Case Report

Page Kidney Complicating Kidney Biopsy after Stopping Apixaban: A Physician's Dilemma

Abstract

Page kidney was described by Page, following very elaborate experiments with animal kidneys in 1939, with persistent arterial hypertension from "cellophane perinephritis." Subsequently, it was reported after trauma, from renal cysts and tumors, and from intrarenal hematoma complicating percutaneous kidney biopsy. We describe Page kidney associated with acute kidney injury 26 days after an uncomplicated ultrasound-guided right native kidney biopsy. Patient was on Apixaban, a non-vitamin K antagonist oral anticoagulant (NOAC) for atrial fibrillation which was withheld 3 days before the procedure. It was restarted 3 days after. The evidence-base supporting guidelines and recommendations for the peri-procedural management of the NOACs is inadequate, sparse, and often conflicted. More research is warranted.

Keywords: *Acute kidney injury, apixaban, guidelines, hypertension, page kidney*

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Introduction

Page kidney is a rare condition that was first described by Page in 1939 resulting from (external) compression of the kidney(s) with renal dysfunction and hypertension.[1] By 2009, about 100 cases of Page kidney had been reported in the literature.[2] Earlier on, most cases were related to posttraumatic episodes from blunt abdominal trauma.[2] More recently, this syndrome has also been described following intrarenal mechanisms such as sub-capsular and renal parenchymal hematomas, renal cysts, and renal tumors.[2,3] We describe Page kidney complicating ultrasound-guided right native kidney biopsy in a 73-year-old Caucasian male after withholding Apixaban, 3 days before the renal biopsy procedure and had restarted the Apixaban 3 days post-procedure. The evidence-base to guide peri-procedural management of NOACs is inadequate.

Case Report

A 73-year-old Caucasian male was transferred to our Emergency Department with 2 h of excruciating mostly nonradiating acute onset right flank pain. There was no trauma. He had vomited up to three times in the past 2 h. He denied fever, chills, chest pain, dyspnea, abdominal pain, dysuria, hematuria, testicular pain, leg pain, or tingling. He acknowledged that since the kidney biopsy, he had experienced a very low level of right flank discomfort. He had taken 1000 mg of acetaminophen without effect. Past medical history included hypertension, heart failure, and atrial fibrillation on Apixaban 5 mg twice daily for over 2 years. He had an ultrasound-guided right kidney biopsy 26 days earlier. Vital Signs were stable. The abdomen was soft, not distended, and nontender. There was no costovertebral area tenderness. He required intravenous morphine sulfate for pain control, and in addition to IV fluids, he received 2,106 Units of prothrombin complex concentrate infused over 20 min.

The right kidney biopsy was indicated by the earlier change in baseline serum creatinine, 3 years ago, together with a new diagnosis of uveitis by his ophthalmologist. About 3 years prior to the kidney biopsy, the serum creatinine had increased from a baseline of 0.90 mg/dL to a new baseline of 1.2–1.4 mg/dL. Furthermore, he had experienced new symptoms of blurred vision and his ophthalmologist, about a year before the biopsy, had made a diagnosis of right-sided anterior uveitis. There was, therefore, a suspicion that he may

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be exhibiting features of Tubulointerstitial Nephritis and Uveitis (TINU). However, serum creatinine had remained stable at about 1.30 mg/dl for 2 years prior to the kidney biopsy. He had withheld the Apixaban for 3 days before the right kidney biopsy. Protime INR was 1.1 and PTT was 13.2s on the day of the kidney biopsy. Using 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 patient tolerated the procedure well and there were no immediate complications. Postbiopsy renal ultrasound was normal. He had restarted Apixaban 3 days after the kidney biopsy. During the kidney biopsy, three passes were made using the 18-gauge core needle. The pathology report described three tan, cylindrical tissues, each 1.2 cm in length and 0.1 cm in diameter. The kidney biopsy demonstrated hypertensive nephrosclerosis, moderate interstitial fibrosis, and mild interstitial chronic inflammation.

Urinalysis showed trace ketones, 2+ blood, and 2+ protein. Serum creatinine was increased at 1.86 mg/dl; it was stable at 1.31 mg/dL in May 2019, a month before the kidney biopsy [Figure 1]. Electrolytes were normal. The WBC was 12 K/cmm, platelet count was 234 K/cmm, and hemoglobin was 11.7 g/dL just slightly lower than a level of 12.0 g/dL, 8 months prior. Admission protime INR was 1.3 (0.9–1.1) and PTT was 15.5s (10.3–13.4).

A contrast-enhanced CT examination of the abdomen and pelvis (100 cc) revealed an intra-parenchymal hematoma in the lower pole of the right kidney measuring up to 5.9 cm with evidence of active intrarenal bleeding. Interventional Radiology was consulted and he quickly underwent a selective renal angiography with coil embolization of a ruptured pseudoaneurysm [Figure 2].

He received IV fluids, and for the leukocytosis, he received empiric antibiotics for suspected pneumonia. During the hospitalization, serum creatinine progressively increased and peaked at 3.60 mg/dL on hospital day 3 and thereafter improved and was 1.96 mg/dl when he was discharged on hospital day 9 [Figure 1]. Notably, within 24 h of the admission, he had developed persistent hiccups that at times were as frequent as 10–15 times/minute. He needed the combination of oral Metoclopramide 5 mg TID, Gabapentin 100 mg/d, and Baclofen 2.5 mg every 6 h to control the hiccups. He was discharged on hospital day 9, feeling much better, with no flank pain and reduced hiccups.

Discussion

The working diagnosis was that of Page kidney producing the initial increase in serum creatinine from a baseline of 1.31 mg/dL to 1.86 mg/dl on admission[1,3] [Figure 1]. Serum creatinine, which was stable for the previous 2 years was 1.31 mg/dL 4 weeks before the kidney biopsy. On admission, the serum creatinine had significantly increased to 1.86 mg/dL, consistent with acute kidney injury associated with Page kidney.[1-3] He subsequently developed reversible contrast-induced nephropathy following the double exposure to iodinated contrast on admission day–first, from the contrast-enhanced CT examination, and second, during the coil embolization procedure[4] [Figure 1].

Our patient exhibited the features of Page kidney on the evaluation of the acute new-onset right flank pain 26 days following an apparently uncomplicated ultrasound-guided right native kidney biopsy given that the post-biopsy sonogram revealed no evidence of hemorrhage. He had withheld the Apixaban 3 days before the biopsy and restarted 3 days following the biopsy. A review of the literature confirmed that in 2019, there is still a paucity of evidence-base to support such guidelines.[5-11] The recommendations as to the length of withholding before procedure, and the appropriate time to restart the NOAC remain unclear and sometimes speculative.[5,7-11] Moreover, the impact of renal impairment, creatinine clearance, the different NOACs, and the risk categorization of procedures remain conflicted.[7-11] Nevertheless, Ema *at*

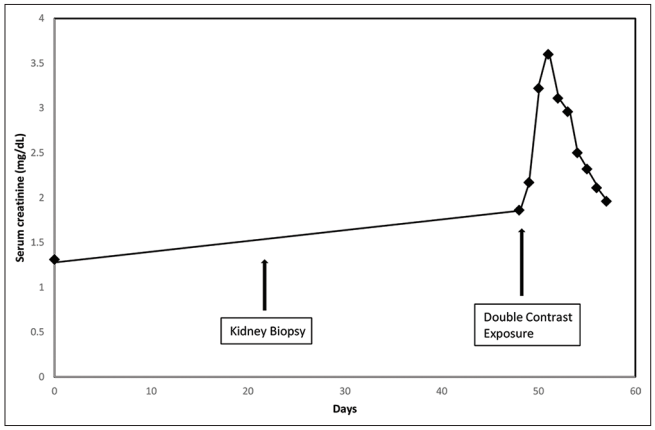

Figure 1: Serum creatinine trajectory before the native kidney biopsy and following recent hospital admission for selective renal arterial embolization

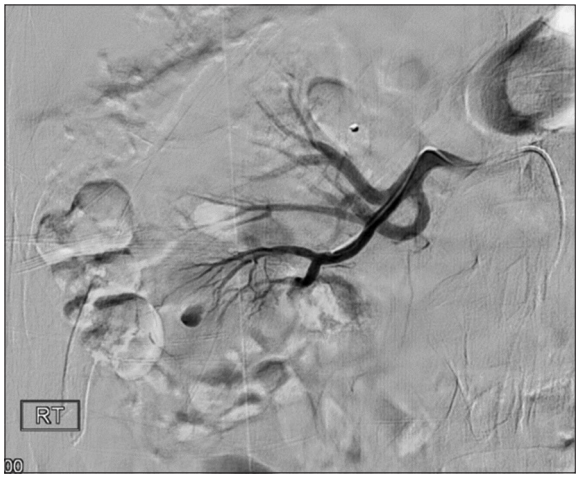

Figure 2: Selective renal embolization of a right renal pseudoaneurysm

el. recently described postoperative hemorrhage after right upper lobectomy in a 76-year-old Japanese man, where Apixaban 5 mg twice daily was withheld for 3 days before the procedure and was restarted 10 days after.[6]

We conclude that the evidence-base for the peri-procedural management of the NOACs remains inadequate. Most reports and recommendations support holding Apixaban for 72 h before high-risk procedures.[5,7-11] The utility of plasma levels of NOACs remains unclear but it would appear that a preoperative plasma level of NOACs below 30 $ng.ml^{-1}$ is a safe bet for postprocedure bleeding risk[5,11] In addition, a standard heparin-calibrated anti-Xa level of <0.1 $IU.ml^{-1}$ is reported to indicate sufficient reduction in the anticoagulant effect of the NOAC[5,11] The impact of limiting the number of passes at kidney biopsy on bleeding complications and compromise on pathologic diagnosis remain uncertain.

One advantage of the NOACs like Apixaban, over Warfarin, is the reduced risk of bleeding complications in treated patients as evident in the ARISTOTLE trial.[12] The rate of major bleeding was 2.13% per year in the apixaban group, as compared with 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60 to 0.80; $P < 0.001$).[12] More research efforts are clearly warranted to revisit these unanswered questions of the appropriate and safe duration of drug withholding of the NOACs before high-risk procedures, when to resume the drug post-procedure and to what extent the degree of renal dysfunction would dictate dose modifications of these agents.[5,8-12]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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