Spontaneous Retroperitoneal Hematoma Simulating Ruptured Infrarenal Aortic Aneurysm in a Patient with End-Stage Renal Disease

JYY Li, MBBS¹ YC Chan, MBBS, BSc, MD, FRCS, FRCS (General Surgery), FCSHK¹ KX Qing, MBBS, PhD¹ SW Cheng, MBBS, MS, FRCS, FCSHK¹

¹ Division of Vascular and Endovascular Surgery, Department of Surgery, The University of Hong Kong Medical Centre, Queen Mary Hospital, Hong Kong

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Address for correspondence Yiu Che Chan, MBBS, BSc, MD, FRCS, FRCS (General Surgery), FCSHK, Division of Vascular and Endovascular Surgery, Department of Surgery, South Wing, 14th Floor, K Block, The University of Hong Kong Medical Centre, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong (e-mail: ycchan88@hkucc.hku.hk).

Abstract

Keywords

- ▶ spontaneous retroperitoneal hemorrhage
- ▶ hematoma
- ▶ infrarenal aortic aneurysm
- ▶ ecchymosis
- ▶ hemodialysis

We reported a case of spontaneous retroperitoneal hematoma (SRH) simulating a ruptured infrarenal aortic aneurysm. A 72-year-old man with a history of infrarenal aortic aneurysm and end-stage renal disease on hemodialysis presented with malaise and nonspecific central abdominal pain and left loin discomfort. An emergency computed tomography scan showed a large retroperitoneal hematoma and clinical suspicion of ruptured infrarenal aortic aneurysm. However, the hematoma was discontinuous with the aneurysm sac and raised the clinical suspicion on dual pathology. The SRH was treated conservatively with transfusion of blood products, and the aneurysm was treated with nonemergency endovascular repair electively. This case demonstrates the importance of recognizing different clinical and radiological characteristics and be aware of dual pathology.

Introduction

Ruptured abdominal aortic aneurysm often presents with severe back pain and abdominal discomfort, symptoms which may be clinically indistinguishable from spontaneous retroperitoneal hematoma (SRH). However, obtaining the correct diagnosis in such cases is vital. Ruptured aortic aneurysm usually requires emergency operation and during the operation intraoperative heparin may be required. On the other hand, SRH in an hemodynamically stable patient can be managed conservatively, with close observation and transfusion of blood products. Trans-arterial embolization should be used for hemostasis in those patients with hemodynamic instability, and open surgery should only be reserved for failure of the above treatment modalities.

This is the first report in the world's literature of a patient with an infrarenal aortic aneurysm who developed SRH.

Case Study

A 72-year-old man presented to his local hospital with malaise and nonspecific central epigastric abdominal pain.

The medical history was significant for end-stage renal disease with hemodialysis for 5 years, chronic obstructive airway disease, and an infrarenal aortic aneurysm with a maximum diameter of 4.5 cm. Ischemic heart disease was diagnosed, and he was prescribed aspirin, clopidogrel, and subcutaneous low-molecular-weight heparin (LMWH; enoxaparin). The patient started to complain of some left loin discomfort a few hours later, together with an hemoglobin drop from 9.6 to 6.6 g/dL within the subsequent 2 days. There was no passage of blood or melena per rectum.

As an investigation for this unexplained anemia, esophagogastroduodenoscopy showed hiatal hernia without any evidence of bleeding. Two packs of red blood cells were transfused, following which his hemoglobin level went back to 11.1 g/dL. An emergency CT scan did not show any abnormality or any radiological evidence of an aortic rupture, and he was treated conservatively with continued hemodialysis. However, he had worsening anemia with a progressive drop of hemoglobin to 7.8 g/dL, 2 days after the transfusion. At this time, aspirin and enoxaparin administration were stopped.

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Fig. 1 (A–D) Emergency CT scan 6 days later showing large SRH and the hematoma seemed discontinuous from the aneurysm sac. The hematoma extended from upper abdomen to the left pelvis. CT, computed tomography; SRH, spontaneous retroperitoneal hematoma.

Ecchymosis was noted over the left loin area. A repeat CT scan performed 6 days after the first one showed a large retroperitoneal hematoma (measuring 9.9 cm × 7.4 cm × 9 cm), which was absent in the previous CT scan (► **Fig. 1**). A clinical suspicion of ruptured aortic aneurysm was raised, and he was therefore urgently transferred for further vascular management.

Upon arrival at our institution, the patient was mildly anemic and had cachexia. His blood pressure was 95/68 mm Hg, with a pulse of 87 beats per minute. He was afebrile and his abdomen was soft and nondistended. The aortic aneurysm was nontender on palpation, and he had full complement of peripheral pulses palpable. He had a large cutaneous ecchymosis of the left loin and lateral abdominal wall measuring 43 cm × 20 cm (► **Fig. 2**), which the patient says had been there for approximately 5 days. Blood tests showed a hemoglobin level of 10.4 g/dL. The electrocardiogram, creatine kinase, and troponin I levels were normal. A detailed review of the CT scans from the referring hospital concluded that the large retroperitoneal hematoma was separated from the aorta, and therefore probably unrelated to aortic pathology. The SRH

was probably a result of the aspirin, clopidogrel, and enoxaparin in the immediate past week, especially when the patient had end-stage renal failure.

After careful discussion with the patient and his family, it was decided that the 4.5-cm aortic aneurysm could be treated

Fig. 2 Development of a large cutaneous ecchymosis (43 cm × 20 cm) in the left loin and lateral abdominal wall.

Fig. 3 Pre- and postendovascular aneurysm repair CT scan showing successful aortic treatment (A, B) and decrease in size and stabilization of the left loin retroperitoneal hematoma (D, F).

at the same clinical admission, as they are not keen for long distance travel and continual surveillance until 5.5 cm. He underwent a successful endovascular aneurysm repair with an Endurant (Medtronic Inc., Minneapolis, MN) stent graft. The patient made an uneventful recovery and a follow-up CT scan after 6 weeks showed that the infraarenal aortic aneurysm was successfully treated, and the SRH was resolving (►Fig. 3).

Discussion

This is the first patient reported in the world's literature who had an infraarenal aortic aneurysm and developed SRH as a

result of receiving aspirin, clopidogrel, and enoxaparin, thereby confusing the clinical diagnosis simulating ruptured aortic aneurysm.

SRH is a distinctive clinical entity that can present in the absence of specific underlying pathology or trauma. Anti-coagulation therapy, bleeding abnormalities, and hemodialysis are the most three common associations.^{1,2} The incidence of retroperitoneal hematoma had been reported at 1.3 to 6.6% of the patients undergoing therapeutic anticoagulation.³⁻⁵ When it comes to the comparison between unfractionated heparin (UFH) and warfarin, the risk of bleeding during UFH therapy has been estimated to be two- to fivefold greater than

that with warfarin.⁶ In a review of 51 cases of patients receiving UFH and developing SRH, most of their dosages were in the therapeutic range.⁷ If the patient is receiving both long-term warfarin and LMWH, the risk of having retroperitoneal hematoma is much higher.^{8–10} In general, patients on chronic hemodialysis have an increased incidence of SRH, especially if they are receiving heparin or warfarin.¹¹

The pathophysiology of SRH was still a mystery and several hypotheses have been proposed. Diffused occult vasculopathy and arteriosclerosis of the small vessels in the retroperitoneum may make them friable and therefore prone to rupture, although such theories were not supported by histology.¹² Qanadli et al¹³ postulated that SRH starts at the microvascular level, and large vessels become disrupted or stretched as the hematoma enlarges.¹⁴ In the presence of heparin- or anticoagulation-induced immune microangiopathy, unrecognized minor trauma in the microcirculation may lead to bleeding.¹⁵ Although, the term spontaneous implies the causes are unknown, many authors have suspected that unrecognized trauma (such as minor trauma in sports and vomiting or coughing) may initiate blood loss if the patient is on anticoagulation. In a retrospective study of 12 patients undergoing anticoagulation therapy who developed large rectus sheath hematoma, 6 patients had a history of coughing fits.¹⁶ Such minor trauma is a recognized inciting factor in hemophilia-related spontaneous retroperitoneal bleed.^{13,17,18} Rarely, SRH may develop if the patient is on clopidogrel.¹⁹

With regard to the association between SRH and end-stage renal disease patients, on hemodialysis, in most cases this may be related to the administration of heparin. A search of the published literature revealed case reports or small cohorts; in most of these cases, the patients were managed

conservatively with blood transfusion and close observation (►Table 1). In the earlier series, most of these patients received unfractionated heparin for their hemodialysis^{6,20,21}; while recently, most of the patients have had LMWH.^{22–24} Chang et al reported one patient using heparin in chronic hemodialysis but the type of heparin was not specified in his case report.²⁵ Embolization was offered to five patients. Three of them received LMWH^{23,26} and one received UFH.²⁶ Moore et al reported a case of chronic heparinized hemodialysis but the type of heparin was not specified.²⁷ For those who ended up with surgical treatment, three of them received UFH^{20,21} and one of them received heparin-free hemodialysis.²⁶ Vaz,²⁷ Carlson et al,²⁸ and Murphy et al²⁹ all reported one patient with SRH but the use of heparin was not mentioned in their case reports. All these studies are summarized in ►Table 1.

Evidence from the literature seemed to suggest that patients who received UFH in hemodialysis were more likely to be managed conservatively with blood transfusion and close monitoring (around 70% of the cases), as compared with those using LMWH (50% of the cases). In the authors' view, this could be attributed to several factors. First, the effect of UFH could be closely monitored with activated partial thromboplastin time, and any overdosing could be detected immediately, and reversed with protamine sulfate and transfusion of blood products.³⁰

LMWH inhibits factor Xa and thrombin. The improved pharmacokinetics permits daily administration once or twice, as compared with continuous infusion in UFH.³¹ Also, laboratory monitoring is not required in LMWH. However, LMWH should be avoided or used with extreme caution in patients with renal insufficiency (RI) due to the delayed clearance.³² Schmid et al³³ suggested that monitoring peak anti-Xa levels

Table 1 Published series on association between development of SRH in patients with ESRD on hemodialysis

Author, year	Number of patients	Type of heparin used			Treatment		
		UFH	LMWH	Others	Conservative	Rx	Surgery
Vanichayakornkul, 1974	2	✓			1	1	
Milutinovich, 1977	6	✓			4		2
Bhasin, 1978	5	✓			5		
Vaz, 1979	1			N/A	1		
Carlson, 2003	1			N/A			1
Farooq, 2004	1		✓		1		
Chang, 2005	1			NM	1		
Moore, 2007	1			NM		1	
Groeneveld, 2008	3			N/A	2	1	
Malek-Marín, 2010	5	✓	✓ ✓	Heparin-free Heparin-free	1	1 1 1	1
Fan, 2012	1		✓		1		
Murphy, 2013	1			N/A			1
Total	28	14	4	10	17	6	5

Abbreviations: ESRD, end-stage renal disease; IV, intravenously; LMWH, low-molecular-weight heparin; N/A, not applicable; NM, type not mentioned; Rx, prescription; SC, subcutaneously; SRH, spontaneous retroperitoneal hematoma; UFH, unfractionated heparin.

in patients with severe RI regularly is crucial to adjust the dosage in the target range. If there is no possibility of measuring anti-Xa levels, the use of LMWH should be prohibited. LMWH with well-documented pharmacokinetics should also be used instead because the ratio of renal clearance in respect of total drug clearance is lower in LMWH with higher mean molecular weight. It can therefore be postulated that the clearance of LMWH with larger molecules, such as dalteparin or tinzaparin, is less dependent on renal function than it is for LMWH with lower mean molecular weight, such as enoxaparin or nadroparin.³³ A meta-analysis of enoxaparin studies showed a relative risk of major bleeding events in patients with severe RI of 2.25 (95% confidence interval 1.19–4.27) as compared with patients with better renal function.³⁴ Repeated administration of therapeutic doses might lead to accumulation in those patients. In these high-risk patients, the use of LMWH was relatively contraindicated although reducing dosage might help in addition to monitoring anti-Xa activity. It should be emphasized that LMWH can cause SRH even in the absence of renal disease.^{35,36}

Our patient was treated with aspirin and clopidogrel, although the association between SRH and aspirin or clopidogrel is rare. Clopidogrel inhibits platelet aggregation and delays clot retraction induced by adenosine diphosphate. There was only one case report by Jurisic et al⁵ in 2006 suggesting that clopidogrel might induce SRH.

The maximum diameter of the infrarenal aortic aneurysm in our patient was 4.5 cm, and the rupture rate could be regarded to be very low. The large majority of screen-detected aneurysms from heterogeneous studies with diameters of < 4.5 cm, showed that the maximum rate of rupture in men, even up to 4.5 cm diameter aneurysm, was only 3.2/1,000 patient-years.^{37,38} This rupture rate was even less than previously quoted by Vardulaki et al of 1,017 patients from the United Kingdom Chichester and Huntingdon Screening Cohorts, showing an annual rupture rate between 1.2 and 2.1% for aneurysms with a maximum size of 4.5 cm.³⁹ The United Kingdom Small Aneurysm Trial of Caucasian population showed a mean risk of rupture of aneurysms of 4.0 to 5.5 cm in diameter of 1.0% per year.⁴⁰

To differentiate SRH from ruptured aortic aneurysm, both clinical and radiological knowledge is important as the distribution of the hematoma might give up some clues. For ruptured aortic aneurysm, the hematoma is more centrally located and intimately related to the aorta, while the hematoma in our patient is more laterally located and discontinuous with the aorta with left psoas involvement. The significance of making such a differentiation is that the treatment modalities for these two conditions are different. Most hemodynamically stable patients with SRH can be managed with fluid resuscitation, correction of coagulopathy, and blood transfusion. Endovascular treatment involving selective intra-arterial embolization or the deployment of stent grafts over the punctured vessel is attaining an increasingly important role. Open repair of retroperitoneal bleeding vessels should be reserved for cases when there is failure of conservative or endovascular

measures to control the bleeding. Open repair is also required if endovascular facilities or expertise is unavailable and in cases where the patient is unstable. If treated inappropriately, the mortality of patients with retroperitoneal hematoma remains high.

Conclusion

This is the first case in the world's published literature reporting a successful management of a patient with dual pathology of infrarenal aortic aneurysm and SRH. Clinical and radiological knowledge is important to differentiate SRH from ruptured aortic aneurysm. This case also reiterates that LMWH should be avoided or used with extreme caution in patients with renal impairment, especially in combination with other antiplatelet agents.

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Conflict of Interest

All authors declare that there are no competing interests.

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