was ~85 mL/min/1.73 m² BSA (body surface area). However, in 2017, for unknown reasons, the patient's serum creatinine level had risen to about 1.3 mg/dL (eGFR ~55-65 mL/min/1.73 m² BSA). This loss of renal function and the simultaneous diagnosis by ophthalmologist of bilateral uveitis in 2018 had raised the possibility of the syndrome of tubulointerstitial nephritis with uveitis (TINU). From a practical perspective, we concluded that sometime in 2017, due to factors that remain unclear to us, he had lost significant renal functional reserve [18-22]. This necessarily placed the patient at a higher risk of either acute kidney injury or indeed chronic kidney disease progression [18-22]. These were the imperatives for the recommendation by our Nephrology Service Department to get a kidney biopsy.

When the patient presented to the ED with the worsening right flank pain, his vomiting was minimal and consisted mostly of nausea. He was not dehydrated and had no evidence for hypovolemia or dehydration. Nevertheless, his serum creatinine level had increased from 1.3 mg/dL (eGFR=54 mL/min/1.73 m²

BSA) in May 2019 to 1.86 mg/dL (eGFR=35 mL/min/1.73 m² BSA), 26 days after the kidney biopsy. This represented a 35% loss in kidney function since the biopsy. Thus, there was clearly significant acute kidney injury with a considerable loss of renal function as evident from a comparison of the eGFR changes (Figure 1).

Typically, significant renal impairment in Page kidney has been described in patients with single functioning kidneys as exemplified by lone renal allografts [23,24]. On the other hand, renal insufficiency is not usually seen with unilateral kidney involvement with 2 kidneys because of normal perfusion of the contralateral kidney which therefore maintains normal renal function [4]. Nevertheless, unilateral Page kidney in patients with 2 kidneys uncommonly can still present with worsening renal failure [15-17]. Indeed, in the Page kidney literature, there have been reports of acute kidney injury despite unilateral kidney involvement in a patient with 2 kidneys [15-17]. For example, McCune et al. described an increase in serum creatinine from 2.7 mg/dL to 3.8 mg/dL in a 32-year old white male with previous chronic kidney disease, 12 hours following a percutaneous ultrasound-guided right kidney biopsy [16]. The measured creatinine clearance had decreased from 0.85 mL/second (51 mL/minute) down to 0.58 mL/second (35 mL/minute). Radiologic imaging confirmed the presence of a large perinephric hematoma [16]. In another report, Wijeyesinghe et al. reported a rise in serum creatinine from 1.23 mg/dL to 1.80 mg/dL, 8 days following a leftsided percutaneous renal biopsy in a 29-year old white male with proteinuria, microscopic hematuria, and an active urinary sediment [15]. Ultrasound examination revealed a large left intrarenal and perirenal hematoma despite a normal appearing right kidney [15]. Furthermore, Babel et al. recounted their experience with an 89-year old hypertensive male with a long-standing history of chronic renal insufficiency who exhibited acute on chronic renal failure 3 weeks after a fall with serum creatinine rising from 1.14 mg/dL to 5.7 mg/dL on presentation to the hospital [17]. A non-contrast CT scan showed a large left subcapsular renal hematoma and a possibly atrophic right kidney [17]. One hypothesis to explain acute kidney injury with unilateral Page kidney in a patient with 2 kidneys is that with pre-existing chronic kidney disease, the impacted kidney was the dominant kidney and that the unaffected kidney was diseased from renovascular or other undiagnosed unilateral renal disease conditions [16,17].

From the foregoing, we strongly argue that our patient did in fact have features on admission consistent with Page kidney. Without a doubt, he subsequently experienced superimposed contrast-induced nephropathy following the CT scan and Interventional Radiology Department interventions (Figures 1–3).

The subsequent acute rise in serum creatinine to peak at 3.60 mg/dL on hospital day 3 and then started to improve thereafter is consistent with contrast-induced nephropathy from double iodinated-contrast exposure from the CT scan and selective renal angiography on the day of admission [14]. Contrast-induced acute kidney injury after coil embolization for aneurysmal subarachnoid hemorrhage has been reported [14]. Of note, reports of contrast-induced kidney injury following super-selective renal embolization procedures is rare. Haochen et al. in 2019 described the successful treatment of 43 patients with bleeding complications following percutaneous renal biopsies with super-selective renal artery embolization and mean serum creatinine before and after the procedure had remained unchanged; one caveat was that in this study, all 31 patients with serum creatinine >300 umol/L underwent hemodialysis after the procedure [13]. Nevertheless, 1 out of 15 patients (7%), who underwent splenic arterial embolization in another report, developed contrast-induced nephropathy [25].

Although our patient exhibited near return to admission serum creatinine levels on discharge at hospital day 9, the contrast-induced nephropathy may have contributed to the hiccups as well as to the prolonged length of stay and therefore increased cost of hospitalization. Arguably, some alternative options for the management of the right renal pseudoaneurysm that could mitigated or totally avoid contrast-induced nephropathy call for mention here. Direct ultrasound-guided percutaneous embolization of renal pseudoaneurysm has been reported as an alternative to super-selective renal artery embolization with the touted benefits of the circumvention of contrast media exposure, mitigating the hazards of irradiation, and avoidance of the complications of angiographic catheterization [26]. The Egyptian report in 2009 posited that this method was recommended as a first-line treatment of actively bleeding renal pseudoaneurysms [26]. The successful use of ultra-low volumes of iodinated contrast during radiological examination has been achieved using iodinated contrast that was further diluted with normal saline [27]. Finally, in a 2014 report, Said et al. reported on the novel use of carbon dioxide arteriography during super-selective coil embolization of a renal artery pseudoaneurysm in an 82-year-old female with complicated past medical and surgical history including hypertension, diabetes mellitus, congestive heart failure, and a recent right heminephrectomy with poor renal function [28]. Pre-embolization serum creatinine was 1.85 mg/dL, whereas post-embolization serum creatinine was stable at 1.97 mg/dL and was even lower at 1.6 mg/dL, 6 months later [28].

Conclusions

We described the unusual presentation of Page kidney following an ultrasound-guided percutaneous native right kidney biopsy in a 73-year old male with 2 kidneys that still produced acute kidney injury despite the unilateral kidney insult. Following double contrast exposure from a contrast-enhanced CT scan and Interventional Radiology Department angioembolization to treat an actively bleeding intrarenal hematoma, our patient experienced further worsening of renal failure from contrast-induced nephropathy. In a bid to reduce the incidence of contrast nephropathy in such circumstances as we experienced with our patient, we posit that the study of alternative methods of renal imaging such as carbon dioxide arteriography, the use of dilute contrast medium and other non-contrast methodologies such as direct ultrasound-guided percutaneous embolization call for more intense study and analysis. The alternate therapeutic options to mitigate contrast nephropathy in this setting are revisited.

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Department and Institution where work was done

Department of Medicine, The Robert Larner, M.D. College of Medicine, University of Vermont, Burlington, VT, USA.

Conflict of interest

None.

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