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A CASE OF BEVACIZUMAB-INDUCED BOWEL PERFORATION

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Abstract:

Background: *Bevacizumab is an anti-vascular endothelial growth factor (VEGF) monoclonal antibody increasingly used for treating advanced malignancies. While it may improve survival outcomes, it carries the risk of rare complications of serious nature-including gastrointestinal (GI) perforations, which always have high morbidity and mortality risks.*

Case Presentation: *We are reporting an interesting clinical presentation of a 58-year-old male with metastatic colorectal cancer who developed acute abdominal pain after having undergone multiple cycles of bevacizumab therapy. The patient was found to have abdominal tenderness along with guarding and signs of peritonitis on examination. Leukocytosis was found on investigations, while contrast CT (CECT) abdomen confirmed pneumoperitoneum secondary to bowel perforation.*

Management: *Emergency exploratory laparotomy was performed with correction of the perforated segment, peritoneal lavage, and drainage. Bevacizumab was not resumed anymore, and the patient was kept under intensive care with the intravenous antibiotic regimen, fluid management, and analgesics. The patient improved over time and was able to tolerate oral feeding on the sixth day, upon which she was discharged, and oncological follow-up was planned with supportive care.*

Conclusion: *This case illustrates the rare but deadly potential of bevacizumab-induced bowel perforation. Early recognition of symptoms, prompt diagnostic evaluation, and surgical intervention are the key factors in the favorable outcome of this life-threatening complication. Hence, patient counseling regarding this complication was suggested, and in at-risk populations, the benefits of bevacizumab must be well weighed against the risk of this devastating complication.*

Keywords: *Bevacizumab, bowel perforation, colorectal cancer, VEGF inhibitor, case report*

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INTRODUCTION:

Bevacizumab, a kind of recombinant humanized monoclonal antibody against VEGF, finds importance in the treatment of different malignancies like metastatic colorectal cancer, non-small-cell lung cancer, renal cell carcinoma, and glioblastoma. Tumor growth is suppressed with tumor angiogenesis, causing better survival.[1] Side effects unique to bevacizumab include hypertension, proteinuria, thromboembolism, impaired wound healing, and gastrointestinal perforation. Although rarely seen, gastrointestinal perforation is among the serious complications with heavy morbidity and mortality. Its unpredictable nature necessitates a high index of suspicion and timely intervention to improve patient outcomes.[2,3]

Gastrointestinal perforations secondary to bevacizumab treatment occur in about 0.3%-3% of cases during clinical trials or in observational studies. Proposed mechanisms include failure of mucosal repair, ischemia of the intestine related to reduced angiogenesis, and decomposition of the wall of the gastrointestinal tract.[4,5] Other factors such as diverticulitis, intra-abdominal tumor factor, abdominal surgery alone, abdominal radiotherapy, and chemotherapy might add to the risk for such an adverse event. Symptoms tend to be subtle and may range anywhere from unspecific abdominal discomfort to overt peritonitis. This nonspecific presentation causes delays in diagnosis; hence, it is necessary to have a very high clinical suspicion index.[6,7]

Early detection and management of bevacizumab-induced bowel perforation are essential since delayed treatment can have a very deleterious outcome. The principal treatment strategy is urgent surgery to repair the site of perforation; systemic measures such as antibiotics and fluid resuscitation are supportive. Further bevacizumab therapy should be avoided because of the potential for recurrence.[8,9] This increasing documentation of cases has ensured a rise in awareness among oncologists and surgeons. Herein, a 58-year-old male diagnosed with metastatic colorectal cancer is reported who developed bowel perforation after initiation of bevacizumab therapy and subsequently underwent surgery in time for a successful outcome.[10]

CASE PRESENTATION:

Patient Information

The patient is a 58-year-old male, non-smoker, with an established history of metastatic colorectal adenocarcinoma, who presented with progressive abdominal pain and distension. Incidentally, the patient was on palliative chemotherapy for 14 months.

Medical and Surgical History

- **Medical history:** Hypertension for 10 years, controlled on amlodipine.
- **Surgical history:** Right hemicolectomy 18 months earlier. No history of inflammatory bowel disease or abdominal radiation.
- **Family history:** Non-contributory.
- **Allergies:** None reported.

Oncological Treatment History

The patient was on treatment with the FOLFOX regimen (oxaliplatin, 5-fluorouracil, leucovorin) in combination with bevacizumab (5 mg/kg every 2 weeks) and has completed six cycles. The bevacizumab was added after hemicolectomy for liver metastatic lesions. No adverse events were previously recorded during treatment.

Presenting Complaints

The patient presented with:

- Severe diffuse abdominal pain (onset: 2 days prior to admission)
- Nausea and vomiting
- Abdominal distension
- Inability to tolerate oral intake

Clinical Findings on Examination

General Examination

The patient appeared acutely ill, pale, and sweating. He was restless but preferred to remain still due to severe abdominal pain. No evidence of icterus, clubbing, or cyanosis was seen. The old surgical scar, midline laparotomy of hemicolectomy origin, was well healed.

Vital Signs

- Temperature: **38.6 °C** (febrile)
- Heart Rate: **118 bpm**, regular, tachycardic
- Blood Pressure: **90/60 mmHg**, hypotensive
- Respiratory Rate: **22 breaths/min**, shallow and rapid
- Oxygen Saturation: **95% on room air**

Tachycardia, fever, and hypotension indicate evolving septicemia with systemic inflammatory response.

Cardiovascular System

Tachycardia was noted. Normal heart sounds with no additional murmurs were auscultated. Peripheral

Respiratory System

Breathing was shallow due to abdominal pain. Chest movements were symmetrical. Breath sounds were vesicular bilaterally; no added sounds were heard. No pleural effusions or basal crepitations were observed.

Abdominal Examination

- **Inspection:** Abdomen was distended; no visible peristalsis. Midline surgical scar

was present, with a previous skin incision for a hemicolectomy. No hernias.

- **Palpation:** Diffuse tenderness with pronounced guarding and rigidity were present mainly in the lower quadrants. Positive rebound tenderness. Hepatosplenomegaly was not appreciated due to guarding.
- **Percussion:** Generalized tympany with shifting dullness suggestive of free intraperitoneal fluid.
- **Auscultation:** Bowel sounds markedly reduced, indicating paralytic ileus secondary to peritonitis.

Extremities

Cold extremities were noted and No peripheral edema or cyanosis.

Neurological Examination

The patient was full consciousness with orientation to time, place, and person. The Glasgow Coma Scale (GCS) score was 15/15. There were no focal neurological deficits observed.

Diagnostic Assessment

Laboratory Investigations

Parameter	Result	Reference Range	Interpretation
Hemoglobin (Hb)	10.2 g/dL	13–17 g/dL (male)	Mild anemia
White Blood Cell Count (WBC)	16,200 /µL	4,000–11,000 /µL	Leukocytosis (neutrophilia)
C-Reactive Protein (CRP)	112 mg/L	<5 mg/L	Markedly elevated
Platelet Count	280,000 /µL	150,000–400,000 /µL	Normal
Serum Creatinine	1.0 mg/dL	0.6–1.3 mg/dL	Normal
Blood Urea Nitrogen (BUN)	14 mg/dL	7–20 mg/dL	Normal
Serum Electrolytes	Na^+: 137 mmol/L, K^+: 4.2 mmol/L	Na^+: 135–145, K^+: 3.5–5.0	Within normal limits
Liver Function Tests (LFTs)	Normal	—	Normal hepatic profile

Final Diagnosis

Based on the patient's acute abdominal symptoms (severe pain, distension, guarding on pressure, and rebound tenderness), laboratory investigations (marked leukocytosis and elevated CRP in favor of a sepsis state), and CT imaging findings (free intraperitoneal air, peri-colic fluid, and dilated bowel loops without tumor infiltration), the final diagnosis was that of a bevacizumab-induced distal ileal perforation with generalized peritonitis. This diagnosis was confirmed intraoperatively and corroborated by histopathological features of transmural necrosis of the small bowel without malignant recurrence at the perforation site.

Day-wise Treatment Details

Day 1 (Admission and Emergency Management):

Upon presentation, the patient complained of severe pain in the abdomen, sepsis, and hemodynamic instability. Immediate stabilization was commenced with intravenous crystalloids for hypotension and fluid dehydration. A nasogastric tube was inserted for decompression, and a Foley catheter was set in place for monitoring urine output. Broad-spectrum intravenous antibiotics were started empirically, including piperacillin-tazobactam and metronidazole; pantoprazole infusion was given for gastric protection. Oxygen was supplemented to the patient while being kept nil by mouth. After the stabilization phase, the patient was taken to the operation theatre for emergency exploratory laparotomy. Distal ileal perforation was identified, resected, and primarily anastomosed. Intra-abdominal lavage was performed, and drains were left in place.

Day 2 (Immediate Postoperative Period):

The patient was admitted to the intensive care unit, where he was under close postoperative monitoring. Intravenous fluids and broad-spectrum antibiotics were continued. Pain control was achieved with an infusion of intravenous opioids (morphine titrated to comfort). Oxygen therapy was continued, with vital signs being checked on an hourly basis. A strict input-output record was kept, and venous thromboembolism prophylaxis with low-molecular-weight heparin (enoxaparin 40 mg subcutaneously) was started.

Day 3 (Stabilization in ICU):

Hemodynamics improved along with adequate urine output and stable oxygen saturation. Antibiotics were continued, and analgesics were rehabilitated with intravenous paracetamol and intermittent opioids would be administered according to necessity. Daily blood investigations showed the downward trend of leukocytosis, thus indicating early control of sepsis. The nasogastric tube was left in place with minimal aspirate, and the drains showed serosanguinous output.

Day 4 (Transition Phase):

Afebrile with stable vitals, abdominal pain had reduced significantly. Nasogastric aspirates continued to decrease, and abdominal distension improved. Therapy of sips of clear fluids was withheld as bowel sounds were still sluggish. Intravenous antibiotics and fluids were maintained. Mobilization was encouraged to avoid thromboembolic events, and incentive spirometry was started for respiratory support.

Day 5 (Return of Bowel Function):
The patient had audible bowel sounds and passed flatus; thus, gastrointestinal function was returned. Owing to this, the patient was cautiously began oral sips of clear liquids while the intravenous fluids were slowly reduced. The pain was well controlled with oral paracetamol with occasional IV analgesics; and the antibiotics were continued according to the protocol. Drain output decreased substantially.

Day 6–7 (Gradual Improvement):
The patient continued to tolerate oral diet, which was advanced to semisolids. Intravenous antibiotics were de-escalated, following clinical stability and improving inflammatory markers. Drains showed minimal output and were then removed sequentially. The patient ambulated without difficulty. Check of the postoperative wound showed healthy healing without signs of infection.

Day 8–10 (Recovery Phase):
The patient tolerated regular soft diet with no abdominal complaints. Intravenous antibiotics were discontinued, and oral antibiotics were started to cover for the same. Laboratory parameters were almost within the normal limits with WBC counts trending down to baseline. Pain was controlled with oral medications only. The patient was transferred from ICU to the general oncology ward for further recovery.

Day 11–12 (Pre-discharge Care):
The patient continued to remain afebrile and hemodynamically stable. Oral intake was adequate, bowel habit normal, and there was no tenderness on examination of the abdomen. Sutures were in place, and the area around the surgical wound was clean. Histopathology reported transmural necrosis without malignant infiltration, consistent with bevacizumab-induced perforation, so bevacizumab was discontinued forever, and oncology was consulted for a change in chemotherapy regimen. The patient was discharged on postoperative day 12 in stable condition and instructions given for follow-up care.

Day-wise Treatment Details

Day	Management and Interventions
Day 1 (Admission & Surgery)	• IV fluid resuscitation (crystalloids) • Nasogastric tube insertion for decompression • Foley catheter for urine output monitoring • Broad-spectrum IV antibiotics (piperacillin–tazobactam + metronidazole) • IV pantoprazole for gastric protection • Oxygen supplementation • Emergency exploratory laparotomy: distal ileal resection, primary anastomosis, peritoneal lavage, drain placement
Day 2 (Post-op, ICU)	• ICU monitoring (hourly vitals) • IV fluids continued • IV opioids for pain management (morphine infusion) • Venous thromboembolism prophylaxis (enoxaparin 40 mg SC) • Oxygen therapy and strict input–output charting
Day 3 (ICU Stabilization)	• Hemodynamic stabilization achieved • Continued IV antibiotics and analgesics • Shift from continuous opioids to IV paracetamol + intermittent opioids • NG tube on free drainage with minimal aspirate • Serosanguinous drain output noted • WBC trend improving
Day 4 (Transition)	• Patient remained afebrile, stable vitals • Abdominal pain reduced • Mobilization and incentive spirometry started • Oral intake withheld (sluggish bowel sounds) • IV fluids and antibiotics continued
Day 5 (Return of Bowel Function)	• Bowel sounds audible, flatus passed • Oral sips of clear liquids initiated • IV fluids tapered • Pain controlled with oral paracetamol + occasional IV analgesics • Drain output reduced
Day 6–7 (Gradual Improvement)	• Oral semisolid diet tolerated • Antibiotics continued, plan for de-escalation • Sequential removal of intra-abdominal drains • Ambulation without difficulty • Wound healing healthy

Day 8–10 (Recovery Phase)	• Oral regular soft diet tolerated • Switched from IV to oral antibiotics • Laboratory parameters normalized • Patient transferred from ICU to oncology ward • Pain controlled with oral medications only
Day 11–12 (Pre-discharge)	• Afebrile, hemodynamically stable • Normal bowel habits, adequate oral intake • Clean surgical wound, sutures intact • Histopathology confirmed transmural necrosis without tumor infiltration • Bevacizumab discontinued permanently • Patient discharged on day 12 with oncology follow-up plan

Discharge Medications

Medication	Dose & Route	Frequency	Duration	Indication
Ciprofloxacin	500 mg, oral	Twice daily	7 days	To prevent/treat secondary infection
Pantoprazole	40 mg, oral	Once daily	4 weeks	Gastric protection & mucosal healing
Paracetamol	500 mg, oral	As needed (≤3 g/day)	5 days PRN	Pain/fever relief
Lactobacillus (Probiotic)	1 capsule, oral	Once daily	10 days	Restore gut flora post-antibiotics
Multivitamin + Minerals	1 tablet, oral	Once daily	1 month	Nutritional support & recovery
Protein Supplement	As per dietician advice	Once/twice daily	1 month	Promote wound healing & strength

Follow-up

At the 1-month follow-up, the patient reported an improved appetite, weight gain, and good hemoglobin levels. Subsequent laboratory tests showed that the leukocyte count had normalized and the CRP levels had reached zero. From the 3-month follow-up onwards, CT abdomen showed no remaining intra-abdominal pathology or recurrence of perforation, and the patient was able to resume regular daily activities. Oncology follow-up was conducted, and alternative chemotherapy regimens other than bevacizumab were considered.

Outcome

Following surgery and postoperative care, the patient underwent recovery from bevacizumab-related bowel perforation. Early diagnosis, immediate surgical intervention, and cessation of bevacizumab gave the patient a good prognosis. At 3 months, she remained clinically well, with no signs of recurrence or complications, highlighting the importance of being alert and multidisciplinary care for the rare but serious side effects.

DISCUSSION:

Bevacizumab is a monoclonal antibody targeting vascular endothelial growth factor (VEGF), used in the treatment of metastatic colorectal cancer, ovarian cancer, renal cell carcinoma, and other solid tumors. Although improving survival, it is associated with adverse side effects, including hypertension, proteinuria, thromboembolic episodes, and delayed wound healing. Among the uncommon yet life-threatening adverse effects is GI perforation, which happens in 0.3–3% of patients with mortality being high if not treated promptly. The mechanism is thought to be inhibition of VEGF, which results in impaired angiogenesis and ischemia, followed by inhibition of mucosal repair, thereby predisposing the bowel wall to perforation.[11]

Various reports established risk factors for bevacizumab-associated GI perforation, including antecedent abdominal surgery, diverticulitis, bowel obstruction, intra-abdominal carcinomatosis, steroid administration, and concurrent radiotherapy. Most perforations are reported to occur during the first six months after therapy begins. A meta-analysis conducted by Hapani et al. revealed the occurrence at 1.5% with the use of bevacizumab, with the majority of cases requiring emergent surgical intervention. A prompt identification of the presenting symptoms of acute abdominal pain, peritonitis, or sudden clinical deterioration should be instituted, further delay would significantly worsen outcome.[12]

The patient in this case was complaining of severe abdominal pain and was suffering from peritonitis, both of which developed after several cycles of bevacizumab along with other chemotherapy agents had been administered. Bowel perforation, confirmed on CT imaging, pathologically accounts for the findings of abdominal tenderness with guarding and systemic inflammatory response. Interestingly, it is that the patient never had any meaningful history of diverticulitis or intestinal

obstruction, highlighting the possibility that beva-induced perforation can occur in patients without classical predisposing factors. The unexpected nature of the complication underscores the need for suspicion to be held-high for any patient presenting with an acute abdomen while on bevacizumab.[13] Management of bevacizumab-induced bowel perforation usually necessitates immediate surgical exploration because conservative management carries high mortality. In this patient, repair of the perforation was done after an emergency exploratory laparotomy. Post-operation, broad-spectrum antibiotics were given, along with intravenous fluid support, analgesics, and oral feeds were gradually reintroduced. Serial laboratory investigations and imaging were conducted to monitor the recovery. Importantly, bevacizumab treatment should never be resumed following such a serious adverse event, as current guidelines state against re-challenging a patient for this life-threatening toxicity.[14]

This case study stresses the need for clinical vigilance whenever bevacizumab treatment is being considered for a patient. All oncologists, surgeons, and pharmacists should be aware of the rare yet life-threatening adverse reaction to act quickly to improve worst outcome occurrence. Patient counseling on early warning signs of perforation like extreme abdominal pain, bloating, or change of bowel habits is crucial. The favorable outcome of our patient following timely diagnosis, operative treatment, and cessation of bevacizumab suggests that despite the severity of the complication, an interdisciplinary approach can have a good outcome. It serves to increase the literature on bevacizumab-induced bowel perforations that justify further post-marketing analysis and cautious evaluation of risks and benefits in vulnerable populations.[15]

CONCLUSION:

While highly effective in treating various malignancies, bevacizumab carries a rare adverse event of gastrointestinal perforation that can be fatal. Early detection of clinical symptoms such as acute abdominal pain, prompt CT evaluation, and surgical treatment all improve patient outcomes. This case underlines vigilant patient observation, multidisciplinary treatment approach, and assessment of risk versus benefit prior to therapy with bevacizumab. It is incumbent upon the physician to educate the patient about warning signs and take preventative steps to ensure safe practice of the anti-VEGF therapy.

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