CASE REPORT

We bleed whole blood: A missed opportunity for antibiotic stewardship in a case of hemarthrosis

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ABSTRACT

We present a case of traumatic hemarthrosis misdiagnosed as a left knee prosthetic joint infection (PJI); a case which serves as an educational opportunity for investigating PJI in the setting of a recent trauma and displays a missed opportunity for antibiotic stewardship.

The patient is a 66-year-old female with a history of left total knee arthroplasty (TKA) who is seen in the emergency department with left knee pain, stiffness, and swelling after a ground level mechanical fall. Her symptoms inhibited ambulation and the arthrocentesis of her left knee showed a white blood cell (WBC) count of 1,466 cells/mcL as well as a 438,000 cells/mcL red blood cell (RBC) count; the differential also showed neutrophil predominance. The patient was subsequently admitted to the hospital on intravenous antibiotics due to concern for PJI. However, upon infectious disease consultation, the diagnosis was identified as traumatic hemarthrosis without accompanying infection. The patient improved with supportive care and had an uncomplicated discharge and outpatient follow up with no further antimicrobial therapy.

In this article we explain the clinical decision making and evidence-based data points which ruled down PJI and serve to exhibit how this case was a missed opportunity for antibiotic stewardship.

INTRODUCTION

We present a case of suspected left knee prosthetic joint infection (PJI) which is heavily confounded by a history of a mechanical fall and grossly bloody arthrocentesis. This case demonstrates how any diagnostic criteria must be applied

within the broader clinical context and highlights the importance of nuanced decision making to preserve antibiotic stewardship and avoid unnecessary invasive interventions. Our goal is to display these principles and show how specifically in the case of suspected PJI, the clinical context and confounding information must be taken into account when considering the differential diagnosis and need for antibiotics.

CASE PRESENTATION

A 66-year-old female with a history of left total knee arthroplasty (TKA) in 2013, which was complicated by subsequent revision surgery due to wound dehiscence, presented to the emergency department for a second visit. She reported a 2-week history of worsening left knee pain following a ground-level mechanical fall onto her left knee. Her past medical history includes morbid obesity, osteoarthritis, chronic obstructive pulmonary disease, bilateral lower extremity lymphedema, and atrial fibrillation requiring chronic apixaban therapy.

The patient reported that since the fall, she had experienced pain, stiffness, and swelling of the left knee. On initial presentation at symptom onset, the patient was able to ambulate without significant issue and was discharged home after largely unremarkable workup. However, on this second presentation to the emergency department two weeks after her initial fall, her symptoms had progressed to the point of inhibiting ambulation due to pain and swelling.

On examination the patient was afebrile with stable vital signs. There was mild erythema over the left knee with a few superficial excoriations, but no drainage or sinus tracts were observed. The patient declined active range of motion testing of the left knee due to pain but reported soreness and discomfort with passive range of motion. The physical exam was confounded by chronic bilateral lower extremity lymphedema, but there was notable increased swelling around the left knee. The remainder of the physical exam was largely unremarkable.

X-ray series of the left knee showed no osseous abnormalities and confirmed an intact, stable total knee arthroplasty, consistent with the X-ray completed 2 weeks prior. Additionally, lab results showed an unremarkable complete blood count (CBC) and comprehensive metabolic panel (CMP), but inflammatory markers were elevated, with an erythrocyte sedimentation rate (ESR) of 75mm/Hr (normal limit: 0-30mm/Hr) and C-reactive protein (CRP) of 3.41mg/dL (normal limit: 0-0.5mg/dL) which had increased during this 2-week interval from 48mm/Hr and 1.15 mg/dL, respectively.

Orthopedic surgery was consulted and arthrocentesis was performed, yielding grossly bloody fluid. Synovial fluid analysis revealed 81% neutrophils, 10% lymphocytes, and 9% monocytes with a total white blood cell (WBC) count of 1,466 cells/mcL and total red blood cell count of 438,000 cells/mcL with no appreciable crystals on microscopy and a negative gram stain. Due to the elevated synovial fluid WBC count and

neutrophil predominance, the patient was started on empiric intravenous antibiotics (vancomycin and ceftriaxone) and admitted to Internal Medicine with concerns for PJI. An orthopedics infectious disease consultation was also obtained after about two days of empiric antibiotics.

Although initial findings raised concerns for PJI, the presence of grossly bloody fluid and the patient's recent trauma history led to a reconsideration of the diagnosis and deferral of surgical intervention. Later, infectious disease recommended discontinuing antibiotics in light of diagnosing traumatic hemarthrosis rather than PJI.

While the patient never exhibited other infectious signs or symptoms after cessation of antibiotics, the synovial fluid culture did eventually report positive for Cutibacterium acnes (Propionibacterium) after 9 days of culture, though this was favored as likely contaminant. Throughout the remainder of her hospital course, the patient remained afebrile and without meaningful elevations on her daily white blood cell count. Her joint symptoms improved with supportive treatment and physical therapy, and she was later discharged to a skilled nursing facility. Subsequent outpatient follow up revealed no further complication after discharge from the skilled nursing facility back to the patient's home and she continued to recover back to her baseline without further antimicrobial therapy.

DISCUSSION

Antibiotic stewardship is a topic of increasing importance and this case helps to demonstrate that nuanced clinical decision making can aid in upholding those principles. PJI can undoubtedly be a challenging diagnosis to make and is frequently confounded by other joint pathologies including inflammatory arthritis, crystal arthritis, and bloody arthrocentesis and/or trauma.[2] Among the literature there are two common criteria for ruling in PJI (for arthroplasty of hips and knees), the European Bone and Joint Infection Society Criteria (EBJIS)[1] and the 2018 Parvizi Criteria.[3] Table 1 displays both criteria with markers for pertinent positives from our case. Based on the criteria and subsequent scoring, we can see how the Parvizi criteria may provide a more nuanced stratification in giving categories for "not infected", "possibly infected", and "infected" rather than just the sole "likely infected" category from the European criteria which can be easily activated from potentially minimal findings; inferring that risk stratification rather than binary diagnostic thinking may aid in the decision to initiate antimicrobial therapy. This assertion is further supported in that the Parvizi criteria have been found to have a sensitivity of 97.7% and specificity of 99.5%.[3] While many scoring systems have high specificity, the Parvizi sensitivity figures exceed that of the EBJIS and Musculoskeletal Infection Society (MSIS) recommendations, another PJI risk calculator, which show sensitivities of 79.3% and 89% respectively.[3,4] The Parvizi criteria, while not designed to supersede clinical

judgement, can be used as a cornerstone tool in diagnosing PJI.

Table S1. Additional Criteria for Use When Single Diagnostic Criteria for Hip or Knee Periprosthetic Joint Infection (Table 3) are Nondiagnostic

European Bone and Joint Infection Society criteria *suggesting* a hip or knee arthroplasty is *likely infected*[12]				2018 Parvizi criteria for classification of hip or knee arthroplasty as infected, *possibly infected*, or not infected[31,a]	
2 *Likely infected*	1	Clinical criteria	History of recent fever or bacteremia		≥6 Infected 2-5 *Possibly infected* 0-1 Not infected
	1		Previous wound healing problems		
	1	Blood tests	C-reactive protein >1 mg/dL *or* D-dimer >860 ng/mL	2	
	1		Erythrocyte sedimentation rate >30 mm/h[b]	1	
	1		D-dimer >860 ng/mL		
		Synovial fluid tests	>3000 leukocytes/mL (<90 days after arthroplasty) or >10,000 (>90 days after arthroplasty) leukocytes/mL or leukocyte esterase ≥ ++	3	
	1		>1500 leukocytes/mL[c]		
			Positive alpha-defensin	3	
			Percent neutrophils >90% (<90 days after arthroplasty) or percent neutrophils >80% (>90 days after arthroplasty)[d]	2	
	1		Percent neutrophils >65%[d]		
	1		C-reactive protein >6.9 mg/L	1	
	1		Leukocyte esterase ≥ ++		
	1	Radiology tests	Positive WBC scintigraphy[e]		
	1		Radiographic evidence of loosening within five years after implantation		
		Preoperative score (from above)		Sum of above	≥6 Infected 4-5 Inconclusive[f] ≤3 Not infected
	1	Intra-operative tests	Positive histopathology	3	
	1		Purulence[f]	3	
	1	Culture	Single positive culture	2	

[a]Listed criteria may not apply with crystal arthropathy, adverse local tissue reaction, inflammatory arthropathy flares, or slowly growing organisms (e.g., *Cutibacterium acnes*, coagulase-negative staphylococci).
[b]Applies >90 days after arthroplasty.
[c]May not apply with adverse local tissue reaction or crystal arthropathy.
[d]Levent et al. (J Arthroplasty 2021;36:3728-33) suggest that percent neutrophils should have an increased score.
[e]WBC scintigraphy positive if uptake increased on 20-hour scan, compared to earlier scans (particularly with corresponding bone marrow scan).
[f]Interpret with caution in the early postoperative period or when other possible causes of inflammation are present, including metallosis, hemarthrosis, crystal arthropathy, active inflammatory joint disease (e.g., rheumatoid arthritis), or periprosthetic fracture.
[g]Consider molecular diagnostic testing.

Furthermore, interpretation of notable data points should be analyzed in the broader clinical context; such as the case for synovial fluid WBC count as in our case complicated by hemarthrosis. As noted in Table 1, the criteria for indicating PJI utilize different thresholds for synovial fluid WBC counts; and it is recommended to use caution while interpreting these results when other possible causes of inflammation may be present. Congruently, Ottink et al suggest a formula for calculating synovial fluid WBC counts in the setting of a bloody arthrocentesis: adjusted WBC synovial = actual WBC synovial - [(WBC blood / RBC blood) × RBC synovial].[2] This tool serves to correct for the gross bleeding of both WBCs and RBCs into the joint space and yield a data point which can specify a reliable synovial fluid WBC count relative to the proportional WBC count of the patient's systemic circulation. When applied to our patient's results from the day of her admission, we find a negative value for a raw synovial fluid WBC count, suggesting remarkable RBC predominance and likely subsequent decline of intra-articular WBCs following the inciting event and initial bleed; thus ruling down a PJI. While there is not widespread data investigating the validity of this formula it may serve as an additional tool when considering the broader clinical context of intra-articular pathology.

As for the culture growing Cutibacterium acnes, this finding must also be taken into the broader clinical context. As discussed, PJI was ruled down throughout hospital course. Additionally, Cutibacterium acnes and its role as an intra-articular pathogen versus contaminant is an area of ongoing study and the body of literature is largest for shoulder involvement.[5] However, data still suggest that this common skin flora can contaminate cultures taken via arthrocentesis and that Cutibacterium acnes can even represent intra-articular colonization without infection.[6] These findings further necessitate nuanced clinical decision making in the case of an intra-articular culture positive for Cutibacterium acnes.

Given the patient's lack of infectious signs or symptoms (no leukocytosis or fever) and data points comprising of the patient's Parvizi score and adjusted synovial fluid WBC count, the diagnosis of traumatic hemarthrosis was favored in place of PJI and further antimicrobials were appropriately withheld. Furthermore, given the role of stewardship demonstrated in this case, it is also important to consider the benefits of a dedicated bone and joint infectious disease

service that works closely with hospitalists and orthopedic surgeons. This specialized team which may function function in addition to a general infectious disease service is not necessarily a new concept but one that could serve to improve stewardship and outcomes amongst patients with orthopedic related infections. Infectious disease colleagues bring qualitative value in recommendations for precise diagnostic testing, expertise in drug selection, and subsequent outpatient monitoring and follow-up.[7] One such example has been demonstrated in cases of osteomyelitis managed by orthopedists in conjunction with an infectious disease specialist which resulted in a markedly decreased risk for relapse as compared to cases managed by orthopedics services alone.[8] It is strongly favored both by infectious disease providers as well as surgeons that infectious disease services should be expanded to support an orthopedics specific service whenever possible.[7,9]

In summation, the data did not support treatment with antibiotics or subsequent surgical intervention. On review, the patient was ultimately treated accordingly through consultation of an orthopedic infectious disease service, but her case serves as a missed opportunity for antibiotic stewardship and provides a specific educational opportunity when considering PJI in the setting of trauma.

Notes

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