Unexplained occurrence of multiple de novo pseudoaneurysms in patients with chronic kidney disease undergoing angioembolization for bleeding following percutaneous renal intervention: Are we dealing with infection or vasculitis?

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ABSTRACT

Background and Objectives: Patients with chronic kidney disease (CKD) are more prone for bleeding following percutaneous renal intervention, as compared to those with normal renal function. Causes are multi-factorial. Finding multiple aneurysms away from the site of renal intervention following initial angioembolization for hemorrhage is very unusual in these patients.

Materials and Methods: Clinical and radiological findings of all the patients who underwent renal angiography for post-intervention bleed for a period of 5 years were reviewed and analyzed.

Results: A total of 29 patients required angiography for post-intervention hemorrhage. Six patients had recurrence of hemorrhage for which they underwent repeat angiography. Four of these patients had appearance of multiple new aneurysms away from the site of percutaneous nephrostomy (PCN)/percutaneous nephrolithotomy (PNL) puncture and the site of previous bleeding. All the patients had CKD (creatinine >2.5 mg/dl). They were on prolonged preoperative urinary diversion and had polymicrobial urinary infection. Three patients had candiduria. None of these patients had re-bleeding after repeat embolization and treatment with antibacterial and antifungal agents.

Conclusions: Development of multiple aneurysms away from the sites of punctures in patients with CKD following percutaneous intervention is very unusual. Its causation including infection with bacteria and fungus, reaction of embolizing material, and angiopathy needs to be explored.

Key words: Angioembolization, chronic renal failure, hemorrhage, percutaneous nephrostomy, pseudoaneurysm, recurrent

INTRODUCTION

Percutaneous nephrostomy (PCN) and percutaneous nephrolithotomy (PNL) are established minimally invasive renal interventions. Improvement in understanding of vascular and renal calyceal anatomy, refinement of the techniques and technology, and increasing experience in the last two decades have led to increased safety and efficacy of these procedures. However, complications still do happen; perioperative hemorrhage is one of the most dreadful complications. Fortunately, most of the hemorrhage is venous in origin and conservative measures are adequate. Arterial bleeding, although rare, needs angioembolization with a high success rate of 93-95%. Recurrent hemorrhage after angioembolization is unusual and is mostly because of failure to demonstrate bleeding vessels at initial angiography or due to migration of embolizing material. Recurrent bleeding is almost always at the site of renal intervention. We encountered unusual findings of bleeding from new lesions away from initial intervention site on repeat angiography with recurrent bleeding after initial angioembolization. We present the management and possible explanations for such occurrences.
MATERIALS AND METHODS

Clinical, microbiological, and radiological findings of all the patients who underwent renal angiography for post-renal biopsy, post-PCN, or post-PNL bleed for a period of 5 years were reviewed. Preoperative renal function, presence of any coagulopathy, renal diversion if any, microbiological status of urine, site of puncture, number of puncture, per-operative bleeding complications, postoperative hematuria requiring blood transfusion, need of embolization, recurrence of bleeding, and their management and outcome were analyzed.

RESULTS

Totally 29 patients underwent angiography for post-percutaneous renal intervention bleeding and 28 of them required embolization of the bleeding vessels; post-embolization check film confirmed successful control of hemorrhage. In one patient, initial angiography did not demonstrate any vascular lesion and the bleeding site. Six patients had recurrence of bleeding and hematuria for which they underwent repeat angiography. In two patients, repeat angiography revealed bleeding from the site of previous puncture; in one of them, bleeding was due to migration of embolizing material and in the second patient previous angiography had not revealed the bleeding site. In the remaining four patients, recurrence of bleeding was due to new pseudoaneurysms located well away from the site of PCN/PNL puncture and the site of previous bleeding [Figures 1-3]. Suitable antibacterial and antifungal agents (Fluconazole) were administered and selective embolization of the bleeding vessel was performed in view of continued bleeding. None of them had recurrence of bleeding during follow-up [Table 1].

DISCUSSION

PCN has become an increasingly acceptable therapeutic alternative, both for high-risk patients and for patients in whom the procedure offers delay or avoidance of major surgery. Lower incidence of major morbidity, early palliation of symptoms, and convalescence are its major advantages. PNL is a relatively safe and reliable operative technique even for large, multiple, and staghorn renal calculi. However, this invasive procedure is associated with a complication rate of 3-18%.[4,5] One of the most serious complications is renal hemorrhage with a transfusion rate of 3-23%.[3,4,6] Venous bleeding can be controlled with conservative measures, such as clamping the nephrostomy, hydration and diuretics, hemostatic medications, and balloon tamponade.[7,8]

Arterial bleeding requiring intervention is uncommon (0.3-1.4%).[6] Arterial injury can cause severe intraoperative bleeding and may lead to formation of pseudoaneurysm or arteriovenous (AV) fistula later. Their rupture can cause delayed bleeding[9] and in the majority (more than 90% of cases) can be managed by superselective embolization.[3,6,10]

Recurrent bleeding after angioembolization is rare. This is mostly because of failure to demonstrate some bleeding vessels at initial angiography, as was observed in one of our
cases. Use of papaverine during angiography has reduced the chances of missing any injured artery because of spasm.\(^ {11,12}\) Rarely, migration or dissolution of embolizing material may lead to recurrent bleeding. Recurrent bleeding is almost always from lesions at the site of previous puncture. Finding recurrence of bleeding from aneurysms located away from the site of puncture is unusual. All of our four patients in whom recurrence of bleeding was detected from aneurysm located away from the site of intervention had initial successful embolization of the bleeding artery documented on post-embolization check angiography. All these patients had single puncture during the procedure, and therefore does not explain the development of new lesions well away from the site of intervention. Despite extensive search of English literature, we did not come across any report of similar occurrence. We are intrigued by noticing such incidences and have tried to find explanations for the same.

All these patients had some common findings:
- Chronic kidney disease (CKD; baseline serum creatinine 2.5-5.0 mg/dl)
- Prolonged urinary diversion (with PCN in three and DJS in one)
- Polymicrobial urinary tract infection (Escherichia coli in two, Pseudomonas in two, and Proteus in one)
- Candiduria (in three patients)
- None of them had recurrence of bleeding after repeat angiembolization and treatment with antibiotic and antifungal agents.

Patients with chronic renal failure (CKD) are known to have coagulopathy and are prone to have more bleeding after any surgery.\(^ {13-15}\) It has been shown that the risk of peri-operative bleeding increases with the degree of renal insufficiency. Patients with advanced renal insufficiency [estimated glomerular filtration rate (GFR) of <40 ml/min] have a sixfold increase in the risk of severe bleeding postoperatively, and even those with mild levels of renal insufficiency (estimated GFR of 61-80 ml/min) have a twofold increase in the risk of serious postoperative bleeding as compared to patients with normal renal function, after adjusting for coagulation status and platelet function.\(^ {16}\) However, CKD per se is not known to cause vascular lesions like pseudoaneurysm and AV fistula. Moreover, in our patients, these lesions developed acutely after initial angiography. All these patients had normal coagulation profile including bleeding time. CKD patients are immune-compromised and are more prone to infection. Polymicrobial colonization of urinary tract of our patients can be attributed to both CKD and prolonged diversion with DJ stent/PCN tube.

One of the possibilities of development of these intrarenal aneurysms is infection. Mycotic aneurysm develops from any infectious process involving an arterial wall. Infection can occur in several ways:\(^ {17,18}\) (1) Lodgment of septic emboli, most commonly at points of branching, sites of rapid tapering, on sharp bends in a normal vascular tree, and with resultant destruction of the media and weakening of the arterial wall; (2) lodgment of bacteria in vasa vasorum or on diseased intima, such as atherosclerotic plaques, with resultant weakening of the wall; (3) contiguous spread from a localized area of inflammation or infection, with destruction of the arterial wall and formation of a pseudoaneurysm; and (4) injury to an artery, with concomitant contamination and subsequent formation of an infected pseudoaneurysm. Once the infection is established, progression depends

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**Table 1: Demographic profiles and clinical details of the patients**

| Age, sex | Disease | Diversion duration | Baseline creatinine (mg/dl) | Urine C/S | Procedure/puncture site | Initial bleeding: Day, site | Re-bleeding day, site | Follow-up period, creatinine level, status |
|----------|---------|--------------------|---------------------------|-----------|--------------------------|-----------------------------|--------------------------|------------------------------------------|
| 22 years, M | B/L renal stone | B/L PCN, 3 months | 2.5 | Proteus, Candida albicans | LT PCNL/ inferior calyx | 3rd day, lower division of anterior middle segmental artery, inferior pole | 8th day, peripheral, upper division of anterior middle segmental artery | 26 months, 2.7 mg/dl, alive |
| 56 years, M | Recurrent stone former, B/L RSD | LT DJS, 2 months | 3.5 | Pseudomonas | LT PCNL/ middle calyx | 2nd day, branch of posterior segmental artery, mid pole | 4th day, anterior apical and upper segmental artery, superior pole | 9 months, 3.9 mg/dl, died of cardiac cause |
| 45 years, M | Solitary functioning LT kidney with stone | LT PCN, 4 months | 5.0 | Escherichia coli, Pseudomonas, Candida albicans | LT PCNL/ middle calyx | 3rd day, multiple anterior middle segmental arteries, mid pole | 7th day, peripheral, anterior lower segmental artery, inferior pole | 21 months, renal transplant 1 year back, alive |
| 47 years, M | B/L ureteric stone | B/L PCN, 4 months | 3.0 | Escherichia coli, Candida albicans | LT URS and Rt PCN change/ inferior calyx | 3rd day, lower division of anterior middle segmental artery, right kidney inferior pole | 9th day, apical and upper segmental branch of anterior div. and branch of posterior segmental artery, upper and mid pole | 37 months, Lt ureterolithotomy 4 months back, 6 mg/ dl, maintenance hemodialysis |

PCN=percutaneous nephrostomy, PCNL=percutaneous nephrolithotomy, URS=ureterorenoscopy, RSD=renal stone disease, M=male, B/L=bilateral
mainly on the virulence of the organism and the rapidity of destruction of the arterial wall.[17,19,20] Mycotic aneurysms have a very high incidence of rupture, with life-threatening hemorrhage as a direct consequence.[21]

All our patients had predisposing conditions for formation of mycotic aneurysm: Longstanding foreign body (PCN/DJ stent), resistant polymicrobial infection, fungal colonization, and immune-compromised status. However, in all these patients, no vascular lesions were seen other than at the site of puncture during the first angiography and angioembolization. All of them had rapid development (4-9 days) of small, often multiple, eccentric, peripherally placed pseudoaneurysms away from the site of previous puncture after first embolization. Whether introduction of micro-organism during angiographic intervention (injection site, catheters, contrast or embolizing materials) was additionally the cause of these aneurysms is difficult to comment upon.

Hence, in the light of above discussion, there is a strong possibility of mycotic aneurysms developing in the contaminated system with immuno-compromised patient. After second embolization, these patients received long course of bactericidal and fungicidal antimicrobials and did not have recurrence of hemorrhage. The limitation of this study was lack of histopathologic or direct microbiological evidence in favor of our “infective” or “vasculitis” hypothesis; this would have required percutaneous renal biopsy from the new pseudoaneurysm site. This was decided to avoid another potential bleeding complication in an already bleeding patient. Therefore, the diagnosis of mycotic aneurysm remains only circumstantial and logical, thus speculative. Nevertheless, despite these limitations, we do believe that in such high-risk infective setting, possibility of mycotic aneurysms should be considered and timely introduction of appropriate antimicrobials is prudent. Further studies would be required to prove our speculation.

CONCLUSIONS

Development of multiple aneurysms at sites away from punctures in patients with CKD following percutaneous renal intervention is very unusual. Its causation including infection with bacteria and fungus and resultant angiopathy needs to be explored.

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