Case Report

Anticoagulant-Induced Intramural Intestinal Hematoma: Report of Three Cases and Literature Review

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Spontaneous intestinal hematoma is a rare complication of anticoagulant therapy. The authors reported three cases of intramural and submucosal small bowel hematoma resulting from warfarin administration. The first patient presented with abdominal pain, had intramural hematoma at jejunum, the most common site of intramural small bowel hematoma. Another patient who had submucosal duodenal hematoma presented with massive upper gastrointestinal bleeding, a rare manifestation of small bowel hematoma. The third patient presented with intramural ileal hematoma that caused abdominal pain and palpable mass after a short period of warfarin therapy. Typical findings on abdominal computerized tomography yielded the diagnosis. All patients rapidly improved after conservative treatment. The history of anticoagulant use with prolonged INR value in patients presented with abdominal pain should alert physicians to search for this entity. It is extremely important to recognize this syndrome in order to avoid an unnecessary operation since the outcome is usually excellent after conservative treatment.

Keywords: *Intramural hematoma, Anticoagulant*

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Case Report

Case 1

A 67 year-old Thai woman came to the ER because of acute abdominal pain. She had epigastric discomfort without any additional symptoms for 1 day. She took warfarin 5 mg/day regularly for Gerstmann's syndrome. Physical examination revealed mild tenderness at epigastrium. Otherwise was unremarkable.

Hemoglobin on admission was 18.8 gm/dl (normal 12.5-15.5 gm/dl.) and platelet count was 503,000/mm^3. Prothrombin time (PT) was 240.4 sec (control 12.8 sec) with INR of 16.2 and activated partial thromboplastin time (aPTT) was 125.4 sec (control 30.9 sec). Other blood tests were in normal range.

During the first day of admission, warfarin was discontinued and vitamin K 1 mg and two units of fresh-frozen plasma (FFP) were administered. However, abdominal pain did not improve and hemoglobin decreased to 8.1 gm/dl. Intra-abdominal bleeding was suspected, therefore, abdominal CT examination (Fig. 1-2) was performed as Fig. 1 and 2 show. Intramural hematoma of the small intestine was established and FFP was transfused until INR returned to normal range. After conservative treatment, abdominal pain

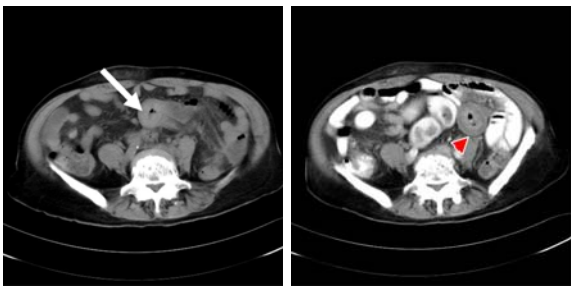

Fig. 1-2 CT scan showed circumferential thickening wall of jejunum (arrow) approximately 14 cm in length with flip-flop phenomenon (arrow head) after contrast administration

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resolved within seven days and she was discharged without warfarin. She has been doing well until now and warfarin was permanently withdrawn.

Case 2

A 70 year-old Thai man was brought to the ER due to acute colicky pain with hematemesis and melena stool for three days. On initial physical examination, he was stuporous and the blood pressure was too low to be measured. He had markedly pale conjunctiva and generalized abdominal tenderness.

He had taken war farin for mitral regurgitation and atrial fibrillation for eight years and the INR value was 3.7 on the last follow up visit.

Hemoglobin was 6.6 gm/dl and platelet count was 298,000/mm^3. PT was over 200 sec (control 12.6 sec). BUN and Creatinine was 34 and 2.9 mg/dl respectively. Other blood tests were unremarkable.

After resuscitation, nasogastric lavage showed fresh bloody content. Three units of packed red cell (PRC), 4 units of FFP and 1 mg of vitamin K were administered. He underwent esophagogastroduodenoscopy (Fig. 3-4) and the diagnosis was submucosal hematoma of duodenum. In total, four units of PRC and 10 units of FFP were transfused until INR was 1.9. With supportive treatment, the pain resolved on day 5. The patient was discharged on day 16 and anticoagulant was withdrawn permanently.

Case 3

A 60-year old Thai man came to the hospital with high-grade fever and persistent abdominal discomfort lasting for two weeks. After receiving antibiotics for one week, he became icterus. On physical examination, the temperature was 38.5□c and moderate icteric sclera was detected. The abdomen was neither distended nor tender.

Laboratory results showed total bilirubin 6.3 mg/dL, direct bilirubin 3.1 mg/dL, SGOT 82 U/L (normal 0-38 U/L), SGPT 82 U/L (normal 0-38 U/L) alkaline phosphatase 207 U/L (normal 39-117 U/L). Abdominal CT results showed as Fig. 5-6. The diagnosis was superior mesenteric vein thrombosis, therefore, heparin was started to prevent further clot formation. The patient was also given ceftriazone 2 gm intravenously for treating E.coli detected in two hemoculture specimens. All symptoms gradually subsided within one week of treatment and warfarin was started and adjusted to 7.5 mg daily. He was planned to discharge with INR value of 2.9. However, he developed acute abdominal pain with a palpable tender abdominal mass 5 cm at right lower quadrant. The repeated INR result was 3.9 and the hemoglobin level was 11.9 gm/dl but dropped to 10 gm/dl on the following day. The diagnosis of intramural bowel hematoma was entertained and abdominal CT (Fig. 7-8) confirmed the diagnosis. Vitamin K 1 mg

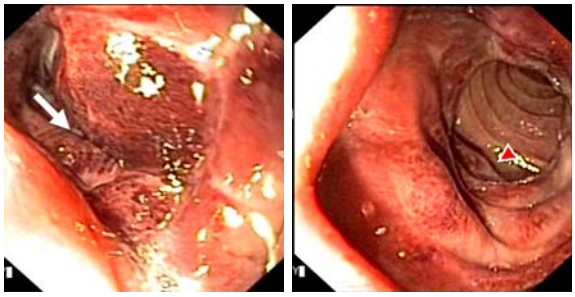

Fig. 3-4 Endoscopic findings showed circumferential markedly edematous bluish hemorrhagic mucosa (arrow) extended from duodenal bulb to the second part of duodenum causing narrowing of lumen with area of transitional zone to normal mucosa (arrow head). The diagnosis was submucosal duodenal hematoma

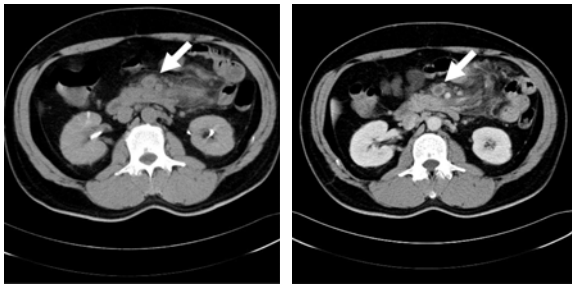

Fig. 5-6 CT scan showed filling defect within the superior mesenteric vein extending to confluent portion with splenic vein, compatible with venous thrombosis

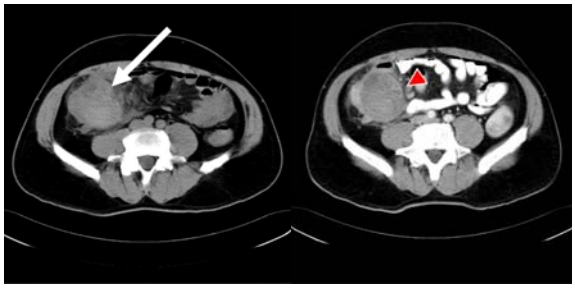

Fig. 7-8 CT scan showed a round inhomogeneous hyperdense mass of 7.5 x 7.2 cm in the wall of terminal ileum (arrow) with flip-flop phenomenon (arrow head)

was injected intravenously and 12 units of FFP were administered until the INR value was 1.1. Two days later, abdominal pain resolved and he has been doing well until now.

Discussion

The authors presented three cases of intestinal hematoma that had uncommon complications of oral anticoagulant therapy. The outcome was excellent after conservative treatment.

Oral anticoagulant was widely used in many indications such as deep vein thrombosis, persistent atrial fibrillation, etc. The most serious complication associated with the use of warfarin is bleeding due to excess anticoagulation, occurring about 7.6 per one hundred patient-years[1]. However, spontaneous intramural intestinal hematoma is an uncommon site of hemorrhage. Small bowel hematoma had been reported as one case per 2,500 anticoagulated patients per year[7] but the lesion in the large intestine had been reported much less in the literatures[2-5]. The authors reviewed retrospective data of cases reports that showed similar clinical characters for five years and six cases were found as shown in Table 1.

Intestinal hematoma should be suspected as the cause of abdominal pain in patients with a history of warfarin use accompanying with prolonged INR value and anemia. This symptom usually presented in all patients[3,8,9] with varying degree from acute abdominal emergency to cramping pain because of partial gut obstruction. Other common symptoms include nausea, vomiting, abdominal distension[10]. Clinically gastrointestinal hemorrhage, hematemesis, melena, or rectal bleeding, is presented in less than half of the patients[3,9-11] and massive bleeding causing hemodynamic compromise like case 2 in our report is rarely reported[12]. Duration of symptoms are usually a few days (varying from 1 day to 3 weeks) before hospitalization[3,9-11,13-15]. On physical examination, abdominal tenderness, either localized or diffuse, with or without signs of peritoneal irritation, is also present in varying degrees. Most patients (85%) have no anemia initially, but it will develop within the first 48 hours after admission[10-11,15]. Laboratory tests usually reveal PT, PTT, and INR value above the range of normal (mean INR value 4.40-11.6)[3,11]. However, it does not appear to be a close correlation between bleeding and the level of prothrombin activity, since there were reported cases of intramural hematoma in patients receiving warfarin with PT in therapeutic range[3,16-17]. There is also no relation between the duration of anticoagulant therapy and the onset of symptoms. The duration of drug use varied from 1-132 months[3] but has been reported as few as 10 days[14]. However, one case in the present report which showed large intestinal hematoma after the use of warfarin for only eight days, which is the shortest time that has been reported in the literature.

The location of hemorrhage is usually in the submucosal layer of the bowel and originating from a small vessel that produces slow bleeding[2,10]. The site of large bowel involvement can occur anywhere[4,5], however, the small bowel is mostly affected in jejunum (64-69%), followed by ileum (26-38%), and duodenum (10-23%) respectively[2,11]. This differs from traumatic small bowel hematoma which most commonly affects the duodenum due to the fixation of this portion of the intestine at the ligament of Treitz with the trauma forcing the fixed retroperitoneal portion of the duodenum against the spine[14,18]. Moreover, it tends to be focal and a shorter segment of the bowel is involved than in nontraumatic spontaneous hematoma[11,14]. The average length of spontaneous small bowel hematoma was 23 cm[11]. Most (85%) are single and non extensive hematoma, but multiple hematoma or small bowel involvement accompanied with hematoma in the large bowel can be found. Intraluminal, intramesenteric, and retroperitoneal hemorrhage can occur with intramural hematoma[12]. Hemoperitoneum occurred in half of the patients[11]. Gut obstruction owing to intramural hematoma has been reported[19,20].

The abdominal ultrasonography and CT are useful radiographic studies to confirm the diagnosis. Although, findings on plain abdominal radiography are not specific, they may be helpful in initial evaluation and suggest the diagnosis of intramural hematoma[9,14,15]. The findings found in two-thirds of patients are the presence of multiple dilated loops of bowel with fluid levels, a generalized haziness of films due to hemoperitoneum, and the presence of a "thick bowel sign"[3]. On sonography, mass in the intestinal wall appears as round or nonperistaltic tubular mass with a central echogenic core of compressed mucosa, surrounded by an anechoic halo which was thickened bowel wall due to hemorrhage[3]. Sensitivity for detection such findings by sonography is 71.4%[3]. CT, which is considered as an imaging of choice, yields the diagnosis in 80-100%[3,11]. Characteristics findings are circumferential bowel wall thickening, luminal narrowing, and intestinal tract obstruction. Intramural hyperdensity that corresponds to hematoma may not be present in all cases (40%)[11]. This can be seen during the first 10 days after the onset and will decrease as the

Table 1. Symptomatic GI complications following prolonged oral anticoagulants used from year 2003-2007 (5-year review)

Author; year	No. of cases	Sex	Age	Symptoms	Signs	Initial INR value	Site of intramural bleeding	Treatment	Results
Krysa J et al, 2003[22]	1	F	75	Abdominal pain, distension, absolute constipation 1 d	Generalized tender abdomen with palpable 10 x 10 cm mass in left iliac fossa	3.4	Rectus sheath	Conservative	Improved within 48 h
Shinozaki S et al, 2004[23]	1	M	57	Postpandrial abdominal distension, nausea, vomiting 2 d	Soft, flat, mild tender abdomen	14.6	Jejunum	Conservative	Improved within a few days
Hsiao CW et al, 2004[20]	1	F	51	Right lower abdominal pain, nausea and vomiting 4 d	Right lower quadrant pain with rebound tenderness	4.57	Ileocecal valve	FFP 8 units and appendectomy	Doing well after 2 years follow-up period
Basile A et al, 2004[24]	1	M	67	Acute pain and palpable mass in lower abdomen	-	-	Rectus abdominis and psoas muscle	Embolization via transfemoral at right inferior epigastric artery and right lumbar artery	Doing well after 9 months follow-up period
Dineen RA et al, 2005[25]	1	F	68	Abdominal pain with refractory hypotension	Central abdominal tenderness with left groin bruising	3.4	Rectus sheath	Palliative treatment	Died
Chen YY et al, 2006[19]	1	M	39	Nausea, vomiting, abdominal pain	-	normal	Duodenum	Conservative	Improved at 1 week
Chaiteerakij R et al, 2007*	3	F	67	Epigastric pain 1 d	Mild tender at epigastrium	16.2	Jejunum	FFP	Resolved within 7 days
		M	70	Hematemesis	Generalized abdominal tenderness	PT over 200 sec	Duodenum	Vitamin K 1 mg, FFP 10 units	Resolved within 5 days
		M	60	Abdominal pain	Abdominal mass at right lower quadrant	3.9	Ileum	Vitamin K 1 mg, FFP 12 units	Resolved within 2 days

* Present report

hematoma ages, then evolves into hypodensity area that can mimic intramural cystic lesion[21].

The mainstay of management is medical treatment, with discontinuing of the anticoagulant drugs, correction of the prothrombin time with intravenous vitamin K with or without FFP, and correction of anemia. Usually, FFP 2-4 units with vitamin K treatment can correct coagulation parameters into normal range within 72 hours[3]. Moreover, symptoms usually subside within a few days and rapid improvement in abdominal pain after correction of coagulation is another clue for the diagnosis[9,15]. If there is no sign of improvement within 48-72 hours after conservative treatment, it is necessary to reconsider the diagnosis[2]. Surgical treatment is considered only if the patients developed complications such as peritonitis, or bowel infarction. Complete resolution of the hematoma usually occurs within 3 weeks after the onset, varying from 10 days to 2 months[2,9,11,14,21]. The factor determining prognosis is the extension of the hematoma[11]. High mortality rate is found in patients with extensive hematoma, such as involvement of more than half the length of the small bowel. Reintroduction of anticoagulant therapy after resolution of hematoma can be done individually with careful risk and benefit evaluation, since the recurrent intramural hematoma has been reported 3 in 5 cases after restarting anticoagulant[2].

Conclusion

Spontaneous intramural small-bowel hematoma is an uncommon complication in patients with excessive anticoagulation with warfarin. The symptoms vary from vague abdominal pain, acute abdomen, to intestinal obstruction or gastrointestinal tract bleeding. Since abdominal pain is usually the presenting symptom, it should alert the physician to search for intramural hematoma in the patient with a history of anticoagulants administration who presented with abdominal pain even if INR value is in the therapeutic range. Abdominal ultrasonography and especially CT scan can confirm the diagnosis. Medical treatment is the treatment of choice with a good outcome. Surgery should be reserved for cases in which the diagnosis is doubtful and for patients who exhibit signs of bowel necrosis or peritonitis.

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รายงานผู้ป่วยที่มีเลือดออกในผนังลำไส้จากยากันเลือดแข็งตัว และทบทวนวรรณกรรมที่เกี่ยวข้อง

รุ่งฤดี ชัยธีรกิจ, สมบัติ ตรีประเสริฐสุข, วโรชา มหาชัย, พินิจ กุลละวณิชย์

ภาวะเลือดออกในผนังลำไส้เป็นภาวะแทรกซ้อน ที่พบได้ไม่บ่อยจากยากันเลือดแข็งตัว ผู้นิพนธ์ได้รายงานผู้ป่วย 3 รายที่มีเลือดออกในผนังลำไส้เล็กหลังได้รับยา warfarin ผู้ป่วยรายแรกมาด้วยอาการปวดท้อง และมีเลือดออกในผนังลำไส้เล็กส่วนเจจูนัม ซึ่งเป็นตำแหน่งที่พบได้บ่อยสุดของลำไส้เล็ก ผู้ป่วยรายที่สองมีเลือดออกใต้ชั้นเยื่อบุผนังลำไส้เล็กส่วนดูโอดีนัม มาด้วยอาการเลือดออกจากทางเดินอาหารส่วนบนเป็นปริมาณมาก ซึ่งเป็นอาการแสดงที่พบได้น้อยของภาวะเลือดออกในผนังลำไส้เล็ก ผู้ป่วยรายที่สามมีเลือดออกในผนังของลำไส้เล็กส่วนไอเลียมมาด้วยอาการปวดท้องและคลำได้ก้อนในท้องหลังได้ยา warfarin ไม่นาน ภาวะนี้สามารถวินิจฉัยได้จากลักษณะเฉพาะที่พบจากภาพเอกซเรย์คอมพิวเตอร์ ผู้ป่วยทุกราย มีอาการดีขึ้นหลังได้รับการรักษาแบบประคับประคอง แพทย์ควรคิดถึงภาวะนี้ ในผู้ป่วยที่มีประวัติ ได้รับยากันเลือดแข็งตัว และมีค่า INR ผิดปกติ และมาด้วยอาการปวดท้อง การวินิจฉัยได้มีความสำคัญ เนื่องจากภาวะนี้ตอบสนองดีต่อการรักษาแบบประคับประคอง และเพื่อหลีกเลี่ยงการผ่าตัดโดยไม่จำเป็น