ISSN: 2755-015X

Journal of Surgery & Anesthesia Research

SCIENTIFIC Research and Community

Case Report

Open Access

Enhanced Recovery through Multimodal Anesthesia in a CDH1 Mutation Carrier with Previous Bariatric Surgery Undergoing Gastrectomy

Gabrielle M Silverio-Alvarado* and Katerina A Neste-Gallisa

Johns Hopkins Bayview Anaesthesiology and Critical Care Medicine, Department of Surgical Oncology Johns Hopkins Bayview Medical Center, 4940 Eastern Ave, Baltimore, MD 21224, United States. San Juan Bautista School of Medicine, Caguas, PR, 00725, USA

ABSTRACT

This study highlights the complexity of perioperative management for CDH1 patients undergoing prophylactic total gastrectomy (PTG) due to the extensive surgery and associated morbidity. Endoscopic surveillance often fails to detect cancers, with studies showing 59.5% of cases remain undiagnosed preoperatively, reinforcing PTG's necessity. A 62-year-old female ASA III with a previous Roux-en-Y gastric bypass (RYGB) presented for PTG. Given her surgical history, aa precise anesthesia plan was premediated with gabapentin and acetaminophen; celecoxib was omitted. Epidural anesthesia (EA) was used for intraoperative pain control, with aa lidocaine bolus (60mg) administered via epidural catheter five minutes before incision, followed by a 2 % lidocaine infusion (3-4 ml/hour), magnesium sulfate, and acetaminophen. No additional opioids were required. The surgery and postoperative course were uneventful. Multimodal anesthesia proved beneficial, providing effective pain control, reduced opioid use, and enhancing recovery. Given opioids' detrimental effects on gastrointestinal function, CDH1 mutation carries require a comprehensive anesthesia strategy to reduce gastric cancer risk and surgical complications. This case underscores the importance of personalized anesthesia management.

***Corresponding author**

Gabrielle M Silverio-Alvarado, MD Candidate, Department of Anaesthesiology and Critical Care Medicine, Johns Hopkins Bayview, 4940 Eastern Ave, Baltimore, MD 21224, United States of America.

Received: March 03, 2025; **Accepted:** March 06, 2025; **Published:** March 17, 2025

Introduction

This case report highlights the effective management of a unique case involving a 62-year-old female with CDH1 gene mutation and a history of Roux-en-Y gastric bypass (RYGB) undergoing prophylactic gastrectomy. The patient's genetic predisposition to gastric cancer, combined with her complex surgical history, needed a careful anesthesia plan strategy to spare opioids and minimize postoperative complications to enhance recovery. The anesthesia plan included general anesthesia combined with multimodal analgesia techniques, including an epidural block, chosen to reduce perioperative opioid requirements and enhance postoperative recovery. Supported by literature, the epidural block ensures superior pain control, reduces systemic opioid consumption, and facilitates early mobilization.

Individuals with CDH1 mutations have a 42–70% lifetime risk of developing diffuse gastric cancer. For patients with a known CDH1 mutation, enhanced surveillance, including regular endoscopic examinations and imaging studies, is recommended for early detection and management of gastric cancer in mutation carriers. Because of the Roux-en-Y gastric bypass, she is not a candidate for endoscopic surveillance, since the area of the stomach removed includes gastrojejunostomy and the excluded gastric remnant (majority of stomach), lymphadenectomy and reconstruction. Surgeon performed a gastrectomy using the same limb for esophagojejunostomy and created an intestinal pouch. Took down the enteroenterostomy and reconstructed the anastomosis of the biliary-pancreatic limb further downstream. Lewis et al were among the first surgeons to recommend prophylactic total gastrectomy for asymptomatic patients with CDH1 mutations. Citation 16. Huntsman et al described in their series of 5 patients from families with CDH1 mutation who underwent prophylactic total gastrectomy. Many patients' pathology specimens showed Hereditary Diffuse Gastric Cancer that on preoperative endoscopy was not found. Citation 16.

Mutations in CDH1 can lead to a loss of E-cadherin function, disrupting cell adhesion and promoting cancer development. E-cadherin is essential for cells to adhere to each other and maintain the structure of epithelial tissues. When CDH1 is mutated, E-cadherin function is compromised, leading to a loss of cell adhesion. This loss of adhesion allows cells to detach from the primary tissue structure, increasing the potential for metastasis. With compromised Ecadherin function, cells become more mobile and can invade surrounding tissues more easily. This increased mobility, progression and metastasis. E-cadherin is involved in various signaling pathways that regulate cell growth, differentiation, and apoptosis. In addition to gastric cancer, CDH1 mutations are also associated with an increased risk of lobular breast cancer.

The anesthetic management of patients with CDH1 mutations requires special consideration due to several factors associated with the genetic mutation and the complex surgical procedures; these

patients often undergo the risk of perioperative complications. These include issues related to anesthesia such as increased bleeding risk, difficulties with airway management due to potential anatomical changes, and the need for meticulous intraoperative monitoring to manage hemodynamic stability. According to a study published in the Annals of Surgery, the perioperative management of patients with CDH1 mutations undergoing PTG is complex due to the extensive nature of the surgery and the associated morbidity. The study highlights the need for specialized anesthetic protocols to manage these risks effectively. A review in Surgical Oncology Clinics of North America emphasizes the importance of a multidisciplinary approach, including anesthesiologists, to optimize outcomes for patients with CDH1 mutations. The review suggests that preoperative assessment, intraoperative management, and postoperative care are critical components that require coordination among surgical, medical, and anesthetic teams. The literature also points out that postoperative morbidity and mortality rates are significant in patients with CDH1 mutations undergoing major surgeries. A study in JAMA Surgery reports that careful anesthetic management can mitigate some of these risks, underlining the necessity of experienced anesthetic care for these patients. The management of pathogenic CDH1 variant carriers (CDH1) presents unique challenges, especially in the context of anesthesia. CDH1 mutations are significantly associated with hereditary diffuse gastric cancer (HDGC) and lobular breast cancer, necessitating complex surgical interventions such as prophylactic total gastrectomy (PTG). This connection between CDH1 mutations and the need for surgical procedures underscores the importance of a multidisciplinary approach, particularly in anesthetic management, to optimize patient outcomes. While the primary focus often lies in the surgical management and clinical outcomes of CDH, the anesthetic considerations are equally critical. The literature suggests that comprehensive anesthetic planning can significantly impact postoperative morbidity (POM) and overall patient survival. Evidence indicates that factors such as patient age, the surgical approach, and the volume of procedures performed at a given center can influence the rate of postoperative complications. A retrospective observational multicenter study was conducted between 2003 and 2021.

The patient's genetic predisposition to gastric cancer, combined with her complex surgical history, needed a precise anesthesia plan strategy to spare opioids and minimize postoperative complications. Despite the patient inability to undergo endoscopic surveillance due to prior RYGB, the possibility for endoscopic surveillance as a potential alternative, the necessity for prophylactic total gastrectomy (PTG) in patients with pathogenic CDH1 variants is underscored by significant limitations and risks associated with endoscopic methods. Studies highlight that a substantial proportion of cancers (59.5%) were undetected on preoperative endoscopy, necessitating a proactive surgical approach. Additionally, risk factors for overall and severe postoperative morbidity (POM), identified using binary logistic regression, further support the need for comprehensive surgical intervention. Specifically, the cancer detection rate post-PTG was 54.5%, with many cancers missed during preoperative endoscopic evaluations, emphasizing the inadequacy of surveillance alone and the critical role of PTG in managing gastric cancer risk in these patients.

Case Presentation

The patient presented with a CDH1 mutation identified during testing for ductal carcinoma in situ (DCIS) of the breast. Her history of RYGB in 2004 complicates endoscopic surveillance. Despite no family history of gastric cancer, her aunt's breast cancer prompted further evaluation. Genetic testing and counseling revealed a high risk of gastric cancer. The patient consented to prophylactic total gastrectomy, following the ERAS protocol with an epidural catheter for multimodal analgesia. This approach aimed to optimize preoperative preparation and postoperative recovery.

A 62-year-old female ASA III with a history of right ductal carcinoma in situ (DCIS) status post lumpectomy and radiotherapy, diabetes mellitus type II, hyperlipidemia and a previous Roux-enY gastric bypass (RYGB) presented for Total Gastrectomy with roux en Y with pouch following a genetic testing that revealed a pathogenic CDH1 mutation, significantly increasing her risk of gastric cancer. Physical exam was normal. The anesthesia plan was general anesthesia combined with multimodal analgesia techniques, including thoracic epidural block. Post-operative pain management was planned with epidural analgesia and opioids for breakthrough pain. Following Enhanced Recovery After Surgery (ERAS) protocol for colorectal surgery, the patient was premedicated with gabapentin and acetaminophen, celecoxib was not given due to her history of gastric bypass surgery. At the OR, standard ASA monitors were placed plus a BIS monitor and 2 large bore peripheral IV lines. After pre oxygenation, induction of general anesthesia was achieved with a combination of midazolam, fentanyl, propofol and rocuronium. Intraoperative pain management was achieved with epidural anesthesia. A lidocaine bolus (60 mg) 5 minutes pre-incision was given through the epidural catheter followed by a lidocaine 2% infusion (3-4 ml/hour) throughout the rest of the case. Magnesium sulfate and acetaminophen were also given as part of multimodal analgesia. No other opioids were needed intra op after induction. The surgery proceeded without complications. In the PACU, vital signs were stable: blood pressure of 124/70 mmHg, pulse of 89 bpm, respiratory rate of 17 breaths per minute, oxygen saturation of 97%, and a temperature of 37.2 °C (99 °F). Pain was well controlled with epidural anesthesia. Bupivacaine 0.0625% continuous infusion rate 6 ml/hr and PCEA dose of 4 ml/hr was used. The patient's postoperative course was uneventful. Thoracic epidural catheter was removed four days later and she was discharged with a plan for follow-up and continued genetic counseling for her family.

Discussion

The anesthesia plan ensured optimal recovery, considering the patient's ASA score of 3 and the complex medication and allergy history. Using ERAS principles, general anesthesia was administered with meticulous attention to maintaining stability and adequate pain control. An epidural block with bupivacaine 0.0625% in sodium chloride 0.9%, and a PCA dose of 4 ml/hr was employed, demonstrating benefits in pain management and recovery. Literature supports epidural analgesia for major surgeries like gastrectomy due to its efficacy in pain relief and opioid sparing.

Prophylactic gastrectomy in patients with a CDH1 mutation presents unique challenges, particularly in individuals with a history of Roux-en-Y gastric bypass (RYGB). The patient's inability to undergo endoscopic surveillance due to prior RYGB necessitated a proactive surgical approach. Multimodal anesthesia (MMA) is beneficial for this patient due to its ability to provide effective pain management, minimize opioid use, and enhance recovery, crucial in complex surgeries like prophylactic gastrectomy with a history of Roux-en-Y gastric bypass. MMA combines medications that act on different pain pathways, such as opioids, NSAIDs, alpha-

2-agonists, ketamines, gabapentinoids, and corticosteroids. Each medication targets specific receptors or mechanisms involved in pain perception, providing more effective pain relief than any single agent alone. By using multiple agents, the reliance on opioids can be minimized, reducing perioperative complications of opioid-related adverse effects such as respiratory depression, constipation, nausea and ileus. Avoiding excessive opioid use helps mitigate the risk of opioid dependency and abuse, which is concerning in postoperative care. MMA improves functional outcomes with patients and enables them to be more likely to engage in necessary activities for recovery without the sedating effects or other limitations imposed by high opioids doses. MMA pharmacological mechanisms include NSAIDS acting by inhibiting prostaglandins, Alpha-2 agonists stimulate alpha-2-adrenergic receptors in the spinal cord, inhibiting norepinephrine release and reducing pain transmission. They have sedative gabapentin effects and can enhance the analgesic effects of opioids without increasing their dosage. Ketamine, an NMDA receptor antagonist that modulates central sensitization and reduces opioid tolerance. It helps prevent hyperalgesia and can lower opioid requirements postoperative.

Gabapentin acts on calcium channels to modulate neurotransmitter release, reducing neuropathic pain and enhancing opioid effectiveness and corticosteroid anti-inflammatory properties that can reduce tissue inflammation and pain supporting early recovery, reducing complications, and enhancing patient outcomes following complex surgeries. Lidocaine (Intravenous) inhibits sodium channels, G protein-coupled receptors, and N-methyl D-aspartate receptors, resulting in analgesic, anti-hyperalgesic, and anti-inflammatory effects. Decreases postoperative pain, improves bowel function, and reduces hospital stay. It's effective in various surgeries and reduces opioid consumption. Intraoperative Opioid-Free Anesthesia (OFA) patients showed significantly greater hemodynamic lability, requiring higher doses of ephedrine (23.67 mg vs. 15.69 mg, $p=0.039$) and more intravenous fluids (1160 ml vs. 925.86 ml, $p=0.007$). While OFA may offer short-term benefits in reducing opioid consumption immediately after surgery, MMA provides more consistent hemodynamic stability and avoids the risks associated with OFA. The choice of anesthesia should consider the patient's overall health, potential for hemodynamic instability, and the need for postoperative pain management and recovery. MMA provided more stable hemodynamic parameters with less need for vasopressor support.

Opioids have significant and often detrimental effects on gastrointestinal function, particularly in the postoperative setting. Opioids can cause esophageal dysmotility, manifesting with dysphagia. In the stomach, opioids can delay gastric emptying, leading to postprandial nausea and early satiety. Postoperative ileus is a common complication after abdominal surgery, μ (mu), δ (delta), and κ (kappa) opioid receptors are G-protein coupled receptors found extensively in the GI tract. The μ receptors are the principal mediators of analgesic effects and are also primarily responsible for the inhibitory effects on the gastrointestinal and colonic motility. Opioid may cause Narcotic Bowel Syndrome, a chronic abdominal pain, commonly accompanied by nausea and vomiting.

Additionally, opioids commonly cause Gastroesophageal Reflux Disease and gastroparesis. Lastly, opioids can increase sphincter of Oddi phasic pressure, leading to biliary pain and delayed digestion.

Epidural anesthesia can effectively spare the use of opioids in patients undergoing gastrectomy by targeting and blocking the pain signals at the spinal level, thereby providing continuous and localized pain relief while attenuating the stress response to surgery. This technique involves the administration of local anesthetics and sometimes opioids into the epidural space, providing pain relief and reducing systemic opioids, which are associated with various side effects. Epidural anesthesia minimizes postoperative ileus by reducing pain, sympathetic activity, and the need for systemic opioids. This leads to earlier return of bowel function and enables early enteral feeding, contributing to better nutritional health and reduced muscle catabolism. Neuraxial blockade, such as epidural anesthesia, has been shown to decrease intraoperative blood transfusions, reducing the associated risks and complications. Epidural anesthesia combined with general anesthesia was associated with significantly fewer postoperative complications ($P<0.001$) and less intraoperative blood loss ($P=0.058$) compared to general anesthesia alone. Multivariate analysis identified reconstruction type, pN stage, and complications as significant factors for prognosis, with epidural anesthesia combined with general anesthesia contributing to fewer complications due to its superior analgesic and anti-inflammatory effects. Studies also found that lymphadenectomy and pN stage were independent prognostic factors for recurrence and metastasis. Mechanistically, epidural anesthesia provides both somatic and visceral pain relief by blocking pain signal transmission at the spinal level, and continuous infusion through an epidural catheter offers prolonged and consistent pain management. This approach reduces the need for systemic opioids, minimizing their associated side effects such as respiratory depression, nausea, vomiting, and constipation. Effective pain control with epidural anesthesia promotes early mobilization, reduces postoperative complications, and accelerates recovery, demonstrating that the combination of epidural and general anesthesia offers significant benefits for patients predisposed to gastric cancer. By mitigating the perioperative stress response and inflammatory reactions, epidural anesthesia enhances immune function, potentially reducing the risk of tumor recurrence and metastasis. These findings collectively demonstrate that combining epidural anesthesia with general anesthesia offers substantial benefits for patients undergoing open gastrectomy for gastric cancer. Epidural anesthesia enhances recovery in patients by reducing supraventricular arrhythmias, thoracic epidural anesthesia (TEA) significantly decreases the incidence of new supraventricular arrhythmias to 10.2% compared to 22.3% in the general anesthesia (GA) group ($P = 0.0012$). Improves pulmonary function, TEA improves maximal inspiratory lung volume in a subset of patients ($P<0.0001$), patients in TEA group have earlier extubation ($P<0.0001$), have incidence of lower respiratory tract infections (15% vs. 29%; P0.0007) and TEA was associated with fewer cases of acute confusion (1.5% vs. 5.4%; $P = 0.031$) and acute renal failure (1.9% vs. 6.9%; $P = 0.016$).

The incorporation of MMA and epidural block in anesthesia can significantly diminish opioid usage and its associated side effects, thereby optimizing perioperative and postoperative care. This approach not only minimizes adverse effects but also enhances the patient outcomes.

Conclusion

This case underscores the importance of a multidisciplinary approach in managing patients with genetic mutations and complex surgical histories. Multimodal anesthesia, including an epidural block, played a crucial role in enhancing postoperative pain management, reducing opioid use, and minimizing

complications. Integration of ERAS protocols further optimized outcomes. Multimodal analgesia represents a paradigm shift in perioperative pain management, offering superior pain relief and improved patient outcomes compared to traditional opioid-centric approaches. By understanding and utilizing the unique mechanisms of action of different analgesic agents, clinicians can tailor treatment strategies to optimize pain management while minimizing risks and enhancing recovery. Continued research and standardized protocols are vital for improving management and outcomes in similar cases [1-19].

References

1. Mirandola S, Pellini F, Granuzzo E, Lorenzi M, Accordini B, et al. (2019) Multidisciplinary management of CDH1 germinal mutation and prophylactic management hereditary lobular breast cancer: a case report. International Journal of Surgery Case Reports 58: 92-95.
2. Petridis C, Arora I, Shah V (2014) Frequency of pathogenic germline mutations in CDH1 in breast cancer patients with lobular histology and family history. Breast Cancer Research 16: 488.
3. Schrader KA, Masciari S, Boyd N, Sara W, Pardeep K, et al. (2008) Hereditary diffuse gastric cancer: association with lobular breast cancer. Familial Cancer 7: 73-82.
4. Prabhakar A, Cefalu JN, Rowe JS, Kaye AD, Urman RD (2017) Techniques to Optimize Multimodal Analgesia in Ambulatory Surgery. Curr Pain Headache Rep 21: 24.
5. Bhatia A, Buvanendran A (2019) Anesthesia and postoperative pain control-multimodal anesthesia protocol. J Spine Surg 5: 160-165.
6. Neal JM, Barrington MJ, Brull R (2018) The second ASRA practice advisory on neurologic complications associated with regional anesthesia and pain medicine: Executive summary 2015. Regional Anesthesia & Pain Medicine 40: 395-406.
7. Sara Kianian, Jahnvi Bansal, Christopher Lee, Kalissa Zhang, Sergio D Bergese (2024) Perioperative multimodal analgesia: a review of efficacy and safety of the treatment options. Anesthesiology and Perioperative Science 2: 9.
8. Mieszczański Piotr, Grzegorz Górniewski, Paweł Ziemiański, Radosław Cylke, Wojciech Lisik, et al. (2023) Comparison between multimodal and intraoperative opioid free anesthesia for laparoscopic sleeve gastrectomy: a prospective, randomized study. Scientific Reports 13: 12677.
9. Martins Thaíza Paula, Danila Malheiros Souza, Daiane Malheiros Souza (2023) Use of multimodal anesthesia in the treatment of postoperative pain. BrJP 6: 427-434.
10. Camilleri M, Lembo A, Katzka DA (2017) Opioids in Gastroenterology: Treating Adverse Effects and Creating Therapeutic Benefits. Clin Gastroenterol Hepatol 15: 1338-1349.
11. Wu Yiquan, Liu Fuli, Tang Hongli, Wang Quanguang, Chen Limei, et al. (2013) The Analgesic Efficacy of Subcostal Transversus Abdominis Plane Block Compared with Thoracic Epidural Analgesia and Intravenous Opioid Analgesia After Radical Gastrectomy. Anesthesia & Analgesia 117: 507-513.
12. Doymus O, Ahiskalioglu A, Kaciroglu A, Bedir Z, Tayar S, et al. (2024) External oblique intercostal plane block versus port-site infiltration for laparoscopic sleeve gastrectomy: A randomized controlled study. Obesity Surgery 34: 1826-1833.
13. Pei JP, Zhang CD, Liang Y, Zhang C, Wu KZ, et al. (2020) Effects of epidural combined with general anesthesia versus general anesthesia alone in gastric cancer surgery: a propensity score matching analysis. Ann Transl Med 8: 473.
14. Adib E, El Zarif T, Nassar AH, Elie WA, Sarah AA, et al. (2022) CDH1 germline variants are enriched in patients with colorectal cancer, gastric cancer, and breast cancer. Br J Cancer 126: 797-803.
15. Tedaldi Gianluca, Chiara Molinari, Celina São José, Rita Barbosa-Matos (2021) Genetic and Epigenetic Alterations of CDH1 Regulatory Regions in Hereditary and Sporadic Gastric Cancer" Pharmaceuticals 14: 457.
16. Shenoy S (2019) CDH1 (E-cadherin) mutation and gastric cancer: genetics, molecular mechanisms and guidelines for management. Cancer management and research 10477-10486.
17. Petridis C, Arora I, Shah V (2014) Frequency of pathogenic germline mutations in CDH1 in breast cancer patients with lobular histology and family history. Breast Cancer Research 16: 488.
18. Prabhakar A, Cefalu JN, Rowe JS, Kaye AD, Urman RD (2017) Techniques to Optimize Multimodal Analgesia in Ambulatory Surgery. Curr Pain Headache Rep 21: 24.
19. Bres Capucine, Voron Thibault, Benhaim Leonor, Bergeat Damien (2022) A Multicentric Retrospective Study. Annals of Surgery 276: 830-837.