Revista Médica del
Hospital General de México

PERMANYER

Check for updates

CLINICAL CASES

Diagnosis of proximal colonic cancer due to hemorrhagic complication of thrombolytic therapy on myocardial infarction

José M. Alanís-Naranjo, Marco A. Muñoz-Pérez, and Francisco J. Cáceres-Castro*

Department of Cardiology, Hospital Regional 1° de Octubre, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Mexico City, Mexico

Abstract

The incidence of major bleeding in patients who receive thrombolytic therapy has been reported at 3.6%, with gastrointestinal bleeding the most common site followed by vascular access bleeds. The most typical cause of gastrointestinal bleeding is peptic ulcer disease. In the literature, few reports of thrombolytic therapy reveal undiagnosed colonic carcinoma. An 82-year-old man presented an acute posteroinferior myocardial infarction; he denied no gastrointestinal symptoms before hospital admission. Tenecteplase IV was administered with an improved clinical condition and an electrocardiogram showed reperfusion criteria. Approximately ten hours later, he experienced hematochezia; blood tests were relevant due to a descent of hemoglobin. A colonoscopy with biopsy revealed adenocarcinoma in the ascending colon. After stabilization, right hemicolectomy confirmed the cecum's invasive adenocarcinoma (T4aN0M0, stage IIB). The tumor was successfully removed, and chemotherapy was initiated. Thrombolytic therapy makes occult bleeding from colonic cancers obvious. Awareness of this fact may lead to earlier diagnosis of colonic cancers in asymptomatic patients and an increased likelihood of survival. Patients who develop gastrointestinal bleeding after thrombolytic therapy should receive a complete workup of the gastrointestinal tract to exclude serious but potentially curable diseases.

Keywords: *Colonic neoplasms. ST elevation myocardial infarction. Thrombolytic therapy. Gastrointestinal hemorrhage.*

Background

Thrombolytic therapy is a vital reperfusion strategy in ST-segment elevation myocardial infarction where primary percutaneous coronary intervention cannot be offered promptly but is well known for its hemorrhagic complications[1-3]. The incidence of major bleeding in patients who receive thrombolytic therapy has been reported at 3.6%, gastrointestinal bleeding the most common site (31.5%), followed by vascular access bleeds (23.8%)[4]. Peptic ulcer disease is the most typical cause of gastrointestinal bleeding after thrombolytic therapy[5]. In the literature, few reports of thrombolytic therapy reveal undiagnosed colonic carcinoma[5,6]. We report the case of a colonic adenocarcinoma diagnosed following thrombolytic therapy on myocardial infarction.

Case report

An 82-year-old man presented to the emergency department with severe, acute precordial chest pain. His past medical history included heavy smoking for 20 years (1 pack/day). An electrocardiogram showed an acute posteroinferior epicardial injury (Fig. 1).

Acetylsalicylic acid 300 mg PO, atorvastatin 80 mg PO, Clopidogrel 75 mg PO, and enoxaparin 60 mg SC

***Correspondence:**
José M. Alanís-Naranjo
E-mail: martin.alanis.n@gmail.com

Date of reception: 16-08-2022
Date of acceptance: 26-12-2022
DOI: 10.24875/HGMX.22000048

Available online: 15-06-2023
Rev Med Hosp Gen Mex. 2023;86(2):73-78
www.hospitalgeneral.mx

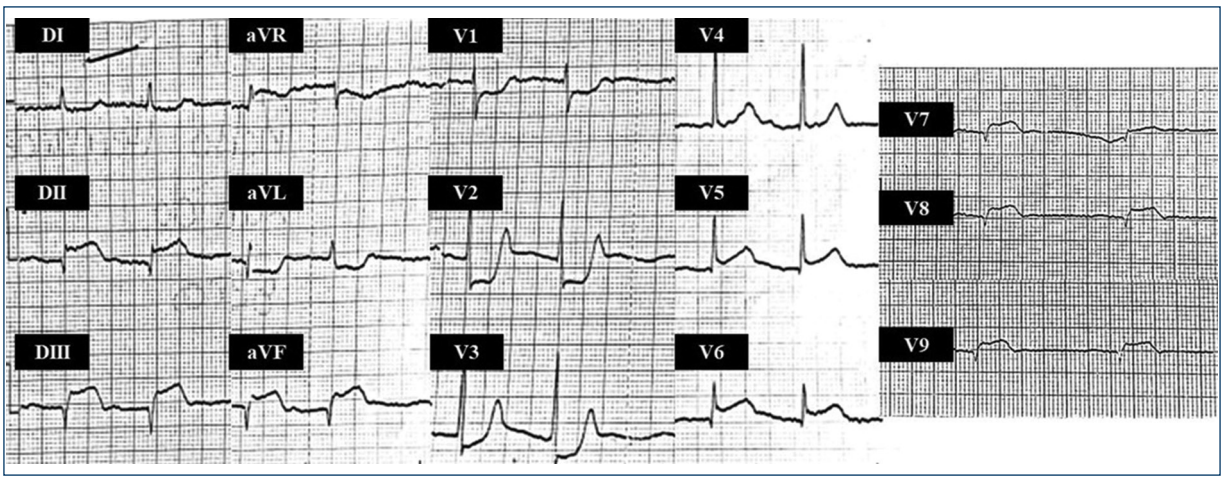

Figure 1. Initial electrocardiogram: elevation of ST-segment in leads DII, DIII, aVF, V7-V9, depression of ST-segment in leads aVL, and V1-V3 (posteroinferior epicardiac injury).

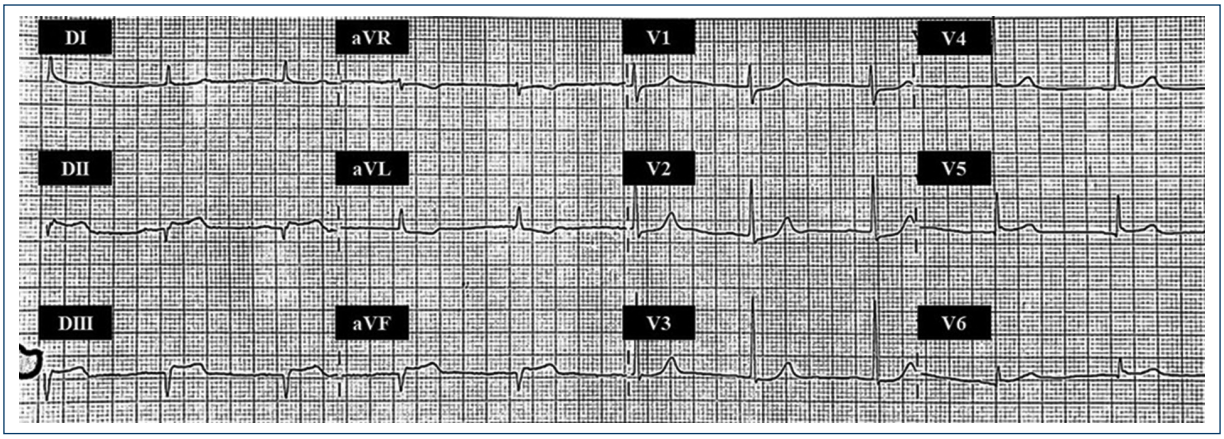

Figure 2. 2 h post-thrombolytic therapy electrocardiogram: depression of ST-segment in leads DII, DIII, aVF with normalization of ST-segment in leads aVL, and V1-V3.

with tenecteplase 20 mg IV were administered. The patient's clinical condition improved, and the electrocardiogram showed reperfusion criteria (Fig. 2).

Approximately ten hours later, he experienced hematochezia; blood tests were relevant due to a descent of hemoglobin (Table 1). He denied no gastrointestinal symptoms before hospital admission. Abdominal and rectal physical explorations were normal. He received a blood transfusion, and a colonoscopy with biopsy revealed adenocarcinoma in the ascending colon (Fig. 3). We continued antiplatelet therapy without recurrent bleeding. He recovered and was discharged home symptom-free 4 days after hospital admission.

He underwent a right hemicolectomy 1 month later. Further, workup confirmed the cecum's invasive adenocarcinoma (T4aN0M0, stage IIB). The tumor was successfully removed, and chemotherapy was initiated.

Discussion

Bleeding is a frequent complication of managing coronary artery disease (CAD) patients, especially those presenting with acute coronary syndromes (ACS). Studies have shown a risk of major bleeding of 1-8% at 30 days in ACS patients. The gastrointestinal tract is one of these patients' most frequent bleeding sources[7]. The literature reports that patients who experience

Table 1. Laboratories on hospitalization

	At admission	At the hemorrhagic event	At hospital discharge	Reference range
Leukocytes, mm^3	8,390	9,790	8,130	5,000-10,000
Platelets, mm^3	222,000	192,000	166,000	130,000-400,000
Hemoglobin, g/dl	13.2	9.9	10.7	14-18
Hematocrit, %	40.7	30	32.7	42-52
Sodium, mEq/L	129	132	135	136-145
Potassium, mEq/L	3.9	4.1	3.8	3.5-5.1
Chlorine, mEq/L	99	104	102	98-117
Magnesium, mg/dl	1.8	1.9	1.9	1.9-2.7
Glucose, mg/dl	111	106	86	74-106
Creatinine, mg/dl	1.12	1.1	0.75	0.7-1.3
Urea, mg/dl.	53	54	24	18-50
Blood urea nitrogen, mg/dl	24	25	11	9-23

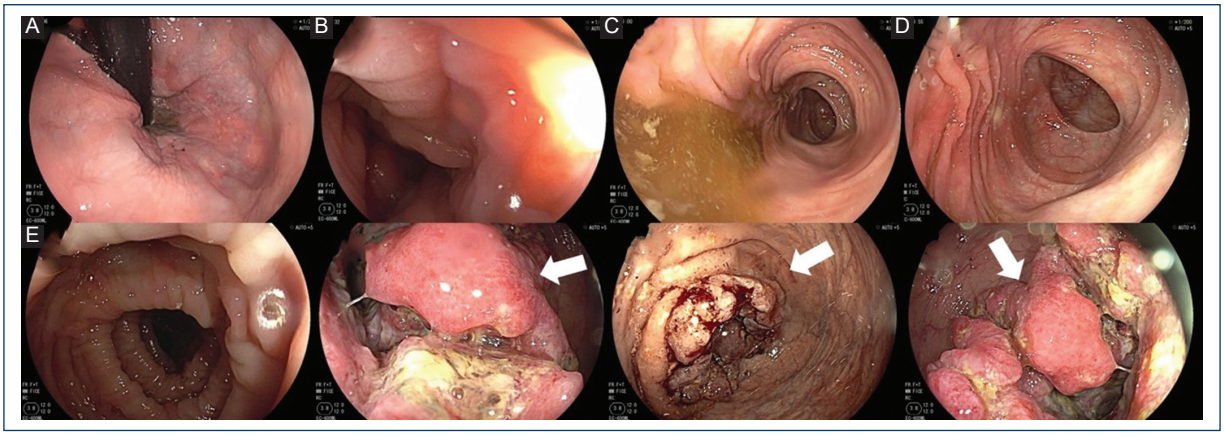

Figure 3. Colonoscopy. **A, B, C,** and **D:** rectum, sigmoid colon, descending and transverse colon preserved shape and architecture, mucosa of normal appearance. **E:** ascending colon: exophytic, ulcerated lesion with irregular edges that occlude 70% of the colonic lumen (arrows).

gastrointestinal bleeding while on anticoagulation or antiaggregant therapy positively diagnose colonic cancer at early stages (Stage I, II)[8-11].

Proximal colon cancer has a poorer prognosis than left colon cancer due to late-stage diagnosis and advanced patient age. Distal colon and rectum cancer symptoms include changing defecation habits, fresh rectal bleeding, mucoid discharge, and obstruction. In addition, proximal colon cancer is associated with anemia and non-specific symptoms. Due to non-specific symptoms such as anemia, abdominal pain, fatigue, and weight loss, it is difficult to diagnose the disease efficiently, resulting in a low survival rate[10].

One-hundred and thirty-five cases of colonic cancers during thrombolytic, anticoagulation, or antiaggregant therapy have been reported in five studies (Table 2). Of the reported cases, 83 patients were diagnosed with the early-stage colonic cancer[5,6,9-11].

The concomitance of very high thrombotic and hemorrhagic risks in a patient with bleeding poses complex treatment decisions[7]. Mehran et al. proposed an objective, hierarchically graded bleeding classification

Table 2. Clinical characteristics of cases of colonic cancer diagnosed due to hemorrhagic complication following thrombolytic, anticoagulation, or antiplatelet therapy

Author	Year	Country	Number of cases	Sex	Age (years)	Therapy type	Dosage	Site	Histology	Colonic cancer stage	Clinical outcome
Baker et al[5]	2002	United Kingdom	1	Male	68	Thrombolytic	Not specified	Descending colon	Not specified	Dukes's B carcinoma (Stage II)	Not specified
Schellhammer et al[6]	2007	Germany	1	Female	57	Thrombolytic	Alteplase; 20 mg	Rectosigmoid colon	Adenocarcinoma	Stage IIIa	Not specified
Norton et al[9]	1997	United Kingdom	8	Not specified	61 to 79	Anticoagulation	Warfarin; Not specified	6 in Caecum 2 in Proximal transverse colon	7 Adenocarcinoma 1 Non-Hodgkin lymphoma	2 Dukes's A carcinoma (Stage I) 4 Dukes's B carcinoma (Stage II) 1 Stage IV Non-Hodgkin lymphoma: Not specified	Alive and well with follow-up ranging from 2 years (lymphoma) to 4 years (Stage IV)
Aday et al[10]	2017	Turkey	27	14 Males 13 Females	34 to 88	Antiplatelet	8 only clopidogrel 9 only aspirin 10 Aspirin + Clopidogrel	Proximal colon	Not specified	20 Stage I/II (74%) 7 Stage III/IV (26%)	Not specified
Symeonidis et al[11]	2012	Greece	98	Not specified	71 (range 52-91)	Antiplatelet	65 Aspirin: 100 mg/d for 15.3 ± 6.51 years. 17 Clopidogrel: 75 mg/d, 5.85 ± 3.46 years 6 Ticlopidid: 250 mg twice daily, 5.85 ± 3.46 years 4 Dipyridamole: 200 mg twice daily, 5.85 ± 3.46 years. 6 Dual therapy; Not specified.	42 Right colon 33 Left colon 23 Rectum	Not specified	56 Stage I/II (57%) 34 Stage III (35%) 8 Stage IV (8%)	Not specified
Alanís et al. (present case)	2022	Mexico	1	Male	82	Thrombolytic	Tenecteplase; 20 mg	Ascending colon	Adenocarcinoma	Stage IIB	Alive and well during the first year follow-up

Table 3. Bleeding academic research consortium (BARC) definition for bleeding

Type	Definition
0	No bleeding
1	Bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a health-care professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a health-care professional
2	Any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: (1) requiring non-surgical, medical intervention by a health-care professional, (2) leading to hospitalization or increased level of care, or (3) prompting evaluation
3 a	Overt bleeding plus hemoglobin drop of 3-< 5 g/dL (provided hemoglobin drop is related to bleed) Any transfusion with overt bleeding
3 b	Overt bleeding plus hemoglobin drop ≥ 5 g/dL (provided hemoglobin drop is related to bleed) Cardiac tamponade Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) Bleeding requiring intravenous vasoactive agents
3 c	Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal) Subcategories confirmed by autopsy or imaging or lumbar puncture Intraocular bleed compromising vision
4	Coronary artery bypass graft-related bleeding Perioperative intracranial bleeding within 48 h Reoperation after closure of sternotomy for the purpose of controlling bleeding Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period Chest tube output ≥ 2 L within a 24-h period
5 a	Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious
5 b	Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation

that serves the clinical community as helpful guidance on managing patients with antithrombotic or anticoagulant drugs who suffer any bleeding. (Bleeding Academic Research Consortium [BARC] Definition for Bleeding) (Table 3)[12]. When the thrombotic risk is higher than the risk of recurrent bleeding in a patient who develops minor (BARC type 2) or major bleeding (BARC type ≥ 3)[12], it is suggested to continue antithrombotic therapy, as long as the bleeding event is not a life-threatening bleed[7]. In the case of resuming antiplatelet therapy after gastrointestinal bleeding, it is recommended to restart a single treatment with low-dose aspirin with restarting the second antiplatelet agent as soon as possible[7].

We present a patient with a colonic carcinoma been revealed due to a thrombolytic therapy complicated by a gastrointestinal major bleeding event (BARC type 3a: Overt Bleeding plus Hemoglobin drop > 3 to < 5 g/dL), a situation few documented in the literature. A colonoscopy with biopsy was performed for further evaluation, showing adenocarcinoma in the ascending colon. After stabilization of a patient with a moderate risk of recurrent bleeding risk (Extracranial major bleeding) but with a very high thrombotic risk (ACS <8 days), antithrombotic therapy was restarted without recurrent bleeding or hemoglobin drop.

Conclusion

This case illustrates a complication of thrombolytic therapy that led to the discovery of undiagnosed colon cancer. Patients with proximal colon cancer have a poorer prognosis due to non-specific symptoms, resulting in a low survival rate. Early-stage diagnosis rates are higher in patients with rectal bleeding and melena. As a result of thrombolytic therapy, occult bleeding from colonic cancer becomes apparent. Increasing awareness of this fact may result in earlier detection of colonic cancer in asymptomatic patients and a greater likelihood of survival. In addition, an examination of the digestive tract should be conducted for patients who develop gastrointestinal bleeding after thrombolytic therapy to exclude serious but potentially curable conditions.

Funding

The authors declare that there was no funding for this article.

Conflicts of interest

The authors declare to have no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were carried out on humans or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

References

1. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European society of cardiology (ESC). Eur Heart J. 2018;39:119-77.
2. Jinatongthai P, Kongwatcharapong J, Foo CY, Phrommintikul A, Nathisuwan S, Thakkinstian A, et al. Comparative efficacy and safety of reperfusion therapy with fibrinolytic agents in patients with ST-segment elevation myocardial infarction: a systematic review and network meta-analysis. Lancet. 2017;390:747-59.
3. Bundhun PK, Janoo G, Chen MH. Bleeding events associated with fibrinolytic therapy and primary percutaneous coronary intervention in patients with STEMI: a systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2016;95:e3877.
4. Moscucci M, Fox KA, Cannon CP, Klein W, López-Sendón J, Montalescot G, et al. Predictors of major bleeding in acute coronary syndromes: the global registry of acute coronary events (GRACE). Eur Heart J. 2003;24:1815-23.
5. Baker JW, Mitchell SJ, Dixon AR. Early diagnosis of colonic carcinoma: a haemorrhagic complication after the use of tissue plasminogen activator. Postgrad Med J. 2002;78:429.
6. Schellhammer E, Pourhassan S, Topp S, Fürst G. Diagnosis of colo-rectal cancer revealed by haemorrhagic complication of intraarterial thrombolysis. Vasa. 2007;36:143-4.
7. Halvorsen S, Storey RF, Rocca B, Sibbing D, Ten Berg J, Grove EL, et al. Management of antithrombotic therapy after bleeding in patients with coronary artery disease and/or atrial fibrillation: expert consensus paper of the European society of cardiology working group on thrombosis. Eur Heart J. 2017;38:1455-62.
8. Landefeld CS, Beyth RJ. Anticoagulant-related bleeding: clinical epidemiology, prediction, and prevention. Am J Med. 1993;95:315-28.
9. Norton SA, Armstrong CP. Lower gastrointestinal bleeding during anticoagulant therapy: a life-saving complication? Ann R Coll Surg Engl. 1997;79:38-9.
10. Aday U, Gundes E, Ciyiltepe H, Cetin DA, Deger KC, Gulmez S, et al. Does antiaggregant administration lead to early diagnosis in proximal colon cancer? North Clin Istanb. 2017;4:173-9.
11. Symeonidis D, Koukoulis G, Christodoulidis G, Mamaloudis I, Chatzinikolaou I, Tepetes K. Impact of antiplatelet treatment on colorectal cancer staging characteristics. World J Gastrointest Endosc. 2012;4:409-13.
12. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research consortium. Circulation. 2011;12:2736-47.