

Case Report

A rare case of hemorrhagic infarction and obstruction of small bowel caused by warfarin therapy and literature review

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Abstract: Hemorrhagic infarction and strangulated obstruction of small bowel caused by non-traumatic spontaneous intramural small-bowel hematoma (n-SISBH) secondary to warfarin therapy is extremely rare. Its non-specific symptoms and signs together with its confusing accessory examination results make n-SISBH a complicated entity for clinical treatment. We report a case of a 67-year-old male patient with long-term use of warfarin sodium complaining of persistent abdominal pain. The diagnosis of hemorrhagic infarction and strangulated obstruction of small bowel caused by n-SISBH secondary to long term warfarin therapy was finally diagnosed during the laparotomy. Partial ileectomy and side to side anastomosis of the remaining small bowel was performed. Three months follow-up showed that the patient had been recovering well. Following this rare case we performed a review of literature to promote the understanding of n-SISBH. N-SISBH is an extremely rare entity. Physicians should be fully alerted with this entity on reception of patients complaining abdominal pain under anticoagulation therapy. Timely conservative therapy works well in many cases, but surgical procedures should be prudently reserved in some cases. Though we have been making progress in understanding n-SISBH, there is still a long way to go before we could reach a standard operation protocol for n-SISBH. Early diagnosis appears to be essential as many patients could then be treated non-operatively with good survival.

Keywords: Non-traumatic spontaneous intramural small-bowel hematoma (n-SISBH), hemorrhagic infarction, warfarin therapy, strangulated obstruction, laparotomy, ileectomy

Introduction

Abdominal pain in elderly patients is common in hospital emergency services with some requiring immediate surgery. It is reported that diagnosis for at least 40% of cases is uncertain. The reason for such large number cases being uncertain is due to the fact that patients come to the emergency wards due to appendicitis, or intestinal obstruction, besides hernias, or cancers/tumors. Hence in this scenario it is rather difficult for the attending physician to anticipate that it could also be intramural hematoma as such cases are very rare. Post-traumatic intramural hematoma of small intestine has only been recognized after its first report in ancient civilization about 177 years ago [1]. Non-traumatic spontaneous intramural small-bowel hematoma (n-SISBH) of small

bowel secondary to anticoagulant therapy is extremely rare, with its incidence being about 1/2500 in patients receiving phenprocoumon therapy [2]. But the incidence of n-SISBH was predicted to increase with the widespread use of anticoagulation therapy in an aging population. Hence the aim of this report was to impart the knowledge that acute abdominal pain could also be due to abdominal obstruction due to n-SISBH, resulting from the use of oral anticoagulants. Hematomas can be ameliorated in many cases with conservative modalities and surgery may not be the option for the treatment, since physical examination could be used to determine the site of tenderness on abdominal quadrants. Further computerized tomography (CT scan) and ultrasonography (US) could be used for diagnosis and the patients may be advised to discontinue warfarin or other antico-



Figure 1. The white arrow indicating homogeneous and circumferential intramural thickening with hyperdense material in the ileum wall of the lower abdomen, measuring up to 24 cm in length, together with the adjacent dilated segment of the ileum.



Figure 2. The white arrows indicating severe ileum wall thickening and lumen narrowing in the cavity comparing with that in **Figure 1**.

of diagnosis of intramural hematoma. However, in this case non-operative therapy could not be performed, which could be the choice of treatment in some cases. Surgery is preferred if generalized peritonitis or intestinal obstruction develops.

Case report

A 67-year-old male was referred to our hospital presented with a 1-day history of persistent general abdominal pain marked in the lower abdomen. 1 day before, he had been admitted to a local hospital because of abdominal pain suffering with nausea or vomiting. His medical history revealed a diagnosis of atrial fibrillation, which had been treated with warfarin sodium (3 mg/day) regularly for about 2 years. Abdominal examination was unremarkable. At the time of admission to the local hospital, prothrombin time (PT) was 68.2 s, and activated partial thromboplastin time (APTT) was 75.0 s, and international normalized ratio (INR) was 5.68. There he received a emergency non-enhanced CT scan, which showed homogeneous and circumferential wall thickening and lumen narrowing of the ileum in the lower abdomen, measuring up to 24 cm in length, together with the adjacent dilated segment of the ileum and little effusion indicating hemorrhagic ascites (**Figure 1**). According to these findings, the diagnostic hypothesis of intramural hematoma and coagulopathy were made. The patient was treated promptly with conservative therapy including bowel rest, nasogastric decompression, warfarin discontinuation, vitamin K₁ (Vit K₁) injection and fresh frozen plasma (FFP). However, after 1-days' conservative treatment (20 mg Vit K₁ and 500 ml FFP in total), the abdominal pain was aggravated. The physical examination showed belly distension and widespread rebound tenderness with guarding. The laboratory data showed that PT was 60.6 s, APTT was 72.5 s and INR was 5.05. He then received a enhanced CT scan, which showed severer ileum wall thickening and lumen narrowing as well as the effusion in the cavity (**Figure 2**) compared with that showed in the non-enhance CT the day before. Based on these findings, acute diffusing peritonitis, hemorrhagic infarction and strangulated obstruction of small bowel due to n-SISBH secondary to warfarin were diagnosed. The patient was sent to our hospital for receiving exploratory laparotomy emergently. Approximately 150 cm

agulant therapies. Herein we report the cases of a male patient with n-SISBH secondary to regular warfarin intake. He underwent laparotomy and partial ileectomy regardless of timely conservative therapy. Furthermore, a review of literature has been performed for a better understanding of n-SISBH.

In this case abdominal US and CT evaluations were performed together will help the accuracy



Figure 3. The necrotic small intestine of a length about 80 cm was resected.

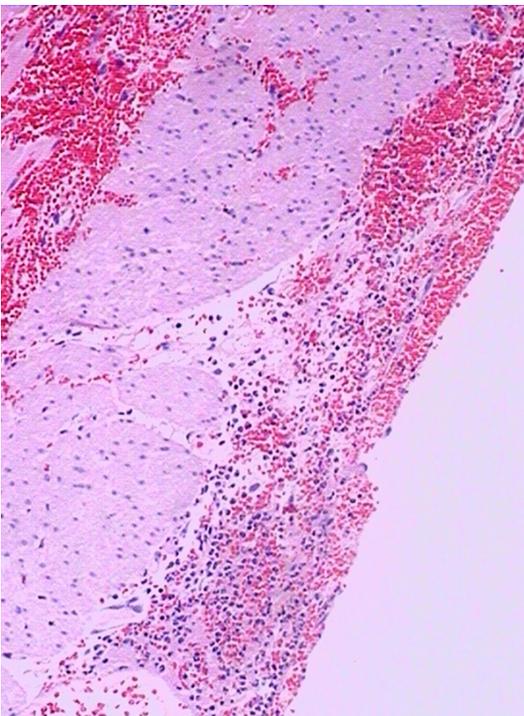


Figure 4. Extensive hemorrhagic necrosis with infiltration of neutrophils appeared in the wall of the small intestine (HE, $\times 100$).

from the ileocecal loop, a segment of the ileum of a length about 80 cm was necrotic (**Figure 3**). Hence, the patient received partial ileectomy and side to side anastomosis by using straight-cut closure. Postoperative pathological diagnosis confirmed ileal hemorrhagic necrosis (**Figure 4**). The patient was discharged uneventfully after 19 days' hospital stay and resumed warfarin treatment at therapeutic dose with international normalized ratio between 2.0 and 3.0.

Discussion

In 1904, Stutherland have reported a case of a nontraumatic hematoma in a child with Henoch-Schonlein purpura. Four years later, von Kahautz diagnosed this condition in a patient with hemophilia [3]. Because of these early reports, n-SISBH has become increasingly recognized as a complication of anticoagulant therapies; bleeding disorders; malignancies; inflammatory and immune diseases. However n-SISBH still has not been well understood [4]. To our knowledge, less than 40 reports about n-SISBH have been issued till now. Due to the rarity of this entity, there is no study that contains sufficient evidence to standardize treatment for this entity either. In the past, exploratory laparotomy, evacuation of hematoma, resection, or intestinal bypass played a role in the diagnosis and treatment of n-SISBH [5, 6]. With the recent advances of cross-sectional imaging, exploratory celiotomy is rarely necessary to establish the diagnosis. The first choice of treatment for several disorders such as pulmonary embolism, deep vein thrombosis, prosthetic heart valves or even persistent arterial fibrillation is oral anticoagulants like warfarin [7, 8].

The first step in the treatment is cessation of anticoagulant administration and correction of coagulation parameters with FFP and Vit K₁. And most cases would recover well avoiding unnecessary operation [9]. But in this case, though timely treated with warfarin discontinuation, Vit K₁ and FFP immediately after the diagnostic hypothesis of n-SISBH and coagulopathy was made, complications such as hemorrhagic infarction and strangulated obstruction of small bowel and peritonitis still arise, leading to exploratory laparotomy and ileectomy without any choice. In this case, as well as other similar cases, we presumed that it's most probably because of the timely positive conservative therapy was unsuitable, or at least inadequate, for reversing the anti-coagulation. That's really a confusing situation pertaining to carrying out an individualized treatment strategy in choosing between conservative therapy and surgical procedures. However, we cannot exclude other reasons such as anatomical and histological difference as well as individual and specie differences, since we still haven't figured out the precise pathophysiological mechanism and diagnosis criteria of n-SISBH yet.

Studies indicated that through the gastrointestinal tract, the small bowel is the most affected region. Regarding the location of the hematoma in the intestinal wall, the jejunum was the most affected (71.6%), followed by the duodenum (29.8%) and the ileum (15.8%) [10]. Nevertheless, it remains unclear why the jejunum is the site of predilection for spontaneous hematoma [7]. The most probable physiopathology of n-SISBH would be characterized by the shredding of the terminal arteries as they leave the mesentery and penetrate the muscularis layer of the intestinal wall. Consequently, the hemorrhage dissects the bowel wall between the muscularis mucosa and the muscularis layers. Some authors speculate that the progression of the symptoms is due to an intramural osmotic gradient caused by the hematoma, leading to its expansion in the intestinal wall with lumen occlusion [11]. It's concluded that over-anticoagulation with warfarin is the most common cause of n-SISBH, followed by other risk factors include hemophilia, idiopathic thrombocytopenic purpura, leukemia, lymphoma, myeloma, chemotherapy, vasculitis, pancreatitis, and pancreatic cancer [3, 12]. However, there is still a lack of predictive factors for the occurrence of n-SISBH. Particular attention should be given to the interpretation of the thickened intestinal wall, which occurs in other afflictions, such as inflammatory, infectious and neoplastic diseases as well as intestinal ischemia [4].

On the other hand, CT scan has proved to be a sensitive diagnostic method [13, 14]. And a few authors even have suggested that non-contrast CT scan should be performed prior to the contrast-enhanced scan [14]. However, there are still no specific biomarkers for reference in surveillance of its progression. That's still a question about when and how to make some adjustment of the conservative therapy before it was fully overruled. Or what if we could take surgical procedures earlier in this case?

Conclusion

N-SISBH is extremely rare with its major complaint of severe stomach pain. Over-dose of anticoagulant therapy with warfarin is the most common cause of n-SISBH.

Diagnostic tests like US and CT scan can be fairly nonspecific, but when we know that the patient has been receiving an anticoagulant

then there is a possibility of accurate prediction of n-SISBH. In such cases Physicians should be fully alerted with this entity on receiving patients complaining abdominal pain under anticoagulation therapy. Early diagnosis with positive conservative therapy could be adopted as the best choice and avoid unnecessary operation in many cases, but it was not possible in this case due to associated complications. Allowing for not only its complicated pathophysiological mechanism but also the absence of its predictive factors and specific biomarkers, there is still a long way to go before we could reach a standard treatment or operation protocol for n-SISBH.

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Disclosure of conflict of interest

None.

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