



CASE REPORT

REVISED Case Report: Large ileal intramural hematoma presenting as an intestinal obstruction in a patient on Warfarin with incidental breast cancer [version 2; peer review: 2 approved]

Maryam Alizadeh Forutan ¹, Fereshteh Araghian Mojarad², Nasrin Rahmani³

¹Gastrointestinal Cancer Research Center, Mazandaran University of Medical Science, Sari, Iran

²Golestan University of Medical Sciences, Gorgan, Iran

³Department of General Surgery, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

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Abstract

Intramural hematoma of the gastrointestinal (GI) tract, which can present as abdominal pain or obstruction, can be a rare complication of oral anticoagulants, in particular Warfarin. In this case report, we describe an 81-year-old female patient presenting with abdominal pain, nausea, and vomiting with a previous history of rectorrhagia. The patient was receiving Warfarin therapy due to cardiac valve replacement for the past 8 years. Laboratory workup revealed elevated INR and anemia. Diagnosis of ileal intramural hematoma was based on ultrasound and CT scan findings. The patient was treated by conservative approaches including administration of fresh frozen plasma, cessation of oral intake, and fluid resuscitation. In CT images, a mass on the left breast and lymphadenopathy on the left axilla were also noticed. Given that most GI intramural hematomas caused by over-anticoagulation are treated non-surgically, considering a patient's drug history, especially in older patients with abdominal pain and obstruction symptoms, is of particular importance.

Keywords

Gastrointestinal Tract, hematoma, anticoagulant therapy, warfarin.

Open Peer Review

Reviewer Status

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version 1 11 Jun 2018	 report	 report

- Kevin W. Olden**, University of Tennessee, School of Medicine, Memphis, USA
- Everton Cazzo** , Faculdade de Ciências Médicas da Universidade Estadual de Campinas (FCM/UNICAMP), Campinas, Brazil

Any reports and responses or comments on the article can be found at the end of the article.

Corresponding author: Maryam Alizadeh Forutan (dr.forutan2@gmail.com)

Author roles: **Alizadeh Forutan M:** Data Curation, Methodology, Project Administration, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Mojarad FA:** Writing – Original Draft Preparation; **Rahmani N:** Supervision

Competing interests: No competing interests were disclosed.

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REVISED Amendments from Version 1

in this version of the manuscript, the discussion section was revised with more focus on hematomas in other GI sites. also, radiologic manifestation and therapeutic strategies were included.

Any further responses from the reviewers can be found at the end of the article

Introduction

Abdominal pain is a common complaint in patients referred to hospital emergency departments and varies from mild and self-limiting to severe and life-threatening conditions^{1,2}. Depending on the location of the pain, symptoms, physical examination and medical history, a differential diagnosis is provided¹. Since mortality and the rate of surgery secondary to abdominal pain is higher in elderly patients, prompt diagnosis of the causative agent is of particular importance³. Non-specific causes, gastroenteritis, irritable bowel syndrome, urologic disorders, and gastroenteritis are among the common etiologies for abdominal pain⁴. An uncommon reason for abdominal pain and bowel obstruction is intestinal intramural hematoma following anticoagulation therapy^{5,6}. Warfarin, a vitamin K antagonist, is widely used to prevent thrombosis formation due to mechanical heart valves, atrial fibrillation, pulmonary embolism and deep venous thrombosis⁷. The occurrence of intestinal intramural hematoma secondary to anticoagulant therapy is an uncommon condition, which affects 1/2500 patients receiving Warfarin⁸. The small intestine is the common site affected by spontaneous intramural hematoma, and intramural hematoma of the colon and rectum are rare⁹. This complication is mostly treated by non-surgical approaches.

This article reports a case of a relatively large ileal intramural hematoma developed following Warfarin use and accidental detection of breast malignancy during a CT scan.

Case presentation

An 81-year-old woman was admitted to the Mazandaran Heart Center, Sari, Iran in February, 2018 with a 4-day history of nausea, vomiting, and abdominal pain. She had been taking Warfarin (5 mg orally once a day) and aspirin (80 mg/day) for 8 years after aortic valve replacement without close monitoring and had a history of hematochezia caused by Warfarin toxicity one year ago. Colicky pain, an increase in bowel sounds and periumbilical tenderness without distension was determined by physical examination. The primary laboratory findings revealed anemia (Hb: 9.8 g/dl; normal value: 11.5–13.5 g/dl) and elevated INR (6; therapeutic range: 2–3.5), liver function and biochemistry tests were within normal values. Normal left ventricular systolic function, LVEF of 55–60%, septal hypertrophy, normal functioning prosthetic valve, and dilatation of the ascending aorta were reported by echocardiography.

During an abdominal and pelvic ultrasound, long mucosal thickening possibly through the ascending and sigmoid colon was observed, suggestive of intramural hematoma. The patient

was placed on *nil per os*, received supportive care and two units of fresh frozen plasma. Due to normal cardiac evaluation and partial relief of symptoms on the second day of admission, the patient was referred to surgical consultation with the possible diagnosis of descending colon and sigmoid intramural hematoma. For re-administration of anticoagulants, heparin infusion (1000 units/hour) began with precise monitoring of prothrombin time.

On the fourth day, CT scan was performed with intravenous and oral contrast (Figure 1) and intramural hematoma of ileum was diagnosed. During the CT, a radiologist noticed a mass on the left breast and a lymph node with a malignant feature on the left axilla. With the improvement of abdominal pain and vomiting (on the fourth day), oral feeding was resumed. After mammography and breast biopsy, pathological examination revealed invasive ductal cell carcinoma with lymphatic and perineural invasion. According to the immunohistochemistry staining, tumor cells were strongly ER positive, PR negative, 15% Ki67 positive and equivocal for HER2. The patient was referred to the oncology-hematology department to receive appropriate treatment.

The patient was discharged 10 days after admission and Warfarin therapy (5 mg/d) was resumed. The patient was visited 2 weeks later with good general health assessment. Letrozole (2.5 mg/day) was started because the patient refused chemotherapy and radiotherapy.

Discussion

The most significant reason for the intestinal intramural hematoma is trauma, while non-traumatic or spontaneous causes include anticoagulation therapy, malignancies, and blood disorders, which are considered to be rare^{10,11}. The intestinal sites involved in the intramural hematoma in order of frequency include jejunum, duodenum, and ileum¹². The intramural hematoma can affect the esophagus, gastric and colon, but these cases are less prevalent. This complication is mostly associated with Warfarin and is more common in male subjects^{10,13,14}; patient's chief complaints are abdominal pain, nausea, vomiting, and absence of bowel movements or flatulence^{6,15}. Melena and jaundice are rare presentation too¹⁶. Hyperechoic bowel wall thickening or free fluid may be noted in ultrasound findings, nevertheless, as a non-unspecific test, normal ultrasound results cannot rule out the possible diagnosis of gastrointestinal intramural hematoma. The diagnostic key test is a CT scan, but there is no agreement in the literature concerning the use of contrast materials, as it may obscure intramural hyper-density and hemorrhage, and also increase the risk of exposure^{17,18}. Bowel wall thickening, luminal narrowing, obstruction caused by edema, picket fence sign can be demonstrated in CT-scan^{19,20}. Products related to hemoglobin breakdown in hematoma site will lead to a high density signal as "ring sign" in MRI which is unique to confirm diagnosis²¹. In the review of fourteen patients by Yoldaş *et al.*, nine patients were treated non-surgically, with eight of them were on Warfarin therapy for heart disorders. Increased INR was also observed in anticoagulant receiving patients¹⁰. In addition to

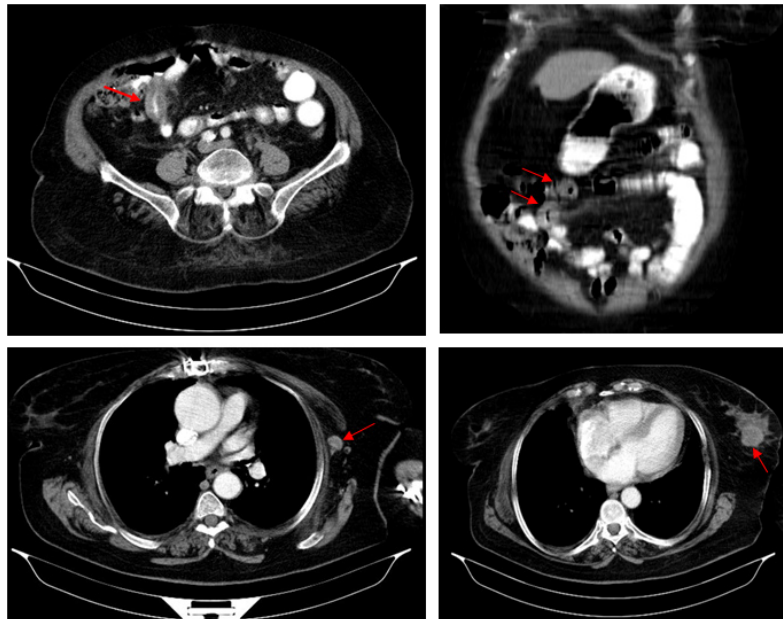


Figure 1. Contrast-enhanced abdominal and pelvic CT. (A) Circumferential thickening of an ileal loop with adjacent fat stranding in Sagittal (1) and Coronal (2) view. (B) LAP on left axilla with malignant feature measuring 18x16mm (3) and 32x26 mm mass in left breast (4).

impaired coagulation tests, increased WBC count and anemia may also present^{15,19}. For early diagnosis of this complication, taking a detailed medical history of anticoagulation use, especially in older patients with abdominal pain, is required. Treatment usually is conservative and includes cessation of oral anticoagulation, serum therapy, and correction of coagulation indices by vitamin K and blood products^{8,19,22}. As this condition is rare, there is no treatment as the best option in the literature but unlike the past, there is a tendency for conservative management of cases today. The patient's condition is the most important consideration in choosing the treatment. Referral to surgery is usually preferred when the patient has peritonitis, obstruction, ischemia or necrosis¹⁶. Accurate recognition of this complication leads to prevention of unnecessary surgical procedures and the risk of bleeding progression. There are also evidence that Warfarin may act as an anticancer agent; Warfarin was shown to lower the incidence of organ

specific cancers including lung, prostate, and breast^{23,24}. Therefore, the development of invasive breast cancer in the present case, despite the long-term use of Warfarin, is interesting.

Finally, the question arises of which anticoagulant can be used as an alternative to Warfarin in patients with frequent life threatening hemorrhagic events, which requires no regular monitoring but has an acceptable efficacy.

Consent

Written informed consent was obtained from patient during admission and follow up for the publication of the patient's clinical information and accompanying images.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

References

1. Cartwright SL, Knudson MP: **Evaluation of acute abdominal pain in adults.** *Am Fam Physician.* 2008; **77**(7): 971–8. [PubMed Abstract](#)
2. Macaluso CR, McNamara RM: **Evaluation and management of acute abdominal pain in the emergency department.** *Int J Gen Med.* 2012; **5**: 789–97. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Lewis LM, Banet GA, Blanda M, *et al.*: **Etiology and clinical course of abdominal pain in senior patients: a prospective, multicenter study.** *J Gerontol A Biol Sci Med Sci.* 2005; **60**(8): 1071–6. [PubMed Abstract](#) | [Publisher Full Text](#)
4. Viniol A, Keuncke C, Biroga T, *et al.*: **Studies of the symptom abdominal pain--a systematic review and meta-analysis.** *Fam Pract.* 2014; **31**(5): 517–29. [PubMed Abstract](#) | [Publisher Full Text](#)
5. Altıkaya N, Parlakgümüş A, Demir Ş, *et al.*: **Small bowel obstruction caused by intramural hematoma secondary to warfarin therapy: a report of two cases.** *Turk J Gastroenterol.* 2011; **22**(2): 199–202. [PubMed Abstract](#) | [Publisher Full Text](#)
6. Avent ML, Canaday BR, Sawyer WT: **Warfarin-induced intramural hematoma of the small intestine.** *Clin Pharm.* 1992; **11**(7): 632–5. [PubMed Abstract](#)
7. Sohrabi MK, Tajik A: **Effective feature selection of clinical and genetic to predict warfarin dose using artificial neural network.** *Tehran Univ Med J.* 2016; **73**(12):

900–5.

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8. Limmer AM, Clement Z: **Extensive small bowel intramural haematoma secondary to warfarin.** *J Surg Case Rep.* 2017; **2017**(3): rjx044.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
9. Lobo L, Koudki R, Prasad HI K, *et al.*: **Colon Obstruction due to an Anticoagulant Induced Intramural Haematoma; A Rare Case Report.** *J Clin Diagn Res.* 2013; **7**(4): 739–41.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
10. Yoldaş T, Erol V, Çalışkan C, *et al.*: **Spontaneous intestinal intramural hematoma: what to do and not to do.** *Ulus Cerrahi Derg.* 2013; **29**(2): 72–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. Birns MT, Katon RM, Keller F: **Intramural hematoma of the small intestine presenting with major upper gastrointestinal hemorrhage. Case report and review of the literature.** *Gastroenterology.* 1979; **77**(5): 1094–100.
[PubMed Abstract](#)
12. Birla RP, Mahawar KK, Saw EY, *et al.*: **Spontaneous intramural jejunal haematoma: a case report.** *Cases J.* 2008; **1**(1): 389.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
13. Dhawan V, Mohamed A, Fedorak RN: **Gastric intramural hematoma: a case report and literature review.** *Can J Gastroenterol.* 2009; **23**(1): 19–22.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Hong M, Warum D, Karamanian A: **Spontaneous intramural esophageal hematoma (IEH) secondary to anticoagulation and/or thrombolysis therapy in the setting of a pulmonary embolism: a case report.** *J Radiol Case Rep.* 2013; **7**(2): 1–10.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. Bekheit M, AlaaSallam M, Khafagy P-A, *et al.*: **Non-traumatic intramural hematomas in patients on anticoagulant therapy: Report of three cases and overview of the literature.** *Afr J Emerg Med.* 2014; **4**(4): e1–e4.
[Publisher Full Text](#)
16. Khan K, Saeed S, Alothman S, *et al.*: **Warfarin induced mesenteric and intestinal hematoma requiring surgical resection to relieve small bowel obstruction: A case report.** *Int J Surg Case Rep.* 2018; **52**: 111–13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
17. Azcón FM, Martínez AM, Chinchilla AS, *et al.*: **Findings in spontaneous intramural intestinal hematoma imaging.** *Rev Argent Radiol.* 2016; **80**(1): 39–44.
Reference Source
18. Sorbello MP, Utiyama EM, Parreira JG, *et al.*: **Spontaneous intramural small bowel hematoma induced by anticoagulant therapy: review and case report.** *Clinics (Sao Paulo).* 2007; **62**(6): 785–90.
[PubMed Abstract](#) | [Publisher Full Text](#)
19. Abbas MA, Collins JM, Olden KW: **Spontaneous Intramural Small-Bowel Hematoma: Imaging Findings and Outcome.** *AJR Am J Roentgenol.* 2002; **179**(6): 1389–94.
[PubMed Abstract](#) | [Publisher Full Text](#)
20. Ou Yang CM, Hsiao TF, Chou YH, *et al.*: **Spontaneous intramural small-bowel hematoma due to a rare complication of warfarin therapy: Report of two cases.** *Journal of Acute Medicine.* 2014; **4**(1): 45–48.
[Publisher Full Text](#)
21. Abdel Samie A, Sun R, Huber A, *et al.*: **Spontaneous intramural small-bowel hematoma secondary to anticoagulant therapy: a case series.** *Med Klin Intensivmed Notfmed.* 2013; **108**(2): 144–48.
[PubMed Abstract](#) | [Publisher Full Text](#)
22. Kones O, Dural AC, Gonenc M, *et al.*: **Intramural hematomas of the gastrointestinal system: a 5-year single center experience.** *J Korean Surg Soc.* 2013; **85**(2): 58–62.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Schulman S, Lindmarker P: **Incidence of Cancer after Prophylaxis with Warfarin against Recurrent Venous Thromboembolism. Duration of Anticoagulation Trial.** *N Engl J Med.* 2000; **342**(26): 1953–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
24. Haaland GS, Falk RS, Straume O, *et al.*: **Association of warfarin use with lower overall cancer incidence among patients older than 50 years.** *JAMA Intern Med.* 2017; **177**(12): 1774–80.
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Everton Cazzo 

Department of Surgery, Faculdade de Ciências Médicas da Universidade Estadual de Campinas (FCM/UNICAMP), Campinas, Brazil

All the comments and suggestions were appropriately addressed.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Gastrointestinal Surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 21 October 2019

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Everton Cazzo 

Department of Surgery, Faculdade de Ciências Médicas da Universidade Estadual de Campinas (FCM/UNICAMP), Campinas, Brazil

This is an interesting and well-written case report of a disease which poses a significant difficulty in relation to its diagnosis and management.

The main comments which I think may improve and enrich this study are the following:

1. The discussion should include a more profound comment on the therapeutic options available for the cases when the bleeding does not stop after interrupting Warfarin, mainly radiological and surgical interventions.
2. The discussion should also include some comments on hematomas which arise on other segments of the gastrointestinal tract, such as stomach and duodenum, since they are close to the topic reported.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Gastrointestinal Surgery

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 05 Nov 2019

Maryam Alizadeh Forutan, Mazandaran University of Medical Science, Sari, Iran

Hello and thanks for your attention.

I will definitely consider and correct the things you have mentioned.

Competing Interests: No competing interests were disclosed.

Author Response 10 Dec 2019

Maryam Alizadeh Forutan, Mazandaran University of Medical Science, Sari, Iran

Dear reviewer,

Many thanks for your attention and points.
We have revised the manuscript according to your suggestions and highlighted them.

Competing Interests: No competing interests were disclosed.

Reviewer Report 12 September 2019

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Kevin W. Olden

Division of Gastroenterology, Regional One Medical Center, University of Tennessee, School of Medicine, Memphis, TN, USA

- The case is well presented, and the clinical details are well written and meticulously enumerated. The case is relevant for practice and will benefit clinicians.
- The only comment I would have is to change the word "ileum" on p.2 (2nd paragraph) to "ileal" and the word "rectorrhagia" to "hematochezia" in order to conform to the more commonly used medical terminology.
- This paper is an excellent case report that presents useful information for the clinician. I would recommend acceptance if the two semantic changes were made.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Functional gastrointestinal disorders

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 14 Sep 2019

Maryam Alizadeh Forutan, Mazandaran University of Medical Science, Sari, Iran

Greetings and regards.

Thanks for bothering to read this case report and for taking the time to review the article.

I will consider the issues raised.

Competing Interests: There isn't any competing interest.

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