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Prathusha Yerramilli
MD, Trinity Health Ann Arbor
Hospital, United States

Asha Shah
MD, Trinity Health Ann Arbor
Hospital, United States

Nonoperative Management of Intestinal Perforation in Metastatic Breast Cancer Does Not Delay Time to Initiation of Chemotherapy

Prathusha Yerramilli and Asha Shah

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Abstract

Immediate surgical intervention is often required for intestinal perforation to avoid the high morbidity and mortality of peritonitis and the complications associated with sepsis. (1, 2). Surgery is a definitive way to establish source control in the presence of intestinal leakage and is an effective approach in cancer patients to avoid delays in chemotherapy. However, micro perforations and contained perforations can be treated nonoperatively, especially in patients at elevated risk for surgery (2, 3, 4). This can also be considered in cancer patients without delaying planned chemotherapy. We report a case of intestinal microperforation in a 59-year-old female patient with metastatic breast cancer to the bone with malignant ascites and peritoneal carcinomatosis. Due to her hemodynamic stability and the high risk of operative complications in the setting of ascites and carcinomatosis, she was treated with nonoperative management. Throughout her hospital course, her vitals and abdominal examination remained stable, and she was safely managed nonoperatively and discharged home. Post hospitalization she had follow-up with oncology and the planned start date for chemotherapy was not delayed due to any concern for ongoing infection from nonoperative management. Management of intestinal perforation should be tailored to the patient's clinical status and comorbidities. Due to this patient's malignant ascites and carcinomatosis, operative intervention carried significant risk of respiratory compromise, marked shifts in body fluids, anastomotic leak, and wound healing complications (5).

Keywords: Microperforation, metastatic breast cancer, intestinal perforation

Introduction

Intestinal perforation carries significant morbidity and mortality due to septic complications from leakage of contents into the peritoneal cavity [1]. Therefore, many patients with perforated viscus undergo operative management, whether by laparoscopy or laparotomy [3, 4]. However, in hemodynamically stable patients, there is an option for nonoperative management with close observation, antibiotics, and bowel rest [3, 4]. Nonoperative management can also be considered for patients who are at elevated risk for undergoing surgical intervention, such as those with malignant ascites and peritoneal carcinomatosis [5, 6]. Often, the preference in patients with cancer is operative intervention, to effectively control infection and allow for timely initiation of chemotherapy. However, this report demonstrates a case where nonoperative management of micro perforation did not delay planned chemotherapy initiation.

Case Report

This case report discusses a 59-year-old female patient recently diagnosed on core needle biopsy with stage 4 lobular carcinoma of the breast, ER+, PR+, HER2 -. On genetic testing, she was found to have RAD51B mutation and CDH1 frameshift mutation. She presented to the emergency room (ER) with a 3-month history of generalized abdominal pain, diarrhea, bright red blood per rectum, and 30-pound weight loss in the setting of an unevaluated breast mass she had for several years. In the ER, she underwent a venous phase 3 cm slice computed tomography of the abdomen and pelvis (CT AP) with intravenous (IV) contrast which revealed diffuse bony metastasis, ascites, and descending and rectosigmoid colitis. This was followed by a venous phase 3.75cm slice CT chest with IV contrast which showed asymmetric thickening of left breast and nipple retraction (Figure 1), 2.6cm axillary lymphadenopathy (Figure 2), as well as redemonstration of diffuse bony metastasis. Diagnostic mammogram then showed a mass in the left breast suggestive of malignancy (Figure 3). Core needle biopsy was performed, which revealed invasive lobular carcinoma.

Corresponding Author:
Prathusha Yerramilli
MD, Trinity Health Ann Arbor
Hospital, United States

Due to bright red blood per rectum, she underwent colonoscopy where a severe rectal stricture was seen and could not be traversed with the GIF colonoscope; biopsies were performed. The endoscopic findings were concerning for malignancy; however biopsies came back negative. Peritoneal fluid was sampled via paracentesis, with 250mL removed. Cytometric analysis of this fluid was positive for metastatic carcinoma consistent with breast primary. The patient was discharged from this encounter with follow up with internal medicine and oncology.

Four days after discharge, she re-presented to the emergency room (ER) with worsening generalized abdominal pain and underwent a 3cm slice venous phase CT AP IV contrast which was concerning for extraluminal gas in the right lower quadrant (Figure 4). The patient's abdominal exam was significant for generalized tenderness, focally worse with voluntary guarding in the right lower quadrant. She was afebrile with blood pressure (BP) 117/70 and heart rate (HR) 90. Given findings of free air, a follow up scan with both oral and IV contrast was obtained which showed an increase in size of the extraluminal gas, but did not reveal extravasation of contrast (Figure 5). Given the location of the free air, it was concluded that she had a contained

microperforation in the region of her terminal ileum/cecum. Given she was hemodynamically stable with a reassuring abdominal exam, non-operative management was undertaken. The presence of ascites and carcinomatosis put her at increased risk for respiratory compromise, marked shifts in body fluids, wound healing complications, and anastomotic leak should operative management be pursued. Nonoperative management (NOM) for this patient included bowel rest, IVF and IV antibiotics (ceftriaxone and flagyl). As her pain and abdominal exams improved, she was transitioned to a clear liquid diet and advanced accordingly. She was discharged on 10 days of oral cefuroxime 500mg twice daily and flagyl 500mg three times daily to complete a 14-day total antibiotic course (IV and oral). The patient followed up with internal medicine clinic 1 week after discharge and was reported to be doing well, with no ongoing abdominal concerns. She also met with the oncology team with plans to start oral chemotherapy (ribociclib) as soon as it could be delivered to her pharmacy. Ultimately, nonoperative management did not delay planned initiation of chemotherapy.

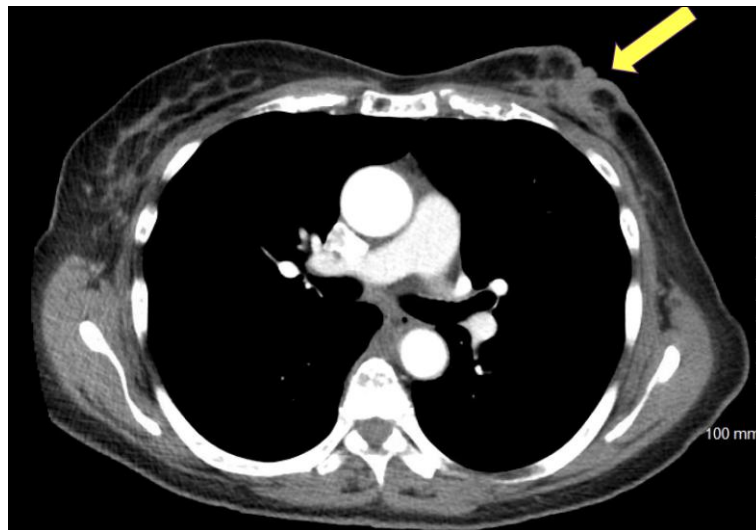


Fig 1: CT chest showing breast asymmetry. The left breast demonstrates concern for mass, skin thickening, and nipple retraction (arrow).

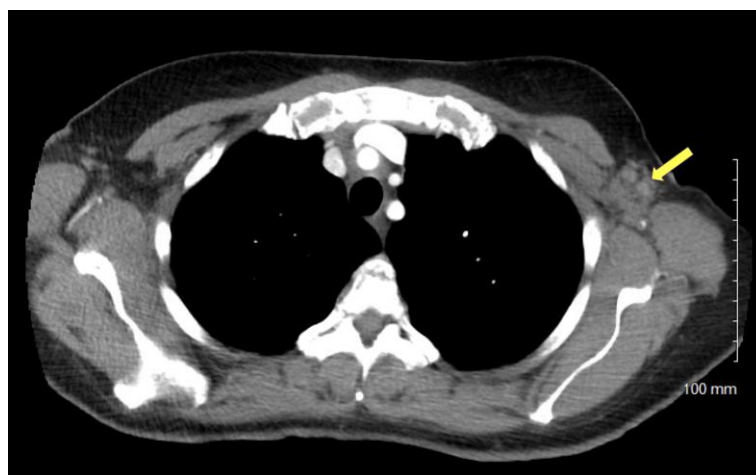
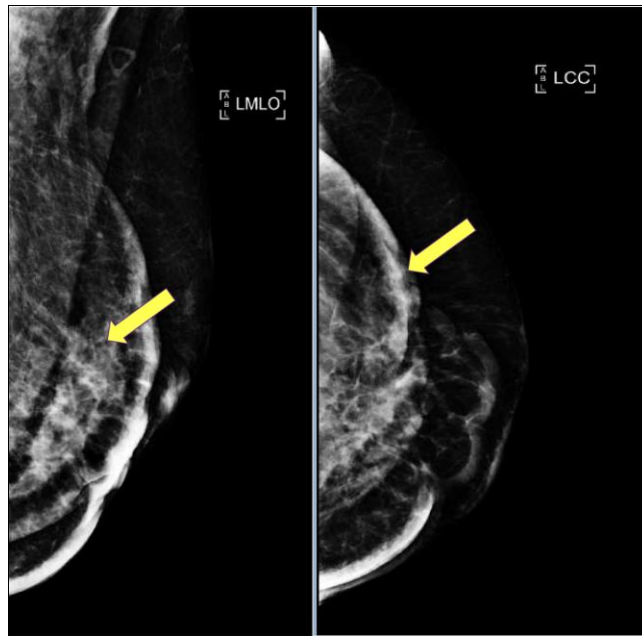


Fig 2: CT chest showing bulky left axillary adenopathy.



MLO = medial lateral oblique; CC = cranial caudal

Fig 3: Diagnostic mammogram of the left breast in MLO and CC views. MLO view demonstrating left breast mass and CC view showing skin thickening and retraction.



Fig 4: CT abdomen and pelvis with IV contrast. The arrow indicates a focus of free air in the right lower quadrant, concerning for contained perforation.

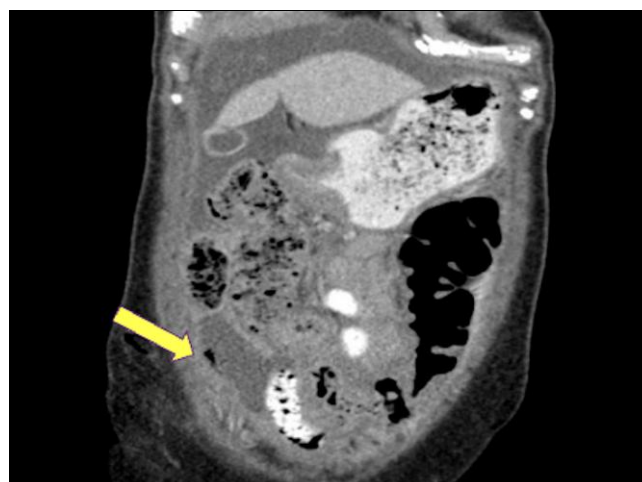


Fig 5: CT abdomen and pelvis with oral and IV contrast. The arrow indicates a focus of free air in the right lower quadrant, which grew in size compared to the IV contrast only study. Lack of oral contrast extravasation supports that the perforation is contained.

Discussion

Intestinal perforation can result due to a variety of disease processes such as infection (diverticulitis, appendicitis), ischemia (bowel obstruction, ischemic colitis), erosion (malignancy or ulcerative disease), or physical disruption (trauma, iatrogenic injury from endoscopy). In this case, the cause for perforation is unknown- her risk factors included rectal stricture, recent colonoscopy, colitis, or possible metastatic cancer erosion. When she re-presented to the ER with worsening abdominal pain, she underwent CT AP with IV contrast notable for extraluminal gas and due to her stability then underwent CT AP with oral contrast, which did not reveal evidence of extravasation. The contained microperforation was managed nonoperatively, especially given her stability and increase risk for complications in the setting of ascites and carcinomatosis [5, 6].

There are known complications of operating on patients with ascites [6]. Specifically, large volume ascites is generally considered a contraindication to major abdominal operation as it can lead to respiratory compromise, marked shifts in body fluids, and infection risks that increase surgical mortality [5]. A study published in the journal of Surgical Oncology looked at mortality after abdominal operation in patients with large volume malignant ascites and concluded that patients with large volume non-ovarian malignant ascites have a high mortality rate following major abdominal operation, despite careful selection of patients felt to have a reasonable chance of surviving the perioperative period. They found the cause of death was generally sepsis and multiorgan failure, likely hastened by surgical intervention [5].

There is a paucity of literature with regards to intestinal perforation in metastatic breast cancer prior to the initiation of chemotherapy. However, it has been shown that intestinal perforation can be a sequela of certain chemotherapies used to treat breast cancer, such as capecitabine [7]. The summary of treatment of patients who underwent surgical intervention after perforation after capecitabine was brief, however it was noted that the patients had "prolonged recovery" (7). With regards to surgical intervention in metastatic cancer not specific to breast cancer, the literature is more robust. One study looked at surgery for intestinal perforation in metastatic ovarian cancer and found that while survival among patients with widely metastatic disease was poor regardless of nonoperative versus surgical management, more patients in the surgery group experienced major complications requiring ICU admission than those who were treated nonoperatively [8]. Furthermore, they also experienced a significantly longer hospital length of stay, putting them at increased risk for delirium, nosocomial infections, medication errors, and diminished quality of life [8].

A study in the Annals of Surgical Oncology looked at 1750 cancer patients with diagnosis of visceral perforation that underwent either comfort care, nonoperative management, or surgery, and found that the surgery group was hospitalized twice as long as the nonoperative group and experienced more complications. In this study, 72 patients underwent surgical intervention including: exploratory laparotomy alone, duodenal repair, small bowel resections, colorectal resections, and stoma creation alone. Of the 4 patients that underwent exploratory laparotomy alone, 3 had laparotomy without identification of causative pathology, and the fourth had severe carcinomatosis precluding further

intervention, and was treated post operatively with comfort care [4]. In our patient, her pneumoperitoneum was small volume without obvious source on oral CT scan. Therefore, it is possible that had she undergone laparotomy the source of the perforation could not be found ultimately leaving her with wound healing and other complications.

From a more basic science perspective, cancer patients are known to have impaired cellular immunity [9] and would be more susceptible to wound complications and possible leak in the event that a bowel resection would be necessary. Additionally, there exists a phenomenon known as the "surgical stress response-" the normal physiological stress response that occurs as a result of surgery including neuroendocrine activation, inflammatory changes, and activation of the HPA axis which, in turn, leads to immunological and hemodynamic changes. Literature has shown that the effect of the stress response may not be beneficial to cancer patients, as specific elements of the stress response are thought to contribute to promoting cancer growth [10]. For example, stress related release of epinephrine and norepinephrine can interact with tumor receptors and increase their invasive and proliferative potential, and release of cytokines, prostaglandins, and cyclooxygenase can inhibit apoptosis and promote angiogenesis and immunosuppression [10].

For this patient, operative intervention carried high risk due to carcinomatosis and malignant ascites. Given her clinical stability, we elected to pursue NOM to avoid the morbid complications associated with surgery. This report demonstrates a case where nonoperative management of intestinal microperforation did not delay planned chemotherapy initiation.

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