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Infectious Arthritis Leading to Rapid Septic Shock in a Patient with SLE, Leukopenia, and End Stage Renal Disease: A Case Presentation and Cautionary Notes

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Abstract

Septic arthritis can be associated with significant morbidity, and cause substantial mortality, especially if the diagnosis is delayed. We present here a case of a young woman with a diagnosis of SLE and chronic pain syndrome that progressed to septic shock within hours of presenting to the Emergency Department. It has been emphasized in that the key to treatment of septic shock is early, almost immediate recognition and the institution of aggressive fluid resuscitation and appropriate antibiotic treatment. The importance of prompt and timely diagnosis of the septic joint is well appreciated, but the time course is usually considered to be within the day, and the notion of the "golden hour" for septic shock is not often considered.

One important consideration is that a synovial fluid WBC of greater than 50,000 or even more specifically 100,000 with differential of 90% PMNs is commonly cited as indicating bacterial arthritis. Our patient, found to be neutropenic, had a joint fluid WBC of 9000. One needs to be vigilant for the possibility of septic arthritis in a neutropenic patient with a low synovial white count.

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Copyright © 2020 Richard J Nierenberg. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Finally, one area which is troubling or illuminating about the care of our patient is to question what effect a prior suspicion of pain medication seeking behavior may have had on the pace of her evaluation. In an era of changing perceptions regarding opioid use and increased sensitivity to the possibility of pain management seeking, one has to be increasingly careful to avoid bias and minimization of symptoms.

Introduction

Septic arthritis is known to be the most threatening of the multiple causes of acute joint pain [1-3], and can be associated with significant morbidity, including permanent joint dysfunction. If the joint infection leads to sepsis it can cause substantial mortality, especially in cases involving immune-compromised patients [4,5], unusual organisms [6-10], and delay of diagnosis [5]. The time frame commonly cited for necessary intervention, however, within the first 48 h, is on a different order than that routinely emphasized for other instances of sepsis. In sepsis the notion of a "golden hour" has been found such that each single hour of delay worsens mortality from sepsis [11]. The caveat of extreme time urgency most emphasized with other presentations of sepsis is not customarily part of the literature of septic joints.

Many times we view, in retrospect, that we have not managed a case as quickly and effectively as we might have liked. Often such reflection falls into the realm of straightforward quality assessment, material considered appropriate for the standard intradepartmental "mortality and morbidity' rounds. There are times, however, when a clinician believes both that he and she might have handled a case more expeditiously and also that the case itself was interesting, unusual, confusing or unanticipated enough that it merits review in a broader forum. When the patient has ultimately done well, it is possible to share that learning opportunity more openly.

We present here a case of a young woman with a diagnosis of Systemic Lupus Erythematosis (SLE), End Stage Renal Disease on hemodialysis (ESRD), and chronic joint pain that progressed into septic shock within hours of presenting to the Emergency Department. We were able to draw lessons from the rapidity of this patient's deterioration that we believe can apply to all patients presenting with joint pain. We also draw lessons with regard to the care of patients who have indwelling venous catheterization, commenting both on the evaluation and use of such devices. Finally we make some

comments regarding the care of patients in whom a suspicion exists of pain medication dependence. Primarily we observe that patients presenting with septic joints merit consideration for being treated in an analogous time frame with other patients who present with sepsis.

Case Presentation

A 26 year old woman with a history of Systemic Lupus Erythematous (SLE) and End Stage Renal Disease (ESRD) on dialysis, presented to the Emergency Department (ED) with a complaint of left knee pain. She had been in the ED the week before for joint pain at which time a diagnosis had been made of Deep Venous Thrombosis (DVT). A prior diagnosis had been recorded on the chart of "drug seeking behavior", and staff, familiar with the patient suspected her of having shown the same. The patient denied fever, chills, nausea, vomiting, chest pain or rash.

On examination initial vital signs showed a temperature of 98.9°F, pulse of 98 bpm, blood pressure 93/46 mmHg and respirations 20 per minute.

She was a well developed, well nourished, and chronically ill appearing female crying in pain. Examination of the head, ears, eyes, nose and throat, heart, lungs and abdomen and neurologic system were without abnormalities. A dialysis 'permacath' catheter was in place in the chest, and not initially noted to appear infected, although the presence or absence of erythema, purulent discharge, swelling or tenderness was not specifically commented upon. Positive findings were confined to the musculoskeletal system which showed a swollen, tender left knee, not noted to be erythematous or hot, but which was very painful to any movement. Skin and neurologic examination was normal.

The patient was initially scheduled for a Complete Blood Count (CBC) and metabolic panel, X-ray of the knee and repeat venous Doppler of the lower extremities. She immediately asked for the proprietary name for an injection of intravenous hydromorphone. Owing to the prior diagnosis of chronic pain and her relationship with a pain consultant familiar with the patient, she was given an oral dose of hydromorphone while a pain management consultant familiar with the patient evaluated her, and recommended an injection of ketorolac and topical 4% lidocaine. The plan was made to obtain X-rays and then perform an arthrocentesis.

Initial blood results returned "Quantity Not Sufficient", and the patient refused several times to permit further attempts at intravenous access. As the patient does not urinate, X-ray was delayed by protocol for a serum BHCG, the repeat venous Doppler obtained first, and X-ray of the knee obtained and resulted three hours after presentation.

The X-ray showed a joint effusion. At that time the patient was seen by her nephrologist and her rheumatologist who, with ED resident staff, performed an arthrocentesis of the left knee and obtained cloudy opaque yellow fluid to be sent for cell count and culture. An orthopedist was contacted upon visualization of the specimen, who asked to be informed immediately when results of cell count and gram stain were available.

The patient was recommended for intravenous antibiotics. She was still "vocally refusing" peripheral IV placement. Use of the hemodialysis catheter, not customarily use for non hemodialysis reasons, was not initially considered. The decision was made to attempt to sedate the patient with intramuscular ketamine to attempt a central line. As the discussion was taking place, the patient was noted to appear increasingly ill, her vocal protestations against line placement appeared less focused, and her BP was found to drop to 75 systolic. The diagnosis was made of sepsis with impending septic shock. After immediate consultation with the patient's nephrologist the decision was then made to access the patient's dialysis port, to give fluid bolus and intravenous antibiotics.

Results of the body fluid analysis returned. The specimen contained 9700 White Blood Cells (WBC), with a differential of 82% PMNs, and 7000 red blood cells. Gram stain showed 1+ Gram positive cocci in clusters. An orthopedist was called with the results. The initial impression was that 9700 WBC was indeterminate and that contaminant bacteria in the cocci family can be found, but upon hearing that the clinical course of the patient was deteriorating an operating room time was set for one hour and the patient was prepared for immediate surgery.

As the clinical condition appeared to worsen, and surgery was imminent, the decision was made to intubate the patient. It was decided to institute vigorous fluid resuscitation and an infusion of norepinephrine was begun. The patient was escorted to the operating room where an incision and drainage of the knee with washout was performed, draining grossly purulent material. Shortly after surgery the laboratory values obtained during access of the central line were available and revealed WBC 0.5, Hgb 5.7, and platelets 28. The patient had been considering renal transplant and family were initially resistant to the idea of transfusion.

The patient remained intubated and on vasopressor support for the first day. Cultures were positive for MSSA from both blood and joint cultures. Suspecting the dialysis catheter to be a likely source of contamination the catheter was removed and cultured, and another later reinserted after several days of antibiotics. The family reconsidered their opposition to transfusion and two units of packed red blood cells were given. White blood count began to return to normal. Over the next few days then patient gradually could be weaned off pressure support and extubated.

Her clinical condition improved steadily, and she was transferred from the ICU to the floor. She had several dialysis sessions as an inpatient, had extensive evaluations regarding continued pain management, was ultimately discharged to rehabilitation and has subsequently done well.

Discussion

We believe that this case presents several management issues which merit review. As has been emphasized in a myriad of literature, the key to treatment of septic shock is early, almost immediate recognition and the institution of aggressive fluid resuscitation and appropriate antibiotic treatment [11-14].

Reviews of the common emergency presentation of a painful joint swelling identify the septic joint as the most threatening possibility among a wide differential diagnosis, and cite delayed identification and treatment as a major cause of morbidity, permanent joint destruction, as well as mortality with a case fatality rate cited as high as 11% to 16% [1,2]. Although the classic presentation is one of sudden onset of a single, hot, swollen, painful joint, which resists any movement, some patients will present with multiple joints and longer onset [2].

One systematic review [15] of eighty better quality studies drawn

from thirty to fifty years of literature review found that: (1) the vast majority of cases were gram positive organisms, with greater than 90% being *staphylococci* or *streptococci*; (2) common risk factors include arthritis, either Rheumatoid or osteoarthritis, prosthetic joints, diabetes, cutaneous ulcers, prior joint instrumentation, and low socioeconomic status, alcohol or intravenous drug abuse; (3) more than a fifth of the cases presented as polyarthritis so that multiple joint presentation cannot be relied upon as suggestive of a more benign etiology; (4) a duration of symptoms is usually in the range of less than two weeks but may be longer with organisms of lower virulence [9] and (5) the absence of fever does not exclude an infected joint [1-3,15].

The importance of prompt and timely diagnosis of the septic joint is well appreciated [3,11-14], but the time course is usually considered to be within the day, and the notion of the "golden hour" for septic shock is not often considered. Most interestingly, in a comprehensive review this year of the most modern approach to septic shock [14], a table showing "potential sources of infection associated with sepsis by organ system", admittedly not exhaustive, did not include septic arthritis. The three most commonly associated sources for sepsis are lung, abdomen and urinary tract and potential septic arthritis is not commonly considered as a high likelihood precipitant of septic shock. Of course, the phrase "septic arthritis", more properly pyogenic or infectious arthritis does not always induce a state of septic shock, and there are "mimics" of the condition [3]. Ours, however, was a case where, we believe, had the onus of time consideration followed septic shock guidelines rather than those usually cited for pyogenic arthritis, the initial course in the department might have been different.

Septic arthritis in immune-compromised patient can have fatal consequences. Salar et al. [5] present a case of a 63 year old female with rheumatoid arthritis who, on a second presentation for joint pain was initially treated for RA exacerbation, but was found ultimately to have multiple septic joints. Despite two joint washouts and 14 days of intensive care and antibiotics, she died in septic shock. The rapid progression from pyogenic arthritis into septic shock is not frequently seen in the same time line as we have come to view the usual presentation of sepsis. In that patient, for example, the interval from presentation with joint pain to hemodynamic compromise was several days.

One factor in which the primary clinician may have been more focused, which may have been used to better advantage in facilitating the care of this patient would have been to have focused greater attention to the possibility of line sepsis in a patient with ESRD and indwelling venous access. Catheter related blood stream infections are the second most common cause of death in patients on hemodialysis, with a 28 fold increase in infection when compared to matched patients without renal failure [16]. Rates of infection have been shown to range from 0.19 up to 5.1 incidence per 1000 patient days [17,18]. This is due to several factors, including comorbidities, disruption of the natural skin barrier, as well as immune dysfunction caused by uremia, which would have been doubly relevant in our patient with SLE. In patients requiring intravenous access for hemodialysis, central venous catheters have been associated with a 15 fold increase in bacteremia [18-21].

While the tunneled central venous catheter for our patient was not initially noted to show clinical signs of infection in our patient, the Infectious Disease Society of America (IDSA) notes that clinical signs of erythema, induration and tenderness are not necessarily reliable when evaluating for bacteremia due to indwelling catheters, so called Catheter-Related Bloodstream Infections (CRBSI) [22]. Rather the diagnosis of CRBSI relies on catheter removal followed by sending both the severed tip of the catheter and peripheral blood for culture. Extra caution is recommended in such patients [16,17], and it is possible that had the risk of bacteremia in presence of an indwelling catheter initially recognized, the association with a painful swollen joint might have immediately led to a greater impetus to initiate vigorous sepsis resuscitation. This consideration mitigates, in some degree, our caution that any septic joint might be a harbinger of septic shock, however does highlight the demand to be particularly vigilant to sources of hematogenous spread to a septic joint, before bacteremia leads to sepsis and shock.

As our patient refused intravenous catheter attempts, which left the dilemma that removal of the catheter would have left no vascular access. Our general practice is to avoid when possible using hemodialysis catheters other than for hemodialysis, and it has been recommended that health care personnel who do so, usually nursing, have specialized training, competence assessment procedures and protocols [23]. As our patient bordered on extremis, it was decided to use the catheter after communication with the nephrology consultants. To eliminate potential communication delays, procedural texts in emergency medicine have recommended accessing hemodialysis catheters by emergency providers in emergent scenarios [24].

The finding of a relative low joint fluid white blood count in what was found to be a septic joint is particularly worth note. The range of joint fluid WBC commonly cited as suggestive of septic joint needs to be tempered with an awareness of the systemic WBC. A synovial fluid WBC of greater than 50,000 or even more specifically 100,000 with differential of 90% PMNs is commonly cited as indicating bacterial arthritis [3]. However patients with peripheral neutropenia can been shown to have decreased joint fluid white blood cell count, and patients with peripheral neutropenia have been reported to have culture proven septic arthritis with very minimal synovial fluid neutrophils [3,25]. One needs to be vigilant for the possibility of septic arthritis in a neutropenic patient with a low synovial white count. A patient with either overwhelming sepsis or SLE can become neutropenic [26,27]. According to our orthopedic author, it was the patient's clinical deterioration, and not the initial joint fluid cell count which prompted immediate surgical intervention.

One review [28] found no single marker in joint fluid aspiration to reliably rule out a septic joint. Of further interest is the fact that serum WBC and inflammatory markers such as ESR and C -reactive protein are useful in monitoring response to treatment, however their absence does not exclude the septic joint. Mcgillicudy et al. [29] report that the previously suggested threshold of 50,000 synovial WBC lacks the sensitivity to be clinically useful in ruling out septic arthritis. Furthermore, one would think that laboratory guideline is even less helpful in a patient with SLE given normal levels are commonly seen approaching 40,000 white blood cells [30].

It has been commonly held that delayed diagnosis can lead to profound, extensive cartilage damage within hours even when sepsis is not present, however not every review has found delay in surgical treatment to have a significant effect on outcome [31,32]. In assessing the need for immediate surgical debridement, some studies have found no difference on mortality or incidence of ICU admission with early surgical debridement. However, each of their patients had diagnostic arthrocentesis and institution of antibiotics. It

Finally, one area which on reflection is troubling, or rather, illuminating about the care of our patient is to question what effect a prior suspicion of pain medication seeking behavior may have had on the pace of her evaluation. Especially in an era of changing perceptions regarding opioid use and increased sensitivity to the possibility of pain management seeking, one has to be increasingly careful to avoid bias and minimization of symptoms. Although there were several elements already mentioned which affected the rapidity of diagnosis and treatment, one must consider whether the perception that this patient had a chronic pain condition, and that the patient had been indicated in the chart as possibly presenting with pain seeking behavior, and that the patient had recently presented with the same complaint and was identified by a staff member from recent memory as a potential drug seeker all may have contributed to moderating the pace of what might have otherwise been a higher priority and more immediate diagnostic endeavor.

There is extensive literature regarding delays in treatment of pain in patients as a function of age [33,34], gender [35,36] and race [37-40], however we did not find prior literature reporting the delay of diagnosis of a significant medical condition based on a perception of drug seeking in the patient. Of course, that might be a situation difficult to report and own up to.

Conclusion

We believe that this presentation of a rapid development of septic shock in a patient presenting with an isolated painful joint serves as a reminder of the importance of rapid identification and institution of treatment of sepsis, in the patient with a septic joint, especially in the immunocompromised state. It is a further reminder of the need for special attention, and sometimes uses of long term indwelling venous access catheters. It also serves to remind us that patients with frequent use and demand for opioid analgesia often, if not always, seek pain relief from frequent and recurrent real pain and that these patients may be doubly at risk for potentially serious and catastrophic consequences when symptoms are viewed through the lens of pain medication seeking.

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