

Methylene blue, an option for minimally invasive pre-procedural colorectal cancer marking. Case Report

Gonzalo Andrés Domínguez Alvarado ^a, María Gabriela Quintero Arias ^b,
Marcela Bermúdez Mantilla ^c, Luisa Fernanda Hurtado Quiróz ^d, Luis Ernesto López Gómez ^e

- a. Physician. Specialist in Epidemiology. Professor. Universidad Autónoma de Bucaramanga. Surgical innovation and research group (GIIQ by its acronym in Spanish). ORCID: <https://orcid.org/0000-0002-7512-8733>
- b. MD. Universidad Autónoma de Bucaramanga. Hospital Nuestra Señora de los Remedios. ORCID: <https://orcid.org/0000-0001-9313-6916>
- c. General Physician. Hospital Universitaria de Santander. ORCID: <https://orcid.org/0009-0003-5451-1850>
- d. General Physician Universidad Industrial de Santander. ORCID: <https://orcid.org/0000-0001-8158-6880>
- e. Physician. Specialist in General and Oncologic Surgery. Fellowship in Obesity, Gastro Obeso Center of São Paulo. Universidad Autónoma de Bucaramanga. ORCID: <https://orcid.org/0000-0002-3666-2159>

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Abstract

Colorectal cancer is a common pathology, that causes approximately 861,000 deaths a year. The case of a 50-year-old male patient with arterial hypertension and type II diabetes mellitus, diagnosed with neoplasia in the descending colon, who underwent a minimally invasive procedure, following tumor marking with methylene blue by endoscopy of the lower gastrointestinal tract, is presented. Adequate postoperative period, without complications. The treatment of choice for colorectal cancer without metastasis is oncological exeresis. Currently the recommended surgical management is by means of a minimally invasive procedure, however, it is a challenge since in some cases the identification of the lesion is difficult and additionally requires a steep learning curve. Therefore, we use methylene blue for preprocedural tumor marking, with excellent results, without complications. Tumor marking with methylene blue prior to the minimally invasive procedure is safe, useful, economical, and low risk.

Keywords: Tumor marking, Methylene Blue, colorectal cancer, oncological exeresis.

Resumen

El cáncer colorrectal es una patología común que causa aproximadamente 861,000 muertes al año. Se presenta el caso de un paciente masculino de 50 años, con hipertensión arterial y Diabetes mellitus tipo II, con diagnóstico de neoplasia en colon descendente, al cual se le realizó procedimiento mínimamente invasivo, posterior a marcación tumoral con azul de metileno por medio de endoscopia de vías digestiva bajas. Postoperatorio adecuado, sin complicaciones. El tratamiento de elección para el cáncer colorrectal sin metástasis es la exeresis oncológica. Actualmente, el manejo quirúrgico recomendado es por medio de procedimiento mínimamente invasivo, sin embargo, es un desafío puesto que en algunos casos la identificación de la lesión es difícil y adicionalmente requiere una curva de aprendizaje pronunciada. Por lo anterior, utilizamos el azul de metileno para la marcación del tumor previo procedimiento, con excelentes resultados, sin complicaciones. La marcación tumoral con azul de metileno previa al procedimiento mínimamente invasivo es seguro, útil, económico y de bajo riesgo.

Palabras clave: marcación tumoral, azul de metileno, cáncer colorrectal, exeresis oncológica.

Introduction

Colorectal cancer (CRC) is a common pathology, which is influenced by both genetic and environmental factors (1).

Worldwide, CRC is the third most commonly diagnosed cancer in men and the second most commonly diagnosed cancer in women. It causes approximately 861,000 deaths per year. The highest incidence rates are found in Australia, New Zealand, Europe and North America, with a direct relationship to dietary and environmental exposure (2).

In Colombia, colon cancer is the third most common cancer and is the fifth cause of death from cancer, with an incidence of 15.8 per 100,000 inhabitants and a mortality of 7.6 per 100,000 inhabitants, being more frequent in men (2). Regarding Bucaramanga, we found that the incidence is 9.6 per 100,000 inhabitants, being 13.7 in women and 14.3 in men (3,4).

CRC is mainly located in the ascending colon and sigmoid colon (54.7%), cecum (16.7%) and transverse colon (14.3%) (5).

Diagnosis is based on clinical history, paraclinical tests and lower gastrointestinal endoscopy (LGE), which is the most effective resource for early detection, allowing complete visualization of the colon, evaluation of the

lesion and biopsy for histological confirmation of the lesion (6).

Treatment depends on the stage of the cancer, with oncologic exeresis being the treatment of choice in the case described in this article. Currently, laparoscopic surgery (LS) is one of the most widely used methods, and being a minimally invasive procedure, better results and shorter hospital stay are obtained (7).

The objective is to show an easy, effective, economical, and replicable method for pre-surgical CRC tumor marking by endoscopy, in order to perform a fast and simple intraoperative identification of the tumor during LS, in addition to a tumor resection with safe margins.

Surgical technique

50-year-old male patient, history of dilated heart disease with left ventricular hypertrophy (LVEF 30-35%), arterial hypertension (AHT) and non-insulin-requiring type II diabetes mellitus. Admitted to the emergency department for diffuse abdominal pain associated with changes in bowel habits, postprandial fullness, and unquantified weight loss.

Physical examination revealed no significant findings. The patient presented previous studies with evidence of fecal occult blood and Magnetic Resonance Imaging (MRI); with findings of thickening and edema of the mucosa of the transverse colon associated with mild inflammatory changes of the adjacent pericolic fat. They considered a gastrointestinal neoplastic process, for which reason LGE was requested with findings of a malignant tumor lesion in the descending colon (Image 1). The patient was evaluated by general surgery, who, in view of the clinical and imaging findings, considered hemicolectomy by laparoscopic technique after endoscopic tumor marking.

Imagen 1. Lesión tumoral de aspecto maligno en colon descendente



Technical Details:

Lower gastrointestinal tract endoscopy pre - procedure:

Materials:

- Endoscope
- Methylene blue or India dye
- Normal saline solution
- Endoscope injector

Hours prior to the definitive surgical procedure and with the same colon cleansing preparation, the colonoscopy study and marking of the lesion is performed. The colonoscopy procedure begins, location of the tumor lesion, the injector previously purged with saline solution and methylene blue is inserted through the working channel of the endoscope (Image 2).

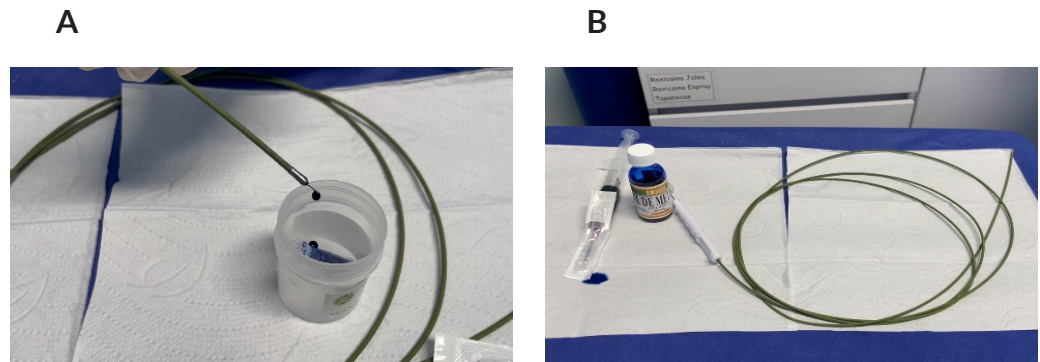


Image 2. Methylene blue in a 1:1 ratio (2.5 c.c. of saline and 2.5 c.c. of methylene blue in a 5 c.c. syringe) B. Injector previously flushed with saline and methylene blue.

It is prepared in dilution with saline solution in a 1:1 ratio (2.5 c.c. of saline solution and 2.5 c.c. of methylene blue in a 5 c.c. syringe), the periphery of the tumor lesion is located and it is proceeded to infiltrate in the caudal, lateral and proximal limits with a total volume of 5 c. c. of methylene blue in the submucosal and colon wall in the adjacent area of the identified tumor lesion, adequate marking is verified and the procedure is completed (Image 3).

« The colonoscopy procedure begins, location of the tumor lesion, the injector previously purged with saline solution and methylene blue is inserted through the working channel of the endoscope. »



Image 3. Lesión Tumor lesion infiltrated with methylene blue in the caudal, lateral and proximal limits with a total volume of 5 cc of methylene blue.

Minimally invasive procedure:

After LGE with the respective marking, the laparoscopic procedure is performed under general anesthesia. The lesion is identified after marking with methylene blue (Image 4), which facilitates the specific dissection maneuvers of the area to be treated. By meticulous dissection the medial descending mesocolon is moved and the dissection line is projected up to the splenic angle to free the hilum. Subsequently, the transverse colon is moved with section of the greater omentum. The descending mesocolon is dissected with progression of this, up to the branches of the middle colic. Mesocolon, tumor lesion and greater omentum are excised in one piece.

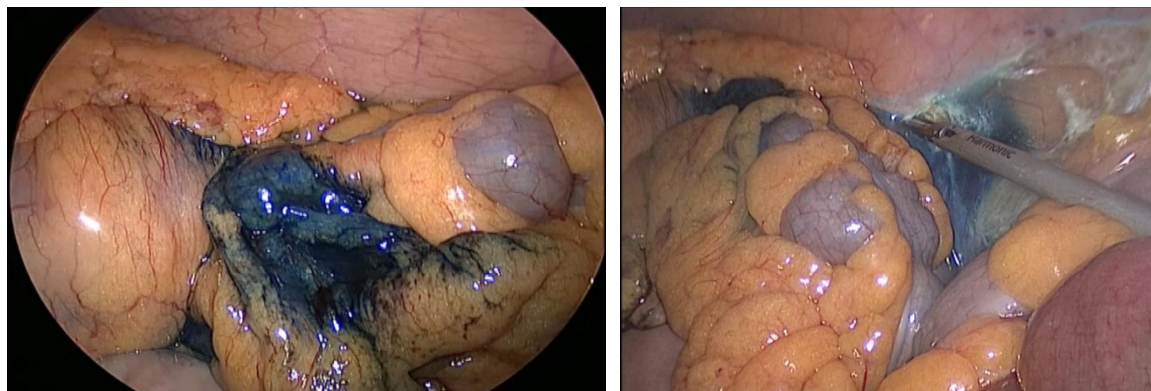


Image 4. Neoplastic lesion at the level of the descending colon previously marked with methylene blue.

The transverse colon was confronted with descending colon and latero-lateral colon-sigmoid anastomosis. Intracorporeal anastomosis with 45 mm linear Endo stapler blue reloading and closure of the entry orifice with laparoscopic hand suture with 3/0 caliber polidoxanone. Extraction of surgical specimen previously introduced in surgical bag through medial mini laparo-

tomy, wound protection technique. Closed peri anastomotic drainage. Closure of mini laparotomy and ports.

Postoperative evolution was stable and satisfactory. Adequate diuresis and ambulation, with abundant liquid stools, adequate pain modulation with conventional analgesia, wound without inflammatory signs, with active peristalsis, without symptoms or signs suggestive of complications. He was discharged on the seventh day after the surgical procedure with outpatient analgesic management and diet recommendations.

Discussion

Within the treatment of CRC, we find that oncologic exeresis is the treatment of choice. The approved techniques are laparotomy and LS. The resection margins and lymph node levels are similar in the two techniques, with the difference being the degree of invasion and less surgical trauma in LS. In Colombia, laparotomy is so far the most widely used (6).

LS has been increasing over the last decade as the procedure of choice for excision of non-metastatic CRC since it has a better short- and long-term oncologic outcome (6). In a recently published meta-analysis we found that LS as a method was associated with shorter operative time, less blood loss, shorter skin incision length, as well as shorter hospital stay with a similar surgical efficacy result (8).

However, it has been documented that LS is a challenge since it requires a steep learning curve on the part of the surgeon, given that the identification of the tumor lesion and an adequate radical resection can be a challenge for the surgeon and more specifically if the neoplastic process does not involve the serosa (9). For this reason, the use of techniques such as tumor marking has been implemented for a better result.

Currently, the use of tumor marking prior to the surgical procedure has been found to be a simple, safe, and economical method; however, in our environment its use has not been documented for colon cancer. Its use is wide, and has been proposed in multiple procedures such as marking prior to sentinel lymph node biopsy in breast cancer, gastric, endometrial and lung cancer by means of substances such as methylene blue, technetium-99 indocyanine green, injection of carbon nanoparticles, among others (10-12).

In this case reported, methylene blue is used, a thiazine dye that works as a tumor marker since it is captured by the intestinal absorptive epithelium; it can detect intestinal metaplasia or dysplasia, with a sensitivity of 92 - 98% and a specificity of 91 - 95%. After its administration, a laparoscopic

study will be performed where the areas affected by the lesion are more easily identified, in addition to the lymphatic drainage (13).

The aim of this technique is to facilitate the location and, therefore, an adequate resection of the margins, in order to offer a radical, safe procedure with fewer postoperative complications and a satisfactory outcome. In the clinical case of the patient described, who presents systemic comorbidities of cardiovascular type, it is essential to perform a quick procedure. From experience we know that the location of the lesion in cases of early or intermediate disease can take surgical time and extend the dissection to areas that do not require it.

In conclusion, endoscopic tumor marking facilitates intraoperative identification of lesions, especially when they are small, do not involve the serosa and do not generate an obstructive component.

The procedure is safe, useful, and economical. It does not generate anti-genic response. It does not expose to ionizing radiation and is low risk.

This option is very useful in the laparoscopic technique and also in the open laparotomy technique.

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E-mail correspondence: gdominguez@unab.edu.co

References

1. Pointet A, Taieb J. Cáncer de colon. *Colloids Surfaces A Physicochem Eng Asp* [Internet]. 2017;21(1):1–7. Available from: [http://dx.doi.org/10.1016/S1636-5410\(16\)81792-4](http://dx.doi.org/10.1016/S1636-5410(16)81792-4)
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J cancer* [Internet]. 2015 Mar 1 [cited 2019 Sep 20];136(5):E359-86. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25220842>
3. Sistema de Información de Cáncer en Colombia [Internet]. [cited 2021 Feb 2]. Available from: https://www.infocancer.co/portal/#!/filtro_incidencia/
4. Global Cancer Observatory [Internet]. [cited 2021 Feb 2]. Available from: <https://gco.iarc.fr/>
5. Et al. Localización y clínica asociada al cáncer de colon. Hospital Nacional Arzobispo Loayza: 2009 - 2013. *Horiz Médico*. 2015;15(2):49–55.
6. Lee GH, Malietzis G, Askari A, Bernardo D, Al-Hassi HO, Clark SK. Is right-sided colon cancer different to left-sided colorectal cancer? - A systematic review. *Eur J Surg Oncol* [Internet]. 2015;41(3):300–8. Available from: <http://dx.doi.org/10.1016/j.ejso.2014.11.001>
7. Vogel JD, Eskicioglu C, Weiser MR, Feingold DL, Steele SR. The American society of colon and rectal surgeons clinical practice guidelines for the treatment of colon cancer. *Dis Colon Rectum*. 2017;60(10):999–1017.

8. Dong B, Luo Z, Lu J, Yang Y, Song Y, Cao J, et al. Single-incision laparoscopic versus conventional laparoscopic right colectomy: A systematic review and meta-analysis. *Int J Surg* [Internet]. 2018;55(1):31–8. Available from: <https://doi.org/10.1016/j.ijso.2018.05.013>
9. Mathis KL, Nelson H. Controversies in laparoscopy for colon and rectal cancer. *Surg Oncol Clin N Am*. 2014;23(1):35–47.
10. Brahma B, Putri RI, Sari L, Karsono R, Purwanto DJ, Gautama W, et al. The application of 1% methylene blue dye as a single technique in breast cancer sentinel node biopsy. *J Vis Exp*. 2019;2019(148):1–6.
11. Cabrera S, Bebia V, Franco-Camps S, Forcada C, Villasboas-Roscolesi D, Navales I, et al. Technetium-99m-indocyanine green versus technetium-99m-methylene blue for sentinel lymph node biopsy in early-stage endometrial cancer. *Int J Gynecol Cancer*. 2020;30(3):311–7.
12. Bara T, Gurzu S, Jung I, Borz C, Baniias L, Bara T. Sentinel node biopsy using intravital blue dye. *Medicine (Baltimore)*. 2019;98(12):e14951.
13. Bottaro, Larsen B. NIH Public Access. *Bone*. 2008;23(1):1–7.
14. Kiesslich R, Fritsch J, Holtmann M, Koehler HH, Stolte M, Kanzler S, et al. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. *Gastroenterology*. 2003;124(4):880–8.
15. Repici A, Wallace MB, East JE, Sharma P, Ramirez FC, Bruining DH, et al. Efficacy of Peroral Methylene Blue Formulation for Screening Colonoscopy. *Gastroenterology* [Internet]. 2019;156(8):2198–2207.e1. Available from: <https://doi.org/10.1053/j.gastro.2019.02.001>