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A retrospective review of patients with non-traumatic spontaneous intramural hematoma

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Background/aims: *Non-traumatic spontaneous intramural hematoma of the small intestine is a rare clinical condition, most commonly caused by over-anticoagulation. In this study, the clinical approach algorithm for patients diagnosed with a spontaneous isolated intramural hematoma of the small intestine associated with over-anticoagulation and the long-term outcomes of the patients are presented.* ***Material and Methods:*** *The records of patients who were diagnosed with intramural hematoma in 3 different medical faculty hospitals between 2007 and 2011 were retrospectively analyzed. After excluding patients with trauma history, hematoma in organs other than the small intestine, and with etiological factors other than over-anticoagulation, 15 patients with an isolated intramural hematoma of the small intestine were evaluated within the scope of the study.* ***Results:*** *The sites of first admission were emergency departments for 10 patients (66.6%) and other clinics for 5 patients (33.3%). Thirteen patients (86.6%) received medical treatment and two patients (13.3%) underwent surgical treatment. During the hospitalization period, a total of two patients (13.3%) died. Out of the 11 patients with an average follow-up of 22 months (range: 4-48 months), no patient had a relapse of intramural hematoma and three patients (27.7%) died due to reasons not related to intramural hematoma.* ***Conclusion:*** *Intramural hematoma diagnosis should be known by all physicians, because the site of first admission may be different clinics, since the clinical presentation begins with non-specific complaints. Early and accurate diagnosis by non-invasive methods will preclude unnecessary surgical interventions.*

Key words: Anticoagulant, over-anticoagulation, warfarin, hematoma, intramural hematoma

Non-travmatik spontan intramural hematomlu hastaların retrospektif değerlendirilmesi

Giriş ve Amaç: *Non-travmatik spontan intramural hematom oldukça nadir görülen bir klinik durumdur ve en sık nedeni aşırı antikoagülasyondur. Bu çalışmada; aşırı antikoagülasyona bağlı olarak spontan ince barsak intramural hematom tanısı koyulan hastalardaki klinik yaklaşım algoritmasını ve hastaların uzun dönem sonuçlarını sunmayı amaçladık.* ***Gereç ve Yöntem:*** *2007-2011 yılları arasında 3 farklı tıp fakültesi hastanesinde intramural hematom tanısı koyulmuş olan hastaların kayıtları retrospektif olarak incelendi. Travma anamnezi olan, ince barsak dışı organlarda da hematom saptanan ve aşırı antikoagülasyon dışı etyolojik faktör saptanan hastalar inceleme dışı bırakıldıktan sonra; izole olarak ince barsak intramural hematomu saptanan 15 hasta değerlendirilmeye alındı.* ***Bulgular:*** *On hastada (%66.6) ilk başvuru merkezi acil servisler iken 5 hastada (%33.3) diğer kliniklerdi. Onüç hastaya (%86.6) medikal tedavi uygulanırken 2 hastaya (%13.3) cerrahi tedavi uygulandı. Hastanede yatış sürecinde 2 hastada (%13.3) tedavi mortalite ile sonuçlandı. Ortalama 22 ay (4-48) düzenli klinik takipleri olan 11 hastanın hiçbirinde intramural hematom kliniği tekrarlamadı, 3 hasta (%27.7) takip sürecinde intramural hematomla ilişkisiz nedenlerden dolayı öldü.* ***Sonuç:*** *Hastaların ilk başvuru merkezleri farklı olabildiği ve başlangıç klinik bulguları non-spesifik olduğu için intramural hematom tüm klinisyenler tarafından bilinmesi gereken bir tanıdır. Non-invaziv yöntemlerle erken dönemde ve doğru tanı koyulması gereksiz cerrahi girişimleri engelleyecektir.*

Anahtar kelimeler: Antikoagülan, aşırı antikoagülasyon, warfarin, hematom, intramural hematom

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INTRODUCTION

Oral anticoagulants have long been used for prophylaxis and treatment of various indications. Parallel to the advances in intensive care conditions, as well as with radiological and surgical developments, the number of patients with indications of oral anticoagulation treatment has increased over the past two decades (1). Corresponding to this common usage, it is clear that patients who develop complications due to the use of anticoagulants will be more frequently encountered. A major complication that can be observed during the use of oral anticoagulants is bleeding (2).

Intramural hematoma (IMH) has been first described in 1838 (3) and is most commonly caused by abdominal trauma. Non-traumatic cases are called spontaneous hematoma and their most common cause is overanticoagulation. Other risk factors include hemophilia, idiopathic thrombocytopenic purpura, leukemia, chemotherapy, vasculitis, and pancreatitis (4). Spontaneous IMH of the small intestine is a very rare clinical condition and its incidence is 1/2500 (5). Generally they are not life-threatening complications and may improve with medical treatment.

This study presents the clinical follow-up course, radiological findings, and long-term results of fifteen patients with an isolated spontaneous IMH of the small intestine that represent the experiences of three different university hospitals.

PATIENTS and METHODS

The records of patients who had been diagnosed with IMH in the General Surgery Clinics of Sakarya University Medical School, Erciyes University Medical School, and Maltepe University Medical School between 2007 and 2011 were retrospectively analyzed. Fifteen patients with spontaneous IMH of the small intestine were evaluated within the scope of the study, after excluding patients with trauma history, hematomas in organs other than the small intestine (including the colon), retroperitoneal hematoma, and etiological factors other than over anticoagulation treatment.

The demographic characteristics, indication for anticoagulation, duration of anticoagulant use, presenting signs and symptoms, time to the onset of signs and symptoms, laboratory and radiological findings, management interventions, hospitalization course, and the long-term outcomes of the patients were evaluated.

The following parameters were used in the computed tomography (CT) examination protocols: 4 x 5-mm collimation, 5-mm slice thickness, 2.5-mm scan interval, 120 kVp, and 250 mAs. Approximately 125 mL of intravenous iohexol (Omnipaque 300; GE Healthcare, Little Chalfont, United Kingdom), Iopromide (Ultravist 300; Bayer-Schering, Berlin, Germany), or Iomeprol (Iomeron 350; Bracco, Milano, Italy) was given to patients who has no contraindications for intravenous contrast agent use.

The below medical treatment algorithm was followed in all patients other than the two (13.3%) who required surgical intervention:

1) termination of warfarin sodium treatment and oral food intake, 2) nasogastric decompression in patients with the complaint of vomiting, 3) fresh-frozen plasma transfusion and vitamin K administration, 4) erythrocyte transfusion in patients with anemia, 5) daily follow-up of blood count and clotting parameters, 6) frequent mobilization, 7) initiation of parenteral nutrition in patients without oral nutrition for more than four days, 8) initiation of oral nutrition according to clinical follow-ups (decrease in abdominal distention, passage of gas-stool), 9) rearrangement of oral anticoagulation treatment when the INR value decreased to the therapeutic level.

RESULTS

Of the fifteen patients who were evaluated in this study, seven (46.6%) were male and eight (53.3%) were female, with a mean age of 63.1 (range: 57-74) years.

The site of first admission was emergency departments for ten patients (66.6%), cardiology outpatient clinics for two (13.3%) patients, nephrology outpatient clinics for two (13.3%) patients, and general surgery outpatient clinic for one (6.6%) patient. Following the first admission, seven patients (46.6%) were hospitalized in general surgery clinics, five (33.3%) in cardiology clinics, two (13.3%) in gastroenterology clinics, and one (6.6%) patient in the nephrology clinic, and their treatment planning was initiated by the respective clinics. Eight patients (53.3%) hospitalized in clinics other than general surgery clinics due to elevated creatinine and/or International Normalized Ratio (INR) values, were transferred to general surgery clinics after a mean period of two days (range: 1-3 days) as their complaints of abdominal pain did not improve.

The patients had been using warfarin sodium for an average period of 17 months (range: 5-60 months) with intermittent dose adjustments and a mean dose of 5 mg/day. The most common indications for the use of warfarin sodium were cardiologic reasons (13 patients, 86.6%). The indications for the use of warfarin sodium are summarized in Table 1.

All patients complained of visceral-type abdominal pain at the time of admission. The mean time between the onset of complaints and hospital admission was 5 days (range: 1-12 days). Two patients (13.3%) had ecchymosis on the abdominal skin, one patient (6.6%) on the left hemithorax and back, one patient (6.6%) on the left lumbar region, and one patient (6.6%) on both upper extremities and right lumbar region. The complaints and signs at admission in all patients are summarized in Table 2.

Laboratory examinations revealed that the INR value was above normal (normal range: 0.85-1.25) in all patients, and the mean value was measured as 6.2 (range: 2.29-9.83). The INR level of the patient with rectal bleeding was above the normal values although it was within the therapeutic dose range (INR=2.2). Furthermore, anemia (Hb<12g/dL) was present in 11 patients (73.3%), and leukocytosis (leukocyte count > 10.000 / mm^3) - in 8 patients (53.3%). The values for the patients' blood count and clotting parameters are summarized in Table 3.

The abdominal radiography and abdominal CT examinations were performed in all patients, while abdominal ultrasonography was performed in only 6 patients. Seven patients (46.6%) had small intestine-type air-fluid levels and the remaining 8 patients (53.3%) had normal abdominal radiography. Upon US examination, 6 patients (6/15, 40.0%) had both segmental wall thickening in the small intestines and small intestinal dilatation, while only one patient was found to have intraabdominal free fluid.

Abdominal CT scan revealed single intramural wall thickening in eleven patients (Figure 1A) and multiple hematomas in four patients [different jejunum segments in two patients (13.3 %), jejunum and ileum segments in one patient (6.6 %), jejunum and duodenum segments in one patient (6.6 %), (26.6 %)] (Figure 1B). Intraabdominal free fluid was detected in five patients (33.3 %) at CT scan. Furthermore, among the patients who were found to have intraabdominal free fluid, three (3/5, 60%) had pleural effusion (Figure 2A and B). Radiologic findings are summarized in Table 4.

Thirteen patients (86.6%) received medical treatment and 2 patients (13.3%) underwent surgical treatment. Surgical treatment was used due to the presence of acute abdomen signs at admission in one patient and due to the development of acute abdomen signs during medical treatment (at 3rd day) in the other patient.

Table 1. The indications for the use of warfarin sodium in all patients (n=15, 100 %)

Indications	n; %
Coronary artery stent (CAS)	4; 26.6
Coronary by-pass (CAB)	3; 20.0
Mitral valve replacement	2; 13.3
Cerebrovascular accident (CVA)	1; 6.6
Lower-extremity deep vein thrombosis	1; 6.6
Atrial fibrillation	1; 6.6
CVA+CAS	1; 6.6
CVA+CAB	1; 6.6
CAB+aortic valve replacement	1; 6.6

Table 2. Complaints and signs of admission in all patients (n=15, 100%)

Complaints	(n; %)	Signs	(n; %)
Abdominal pain	15; 100	Abdominal tenderness	15; 100
Vomiting	8; 53.3	Moderate abdominal distension	11; 73
Weakness	6; 40	Anemic appearance	6; 40.0
Anorexia	4; 26.6	Ecchimosis	5; 33.3
Hematochezia	2; 13.3	Dehydrated appearance	2; 13.3
Diarrhea	1; 6.6	Melanotic stool	2; 13.3
Constipation	1; 6.6	Rebound tenderness	1; 6.6
Haematuria	1; 6.6	Haematuria	1; 6.6

Table 3. Patients' blood count and clotting parameters

Patient No	Age	Sex	Hb	Htc	WBC	Platelet	INR
1	74	M	8.2	24.5	28.100	248.000	>5
2	59	M	7.9	26.7	13.200	203.000	>5
3	68	M	8.3	23.6	5700	211.000	8.5
4	64	F	10.4	29.4	14.300	252.000	9.2
5	68	F	8.0	21.7	8.200	46.000	2.2
6	67	F	9.1	28.4	10.210	245.000	3.5
7	58	M	11.7	34.9	8.000	109.000	9.8
8	62	M	10.2	28.2	11.200	134.000	7.2
9	58	M	13.2	33.1	7.800	145.000	6.9
10	67	M	12.0	32.1	13.400	121.000	7.2
11	62	F	12.4	33.2	11.200	230.000	6.2
12	57	F	8.3	24.5	16.500	234.000	3.2
13	59	F	13.3	36.4	13.400	322.000	4.5
14	65	F	10.2	30.2	9.200	229.000	5.4
15	57	F	11.7	35.4	8.700	313.000	5.3

Abbreviations; M: Male, F: Female, Hb: Hemoglobin (g/dL), Htc: Hematocrit (g/dL), WBC: White blood cell count (cells/mm^3), Platelet: Platelet count (cells/mm^3), PT: Prothrombin time (seconds), aPTT: Activated partial thromboplastin time (seconds), INR: International Normalized Ratio

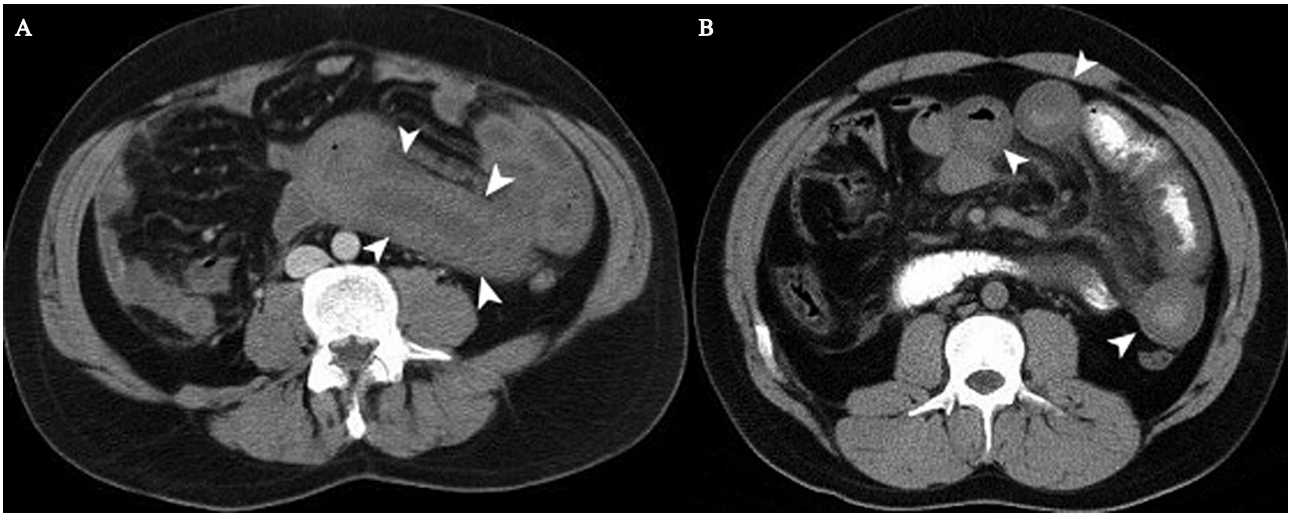

Figure 1. Abdominal CT imaging; **(A)** a 68-year-old male patient; homogenous and symmetrical wall thickening in the jejunum segment on CT examination. The hyperdense appearance in the wall, which is characteristic of early hematomas, can be clearly identified (arrow heads). **(B)** A 58-year-old male patient; symmetrical and homogenous wall thickening can be seen in different jejunal segments on CT examination (arrow heads).

During the hospitalization period, a total of two patients (13.3%) died (a patient who underwent surgery and a patient with chronic renal failure who received medical treatment).

Nasogastric decompression was performed for a mean period of three days (range: 2-4 days). Fresh-frozen plasma (FFP) transfusion was planned so as to administer a maximum 3 units per day until the INR level falls to the therapeutic range. Each patient required 6 units (range: 5-13) units of FFP transfusion on average. The patients who were found to have anemia at the time of ad-

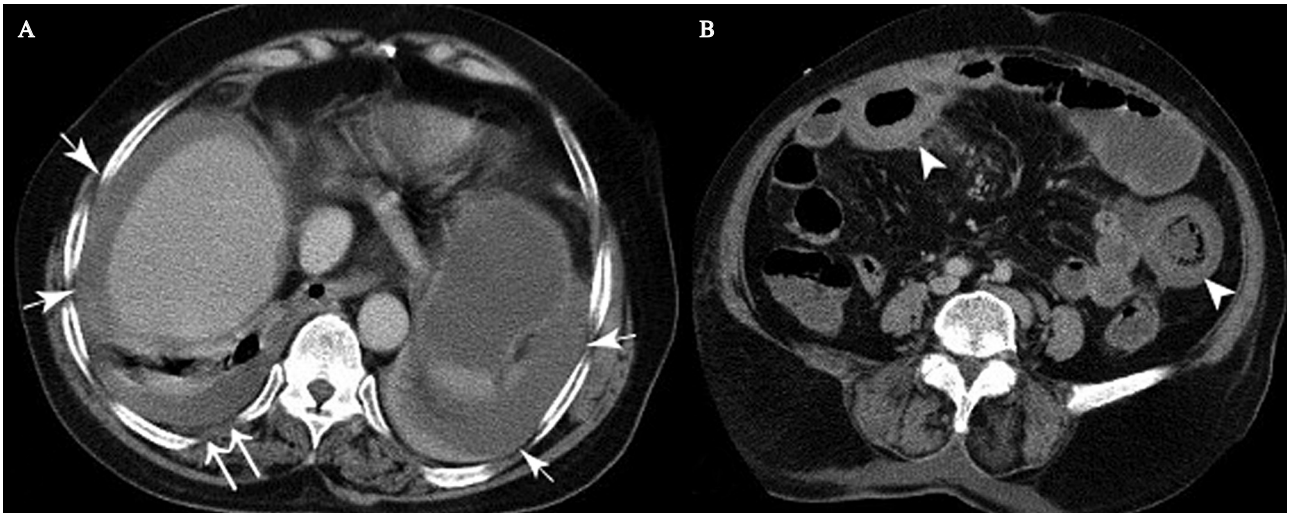

Figure 2. A 64-year-old female patient; abdominal CT imaging; **(A)** there is fluid in the right hemithorax (double arrow) together with intraabdominal free fluid around the liver-spleen (arrows) on the upper sections; **(B)** symmetrical and homogenous wall thickening in different jejunal segments on the lower sections (arrow heads).

Table 4. Radiologic findings in patients with spontaneous intramural hematoma at admission

Radiologic tool	n; %
Abdominal radiography (n=15; 100%)	
• Air-fluid levels	7; 46.6
• Normal	8; 53.4
Abdominal USG (n=6; 100%)	
• Segmental small bowel wall thickening	6; 100
• Dilated bowel loops	6; 100
• Intraabdominal free-fluid	1; 16.6
Abdominal CT (n=15, 100%)	
• Segmental small bowel wall thickening	15; 100
• Partial obstruction signs	15; 100
• Intraabdominal free fluid	5; 33.3
• Single hematoma	11; 73.3
• Multiple hematoma	4; 26.6

mission were administered erythrocyte transfusion and each patient received 3 units (range: 2-5 units) of erythrocyte transfusion on average. No patient required platelet transfusion.

INR levels decreased to the therapeutic range after a mean period of 3.7 days (range: 2-7 days).

The mean duration of hospitalization was 6.8 days (range: 4-13 days).

Except for the two patients who were lost to follow-up, among the eleven patients with an average follow-up of 22 months (range: 4-48 months), no patient had a relapse of IMH and three patients (27.7%) died due to reasons not related to IMH.

DISCUSSION

Intramural hematoma is a clinical condition known for approximately 100 years and the currently accepted theory for its development is a separation of the intestinal wall layers by hemorrhage caused by damage in the terminal arteries in the intestinal wall (6).

Since the clinical triad (abdominal pain, signs of small intestinal obstruction, and multiple hemorrhagic symptoms) typical of IMH may not be observed in all patients, keeping this rare possibility in mind is the first and basic requirement for enabling diagnosis (7-10). This is due to the fact that abdominal pain, nausea and vomiting are the most common symptoms in IMH cases (7-11) and these are non-specific symptoms that are nearly the most frequently encountered symptoms in emergency departments. Abdominal pain and vomiting were also the most common symptoms in the cases in this study, with rates of 100% and 53.3%, respectively.

After considering the possibility of an intraabdominal problem associated with over-anticoagulation, blood count and coagulation parameters should be measured. Although the most common reason for IMH is the use of warfarin sodium, it should be kept in mind that it may also develop in so-

me hematological disorders (e.g., hemophilia, leukemia, thrombocytopenia) (4). While higher than normal values for coagulation parameters, particularly INR, is an expected result since these parameters are used for the adjustment of the warfarin dosage (10), it should be noted that bleeding may also be present when these values are within therapeutic limits (6,9,12,13). Only patients using warfarin were included in this study and the INR level was above the therapeutic limits in all patients, except one.

Clinical series of spontaneous IMH involving a high number of patients are quite rare and the literature data mainly consist of case reports. When the few available clinical series were reviewed, it was observed that the presence of leukocytosis was a frequently reported finding, while different data were found about the presence of anemia. Abbas et al. (7) in their series of thirteen patients reported that only one patient (7.6%) had anemia at the time of admission, while eleven patients (84.6%) developed anemia within the first 48 hours following hospitalization and attributed this result to vigorous fluid resuscitation. Polat et al.(9) in their series of seven patients reported that six patients (85.7%) had anemia at the time of admission. Consistent with the results of Polat et al., the rate of presence of anemia at the time of admission was 73.3% (11/15 patients) in this study. Similar to Abbas et al., (7) in this study, fluid resuscitation was performed during the course of clinical follow-up but a decrease in hemoglobin values were not observed in any patients within 48 hours. This can be attributed to the fact that we administered erythrocyte transfusion, in addition to fluid resuscitation, since a great majority of the patients were already anemic at the time of admission.

Though the presence of anemia at the time of admission is an important finding, it should not be considered as a finding that shows the severity of the clinical condition (e.g., the size of the IMH, the width of the affected intestinal segment, or the amount of intraabdominal free fluid). The presence of anemia at the time of admission should not be used as a supportive finding in surgical decision making. It would be more logical to relate a sudden decrease in hemoglobin levels in a patient belonging to a younger age group who uses warfarin, as in the case reported by Avent et al. (14) directly to IMH. Although anemia was found in a great majority of the cases in this study (73.3%) at the time of admission, the rate of intraabdominal free fluid was only 33%, and the rate of medical treatment was 86.6%, supporting our opinion.

After clinical and laboratory examinations, the next step in the diagnosis is radiological examination, which provides the most valuable information. In abdominal radiographies, findings suggestive of intestinal obstruction (gastric dilatation and/or an air-fluid level) may be found, while these findings are non-specific and may suggest the possibility of IMH only if it is known that the patient uses anticoagulants (15). Several appearance features were defined, which can be found in a majority of IMH cases using barium-enhanced radiography (16, 17). However, none of these findings are specific. Moreover, these definitions belong to the period before the introduction of ultrasonography and CT, and today, the indications for use of passage radiographies in patients with signs of intestinal obstruction are very limited (18). In this study, the rate of findings suggestive of intestinal obstruction (air-fluid levels) on abdominal radiography was 46.6%, while 53.3% of the patients had no findings. Barium-enhanced radiography is not routinely used in patients who present with abdominal pain and who are thought to have intestinal obstruction in the centers participating in the study.

Currently, abdominal ultrasonography and CT, which were introduced in routine practice, provide incredibly valuable information in the diagnosis of IMH. Small intestinal wall thickening and intraabdominal free fluid are detectable with ultrasonography in IMH cases; however, these findings are non-specific and may also be seen in various diseases of the small intestine (inflammatory bowel disease, small intestinal ischemia, infectious diseases) (19). There is consensus in the literature that abdominal CT is the most valuable imaging method in the diagnosis of IMH (4, 9, 10, 20, 21).

In contrast to traumatic hematomas, spontaneous IMH usually occur in the jejunum (traumatic hematomas generally occur in the duodenum) and a longer segment involvement is present. Multiple segment involvement may be present, while it generally involves a single segment and bleeding is slower (7, 10). The jejunum was also the most commonly affected segment in our study with a rate of 69% and the rate of multiple hematoma was 26%. Duodenal hematoma was detected in only one patient, while none of the patients had mesenteric hematoma.

When the literature was reviewed for the treatment approaches used in IMH, the opinions that come to the forefront were that medical treatment options starting with the termination of anticoagulation treatment and the administration of vitamin K should be the first-line treatment of choice, while the surgical treatment option should be reserved for cases that cannot be controlled with medical treatment, cases with acute abdomen signs at the time of admission, cases who develop acute abdomen signs during medical follow-up, and in patients who have active bleeding (6, 7, 9, 10, 13, 22-27).

Primarily medical treatment was administered to the patients in this study (13/15 patients, 86.6%). An improvement rate of 92.3% was achieved following a mean clinical follow-up of 6.8 days in patients who received medical treatment. Mortality occurred with medical treatment in only one patient (1/13 patient, 7.6%). Surgical treatment was used in two cases (13.3%): due to the presence of acute abdomen signs at admission in one patient and due to the development of acute abdomen signs during medical follow-up in the other patient.

In conclusion, IMH of the small intestine associated with overanticoagulation is a very rare clinical condition. Keeping this diagnosis in mind is important for early diagnosis and may have a significant effect on the success of the treatment. This condition, should be known by all physicians, because the clinical presentation begins with nonspecific complaints, the site of first admission may be different clinics, and it has a high rate of recovery with medical treatment. Early and accurate diagnosis by non-invasive methods will preclude unnecessary surgical interventions.

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