

CLINICAL VIGNETTE

CHEMOTHERAPY AND CLOSTRIDIUM

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A 44-year old female presented with a new palpable, left breast mass. Imaging was consistent with possible locally advanced breast cancer, and biopsy confirmed a triple negative invasive ductal carcinoma. After consultation with a breast surgeon, it was determined that neoadjuvant chemotherapy was her best option to improve final surgical outcome. After discussion regarding usual chemotherapy toxicities, the patient proceeded with her first cycle of docetaxel and cyclophosphamide. The following day she received pegfilgrastim. At her one-week follow-up (Day 8) she reported feeling well until the evening prior when she started to have increasing nausea and some mild, abdominal cramping. She had no fevers, chills, diarrhea, constipation, bright red blood per rectum, melena, or other symptoms. Her vital signs, physical exam, and laboratories were unremarkable beyond a white blood cell count (WBC) of 3.1 and absolute neutrophil count (ANC) of 900. Her symptoms were not atypical after chemotherapy. Adjustments were made in her nausea medications and analgesic regimen, and she was to follow-up in 2 days for follow-up of her symptoms and blood counts.

The next morning (Day 9) the patient presented to the office needing to be seen immediately. Her abdominal cramping had intensified, and she was unable to tolerate any oral intake since the prior afternoon. She stated that she could not sleep due to the pain and nausea. Her abdominal exam was benign, but she was mildly hypotensive (BP 89/47) and tachycardic (HR 115). She received some hydration and intravenous (IV) anti-emetics in clinic with only a mild improvement in the above symptoms and vital signs. Her WBC and ANC had now normalized. She was subsequently admitted for closer observation.

In the hospital she received IV antiemetics, hydration, analgesics, and later that evening she felt her symptoms had almost completely resolved. However, her vital signs still showed a worsening tachycardia (HR=140s), and her blood pressure remained at the lower end of normal (SBPs 90s-100s). She remained afebrile. At 5AM (Day 10) the nurse called the on-call hospitalist to report the patient was more confused. She was assessed

immediately and while she seemed tired, she was alert and oriented x4. The physician noted a small ecchymosis above her knee, and the nurse reported an unwitnessed fall when the patient went to the bathroom a few hours prior. A CT of the head was ordered.

Within the next hour she became more confused and was transferred to the ICU for higher level of care. Upon transfer the patient became unresponsive and in pulseless electrical activity. She was resuscitated and intubated. Reexamination showed worsening of the ecchymotic-like skin changes above the knee extending up to the hip, and subcutaneous air appeared to be present. X-rays confirmed the subcutaneous air along the upper leg and right shoulder. Labs delineated liver and kidney failure, and dialysis was initiated. Over the next couple hours her leg exam worsened, and she developed worsening bullae. Microscopic examination of fluid from the bullae was consistent with gram-positive rods. The patient continued to decompensate over the next several hours, and the family decided to withdraw care.

A few days later, microbiology culture from the above fluid identified the offending organism to be *Clostridium septicum*.

While toxicity from chemotherapy is not uncommon, death from treatment is fairly rare due to improvements in dosing, patient selection, and the addition of supportive medications like growth factors and anti-emetics. However, unexpected complications do occasionally occur. *Clostridium septicum* infections are rare and generally associated with colorectal pathology, malignancy, and immunosuppression¹. Presumably the patient's chemotherapy caused enterocolitis and during her brief neutropenia despite Neulasta administration, the infection was able to inoculate her bloodstream.

In one review, confusion is reported as the earliest symptom as was noted in the patient above². Her abdominal pain out of proportion to exam findings, ongoing tachycardia, and early purplish skin changes are typical features. Unfortunately her early gastrointestinal symptoms were also consistent with

the anticipated chemotoxicity. *C.septicum* produces toxins that decrease blood flow and lead to cell death, rapid tissue destruction, gas production, bullae and subsequent myonecrosis³. The purple, ecchymotic-like lesions noted in the patient were related to this vascular compromise. Treatment can include antibiotics, surgery to remove necrotic tissue, or hyperbaric oxygen. As was seen with our patient, even with immediate and aggressive treatment most cases are lethal (70-100%) within 24 hours due to vague early symptoms and rapid progression².

REFERENCES

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