

Recurrent Gemcitabine-Associated Pseudocellulitis in a Patient with Pancreatic Adenocarcinoma: A Clinical Vignette

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Case Presentation

A 59-year old woman with a past medical history of diabetes, atrial fibrillation, hyperlipidemia, and COPD initially presented to the Emergency Department with obstructive jaundice and acute renal failure. She was ultimately diagnosed with pancreatic adenocarcinoma. Surgical oncology determined that the patient's tumor was borderline resectable. Oncology recommended neoadjuvant chemotherapy with a combination of gemcitabine and nab-paclitaxel. She was also initiated on hemodialysis. Notably, the patient did not recover renal function and became hemodialysis-dependent.

One week later, prior to initiation of chemotherapy, the patient presented to the Emergency Department for bilateral lower extremity redness and swelling. She denied fever or chills. In the ED, she had one recorded temperature to 100F. Physical exam showed warm bilateral lower extremities with 2-3+ pitting edema and confluent erythema from the feet to the knees. Initial WBC was 12, and lactic acid was 3.0. Lower extremity dopplers were negative for DVT. She was started on vancomycin, ceftazidime, and doxycycline then reduced to vancomycin alone. It was suspected that the patient had stasis dermatitis with possible cellulitis. Blood cultures were negative. No tissue biopsy was performed.

Four months after starting chemotherapy, the patient again presented to the Emergency Department complaining of bilateral lower extremity warmth, swelling, and tenderness. She had received chemotherapy earlier in the day preceding her presentation. Physical exam revealed generalized blanching erythema, warmth, and 2+ pitting edema of the bilateral lower extremities from the feet to the mid-thighs. Peripheral pulses were intact. Her initial WBC was 4.4, and lactic acid level was 0.9. Lower extremity dopplers were again negative for DVT. While admitted, she was started on vancomycin and cefepime, then reduced to vancomycin. She was discharged to home after three days with a prescription for doxycycline to cover for possible cellulitis, though pseudocellulitis was suspected. Her physical exam at discharge was mildly improved over her initial one. WBC remained within normal limits, and blood cultures were negative. No tissue biopsy was performed.

One month later, the patient presented to the ED a third time with bilateral lower extremity swelling, redness, and pain. Patient was unable to bear weight on the legs due to pain. She had received chemotherapy one week prior. Onset of her symptoms was two days after her infusion. She had also missed a dialysis session one day prior to presentation. She denied fever and chills and was objectively afebrile. Physical exam showed bilateral erythema and edema from the feet to the knees. Also present was blistering of the feet. WBC was 3.5, lactic acid was 0.6, and lower extremity dopplers were negative for DVT.

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The patient was started on daptomycin and cefepime to cover for superinfection; however, antibiotics were discontinued after four days when suspicion for infection abated. WBC remained within normal limits, and blood cultures were negative. No tissue biopsy was performed. Patient's symptoms and physical exam improved over the course of her admission. She was discharged after five days with prescriptions for amoxicillin/clavulanic acid and doxycycline to treat a pneumonia. The working diagnosis for the patient's presentation was drug reaction, namely, pseudocellulitis secondary to gemcitabine.

The patient continued her chemotherapy for a total of six cycles before undergoing a successful Whipple procedure. Since completing her chemotherapy, the patient has had no additional presentations for lower extremity symptoms.



Figure 1. While no photo of our patient's lower extremities is available, this photo—from the 2012 article by Singh and Hampole—is representative of the appearance of our patient's lower extremities. Confluent erythema is seen bilaterally. Used with permission of the authors.

	Presentation 1	Presentation 2	Presentation 3
Initial WBC (x 10 ⁹ cells/L)	12	4.4	3.5
Lactic acid	3.0	0.9	0.6
Lower extremity dopplers	Negative	Negative	Negative
Blood cultures	Negative	Negative	Negative

Table 1. Patient Clinical Data, By Presentation

Discussion

Bilateral red legs in cancer patients with weakened immune systems, particularly in those with a history of chronic venous stasis and/or lymphedema, can pose a diagnostic challenge. Such patients are at risk for developing cellulitis and, as in our case, are often treated empirically with antibiotics. In our case, the patient had a history of probable venous stasis and recent renal failure. Her first presentation with bilateral red, swollen, painful legs occurred prior to beginning chemotherapy with gemcitabine while her subsequent two presentations occurred after initiating chemotherapy. We posit that the diagnosis for her first presentation was stasis dermatitis and the diagnosis for her second and third presentations was gemcitabine-associated pseudocellulitis. Despite experiencing lower extremity symptoms both before and after initiation of chemotherapy, the Naranjo algorithm suggests that an adverse reaction to gemcitabine was probable in our case¹. Gemcitabine-associated pseudocellulitis, though an uncommon drug reaction, has been previously reported in the literature²⁻¹¹. The literature also contains a handful of recurrent presentations^{3,6}. The literature suggests that patients typically present within 1-2 days of gemcitabine exposure, often after their initial exposure^{2,8}. However, patients who have received treatment with gemcitabine for months, even years, have also presented with associated pseudocellulitis^{6,7}. Authors of previous case reports of this adverse effect note that lack of early identification of the likely diagnosis results in unnecessary use of antibiotics⁴⁻⁷. We echo this sentiment. Lastly, our case highlights the importance of familiarity with chemotherapeutic side effects for the hospital provider, as patients may require hospital-based care following their chemotherapy.

Conclusion

Gemcitabine is a chemotherapeutic agent used for neoadjuvant treatment of pancreatic cancer. Pseudocellulitis is an uncommon side effect of this drug. Our patient, who likely suffered from chronic venous stasis as well as acute renal failure, presented with gemcitabine-associated pseudocellulitis on two occasions several months into her treatment and was treated with antibiotics each time to cover for possible cellulitis. Presentations for bilateral red legs, particularly recurrent presentations in a patient on gemcitabine, should prompt hospital providers to seek an alternative diagnosis to cellulitis. As our case shows, the pseudocellulitis reaction is possible even after months of chemotherapy. Making the correct diagnosis and providing antibiotic stewardship are twin responsibilities of the hospital provider. Our case highlights the importance of both for the hospitalized cancer patient.

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