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Permalink

<https://escholarship.org/uc/item/24x4j10s>

Journal

Journal of Endourology Case Reports, 6(4)

ISSN

2379-9889

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Publication Date

2020-12-01

DOI

10.1089/cren.2020.0019

Peer reviewed

Thrombocytopenia Preceding Urosepsis in an Otherwise Asymptomatic Patient After Bilateral Retrograde Intrarenal Surgery

Lillian Xie, BA, Catherine Nguyen, MD, and Ralph V. Clayman, MD

Abstract

Introduction and Background: Urosepsis is commonly predicted by the systematic inflammatory response syndrome (SIRS) criteria. We report a case of urosepsis preceded only by thrombocytopenia.

Case Presentation: An 80-year-old Caucasian female presented with recurrent urinary tract infections, type 1 second-degree heart block (Mobitz I), and chronic deep venous thrombosis for which she was taking apixaban. Computed tomography (CT) revealed a 1.3 cm right upper pole calculus (Hounsfield units (HU)=704) and a left 5 mm nonobstructing interpolar calculus (HU=904). A preoperative urine culture was sterile as the patient was on antibiotics. While on antibiotic coverage, the patient underwent bilateral retrograde intrarenal surgery with bilateral stent placement: the procedure time was 188 minutes. She was continued on vancomycin and gentamicin immediately postoperatively. On postoperative day (POD) 1, she was feeling well; her vital signs were within normal limits. However, the hemoglobin and the platelet counts declined from 12.4 to 10.0 g/dL and from 215 to 58/mm³, respectively. Because of the unexplained thrombocytopenia, the patient was kept at the hospital. In the afternoon, she became hypotensive (78/37 mm Hg) and a rapid response was called. She was admitted to the surgical intensive care unit and antibiotics were broadened. On POD 2, the patient met sepsis SIRS criteria with white blood cell (WBC) of 2.9/mm³ and heart rate of 92 bpm. Stone culture was positive for methicillin-resistant *Staphylococcus aureus* (MRSA). On POD 3, her blood pressure had returned to 116–142/47–84. On POD 5, platelet count recovered to 94/mm³ and WBC to 3.8/mm³. She was discharged on POD 6 with a 2-week ongoing course of intravenous vancomycin. On follow-up 7 weeks postoperatively, she was asymptomatic with WBC of 6.5/mm³ and platelet count of 206/mm³. Follow-up CT demonstrated normal renal anatomy with subcentimeter calculi clustered within the left renal parenchyma and no stones on the right side.

Conclusion: This case shows an uncommon non-SIRS presentation of postoperative urosepsis signaled only by thrombocytopenia.

Keywords: urosepsis, thrombocytopenia, bilateral retrograde intrarenal surgery

Introduction and Background

THE CLASSIC SIGNS AND SYMPTOMS of sepsis are fever, tachycardia, tachypnea, and respiratory alkalosis. Laboratory evaluation usually reveals leukocytosis or leukopenia. The systemic inflammatory response syndrome (SIRS) criteria identify four conditions for predicting patients with sepsis: temperature >38°C or <36°C, heart rate >90 bpm, respiratory rate >20 or PaCO₂ <32 mm Hg, and white blood

cell count (WBC) >12,000/mm³ or <4000/mm³. To meet SIRS criteria, patients must demonstrate ≥2 of the conditions.¹ We report an unusual case of urosepsis preceded only by thrombocytopenia in the absence of SIRS criteria.

Case Presentation

An 80-year-old woman presented with a history of recurrent urinary tract infections (UTIs) with methicillin-resistant

Staphylococcus aureus (MRSA), type 1 second-degree heart block (Mobitz I), and chronic deep venous thrombosis for which she was receiving apixaban. The patient's surgical history included a colostomy for diverticulitis and a bowel resection for a rectal to gluteal skin fistula. Medical history and family history were negative for urolithiasis. Review of systems was unremarkable. Physical examination revealed blood pressure of 129/64, heart rate 74 bpm, and respiration rate of 16; there was a Grade 3 systolic ejection murmur. Laboratory results showed hematocrit 37.2%, hemoglobin 12.4 g/dL, platelet count 215/mm³, WBC 5.8/mm³, and creatinine 0.7 mg/dL, with normal electrolytes including calcium of 9.6 mg/dL.

Renal ultrasonography demonstrated bilateral nonobstructing urolithiasis without hydronephrosis. Subsequent computed tomography (CT) scan revealed a right-sided 1.3 cm upper pole calculus (HU = 704) and a 5 mm nonobstructing left interpolar calculus (HU = 904 without hydronephrosis (Fig. 1). Given the recurrent infections with MRSA, the patient was scheduled for elective bilateral ureteroscopy, holmium laser lithotripsy, and stent placement. Her urine culture was sterile preoperatively.

The patient received 1000 mg of vancomycin prophylactically. After placement of a 14F access sheath on the right, the patient underwent flexible ureteroscopic RIRS with a reusable Storz Flex XC 8.5F ureteroscope, holmium laser lithotripsy (270 μ m laser fiber at 1 J and 10 Hz), stone basketing, and stent placement; irrigation pressure was 100 mm Hg at time of access sheath insertion and varied between 150 and 200 mm Hg during the procedure whenever the working port was occupied with a laser fiber or a stone basket. This process was repeated on the left side. The procedure time was 188 minutes. No stones were identified when all calices were initially inspected. However, a pinhole dimple was noted where one would have anticipated a middle caliceal infundibulum on the left. When the laser was used to further open this area, stone fragments were found and cloudy fluid drained from the obstructed calix. Owing to concern that this might be infected stagnant urine, genitourinary irrigant was immediately added to the regular irrigant as further antibiotic protection while irrigation pressure was maintained given the passage of the laser fiber at this point in the case. The stone fragments were washed out completely from the calix. At the end of the case, the left

ureter had a Post-Ureteroscopy Lesion Score (PULS) of 0 and the right ureter had a PULS of 2.

That evening, the patient received a second dose of vancomycin and was started on gentamicin because of suspected stone infection. She was given one dose of heparin as apixaban was discontinued preoperatively. She was kept overnight because of the concern of possible sepsis. However, on the morning of postoperative day (POD) 1, she was feeling well, urine was clearing nicely, and her laboratory results were within normal limits except for an inexplicable acute thrombocytopenia: 58/mm³. As such, it was elected to not discharge her as previously planned.

At 5 PM, she had an episode of hypotension to 78/37 for which a rapid response was called. Her temperature was 99.0°F, heart rate was 46 bpm, and respiratory rate was 15. Heparin-induced thrombocytopenia (HIT) antibody count was 0.072 (normal \leq 0.399).

The patient was transferred to the surgical intensive care unit and antibiotics were broadened to include vancomycin and tazobactam/piperacillin. Blood cultures were negative. However, the stone culture was positive for MRSA. Hematology was consulted given acute changes in blood count and recommended continuing heparin 2.5 mg twice daily. Of note, it was not until POD 2 that she met SIRS criteria with WBC of 2.9/mm³ and heart rate of 92 bpm. By POD 3, her hypotension had resolved. Prothrombin time (PT) was 15.6 seconds, partial thromboplastin time (PTT) was 33.8 seconds, fibrinogen was 395 mg/dL, and D-dimer was 450 mg/mL. Blood count demonstrated a platelet count of 31/mm³ and WBC of 2.3/mm³. On POD 5, platelet count was 94/mm³ and WBC was 4.8/mm³. The patient was discharged on POD 6 with a 2-week course of vancomycin. Her stents were removed without incident 1 week later. On follow-up 7 weeks postoperatively, she was asymptomatic with WBC of 6.5/mm³ and platelet count of 206/mm³, although repeat urine culture was positive for gram negative rods and yeast. No treatment was elected at the time as the patient was asymptomatic; however, the department of hematology and oncology elected to analyze her IgG counts given her history of recurrent UTI. Her follow-up CT scan showed normal renal anatomy with a 2 mm and 4 mm calcification side by side in the lower pole suggestive of a dilated calyx or dystrophic calcification within scarring, and no stones on the right side.



FIG. 1. Preoperative CT scan showed (A) 12.9 mm right-sided calculus (HU = 704) and (B) 5 mm left-sided calculus (HU = 904). HU, Hounsfield units.

TABLE 1. PLATELET-TO-LEUKOCYTE RATIO OF PATIENT OVER TIME

	Platelet count (/mm ³)	WBC (/mm ³)	PLR	Notes
6 months preoperation	218	8.2	33.0	
4 months preoperation	197	6.6	34.6	
1 month preoperation	215	5.7	37.1	PLR >18.4 at baseline
POD 1 05:10	58	5.8	10.4	BP 99/54 HR 88 RR 16 Temp 98.3 F
POD 1 10:15	54	5.6	11.7	BP 109/55 HR 88 RR 18 Temp 99.1 F
POD 1 17:10	41	4.6	14.6	Rapid response called for BP 78/37. HR 46 RR 15 Temp 99.0 F.
POD 1 23:00	35	2.8	12.1	Patient first satisfies SIRS criteria.
POD 2	31	2.3	13.5	
POD 3	32	3.0	10.7	
POD 4	52	3.8	13.7	
POD 5	94	4.8	19.6	

BP, blood pressure; HR, heart rate; PLR, platelet-to-leukocyte ratio; POD, postoperative day; RR, respiratory rate; SIRS, systematic inflammatory response syndrome; WBC, white blood cell.

Discussion

Thrombocytopenia can be associated with sepsis.² The up-regulation of surface cluster of differentiation markers leads to increased platelet activation and consumption of platelets in septic patients. The severity of thrombocytopenia correlates with the likelihood of organ failure; severe thrombocytopenia (platelet count <50/mm³) is associated with increased mortality, increased disease severity, and poorer prognosis.² Although 20%–58% of septic patients develop thrombocytopenia,² it is less clear whether thrombocytopenia by itself might be the initial harbinger of sepsis.

In a literature review, we found no case reports demonstrating postoperative thrombocytopenia as the sole sign of pending urosepsis. However, with regard to thrombocytopenia and infection, Elbaset et al. reported that among patients with emphysematous pyelonephritis, a low platelet-to-leukocyte ratio (PLR) (i.e., ≤18.4) was a risk factor for urosepsis.³ Our patient's preoperative PLR ranged from 33.0 to 37.1 (Table 1); however, within 18 hours of surgery, it fell to 10.4 because of her severe thrombocytopenia. Of note, our patient did not meet SIRS criteria until 20 hours after her initial PLR of 10.4 (Table 1). By POD 5, her PLR had returned within the normal range at 19.6.

The differential diagnosis for acute thrombocytopenia includes disseminated intravascular coagulation (DIC), antiplatelet antibodies, and pathogen-induced thrombocytopenia. DIC is diagnosed by a rise in PT, PTT, and D-dimer, and decreased fibrinogen. These laboratory values were all within normal range for our patient, except for a slightly elevated PT. With regard to the possibility that antiplatelet antibodies caused acute thrombocytopenia, our patient was on heparin before and after surgery and had a negative HIT antibody assay. In our case, the most likely cause of the thrombocytopenia was pathogen induced; this has been reported in 20%–30% of *Staphylococcus* infections, with the majority associated with septicemia.² Our patient's blood cultures were negative; it is of note that when they were drawn, she was already receiving antibiotics for suspected MRSA given her medical history and the findings at ureteroscopy. In addition, suspicion for infection was high given the pinpoint appearance of the right-sided infundibulum and drainage of cloudy fluid when the infundibulum was opened. The use of higher irrigation pressures could have also increased the

likelihood of urosepsis; however, use of an access sheath has been shown to mitigate the intracaliceal and ureteral pressures significantly and protect against pyelovenous backflow.⁴

In sum, isolated thrombocytopenia in the absence of SIRS proved to be the only sign of impending urosepsis; we call attention to the importance of recognizing sudden postoperative thrombocytopenia as a possible harbinger of life-threatening urosepsis, especially in an elderly patient.

Disclosure Statement

No competing financial interests exist.

Funding Information

Funded through the Curiosity and Innovation Laboratory within the Department of Urology at the University of California - Irvine.

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Abbreviations Used

BP = blood pressure
CT = computed tomography
DIC = disseminated intravascular coagulation
HIT = heparin-induced thrombocytopenia
HR = heart rate
HU = Hounsfield units
MRSA = methicillin-resistant *Staphylococcus aureus*
PLR = platelet-to-leukocyte ratio
POD = postoperative day
PT = prothrombin time
PTT = partial thromboplastin time
PULS = Post-Ureteroscopy Lesion Score

RIRS = retrograde intrarenal surgery
RR = respiratory rate
SIRS = systematic inflammatory response syndrome
UTIs = urinary tract infections
WBC = white blood cell

Cite this article as: Xie L, Nguyen C, Clayman RV (2020) Thrombocytopenia preceding urosepsis in an otherwise asymptomatic patient after bilateral retrograde intrarenal surgery, *Journal of Endourology Case Reports* 6:4, 256–259, DOI: 10.1089/cren.2020.0019.