Case Report

A super-elderly case of abdominal aortic aneurysm associated with chronic disseminated intravascular coagulation

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ABSTRACT

Chronic disseminated intravascular coagulation (DIC) is a well-known complication of aortic aneurysm. A 91-year-old Japanese woman was admitted to our hospital because of massive purpura of the lower limbs. The presence of abdominal aortic aneurysm (AAA) had been pointed out from the age of 80 years, and its diameter had gradually increased. The AAA was composed of two portions, that is, a large upper and a small lower portion, and a large mural thrombosis was observed in the lower portion. The laboratory data led to the diagnosis of DIC, and AAA was the only identifiable cause of coagulopathy. The time course of exacerbation of AAA was consistent with the progression of thrombocytopenia and purpura. Therefore, we concluded that AAA was the underlying cause of DIC. Since DIC in aortic aneurysms is associated with excessive fibrinolysis, tranexamic acid was administered as anti-fibrinolytic therapy. After that, coagulopathy was drastically improved. Our patient responded successfully to anti-fibrinolytic therapy for coagulopathy. The present case illustrates the importance of evaluation of the diameter of an aneurysm as well as intraluminal thrombosis, which may play an important role in coagulopathy including DIC. It is necessary to monitor coagulation and fibrinolysis for the follow-up of patients with AAA.

<Learning objective: We present a case report of an aged Japanese woman with abdominal aortic aneurysm associated with disseminated intravascular coagulation, and anti-fibrinolytic therapy drastically ameliorated her condition. Our case illustrates the importance of evaluation of the diameter of an aneurysm as well as conducting follow-up monitoring of coagulation and fibrinolysis.>

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Introduction

Societies are aging at a greater rate worldwide, particularly in Japan, and are creating a burden on healthcare systems to maintain adequate levels of care for aged patients with atherosclerotic cardiovascular diseases, including aortic aneurysm. For example, the number of patients with abdominal aortic aneurysm (AAA) is increasing [1,2]. The surgical or intravascular treatment of AAA is well established; however, the presence of other diseases associated with AAA complicates the therapeutic strategy.

Disseminated intravascular coagulation (DIC) is a characteristic complication of aortic aneurysm that was first reported by Fine et al. in 1967 associated with a case of dissecting aortic aneurysm [3]. Among preoperative patients with aortic aneurysms, 40% have elevated levels of fibrinogen degradation products and 4% experience clinically overt DIC [4]. The clinical picture of DIC in aortic aneurysm includes distinctive features of typical DIC manifested as sepsis, in which fibrinolytic processes are activated and are associated with greater risk of bleeding. Here, we describe the case of an aged Japanese woman with AAA associated with DIC, who was successfully treated with anti-fibrinolytic therapy.

Case report

A 91-year-old woman was admitted to our hospital because of massive purpura of bilateral lower limbs. The presence of AAA had
been pointed out from the age of 80 years, and its diameter had gradually increased. Therefore, surgical therapy was recommended to her several times; however, she refused obstinately for the operation. Her medical history included a partial gastrectomy for gastric cancer. Six months before the admission, she noticed mild subcutaneous bleeding at a bruise on a lower limb that was spreading widely to both limbs. On admission, the blood pressure was 114/70 mmHg and pulse rate was 60 beats per minute, and skin oxygen saturation was 98%. The jugular vein was not dilated, and ejection systolic murmur at the 2nd right sternal border was audible. A large pulsating mass (7 cm x 11 cm) was palpable on the abdomen, and marked purpura was observed on her lower legs (Fig. 1). Laboratory data indicated anemia, thrombocytopenia (hemoglobin 5.1 g/dl, platelet count, 4.4 x 10^9/μl), and abnormal levels of serum coagulation factors (fibrinogen, 82 mg/dl; fibrin/fibrinogen degradation products (FDP), 107.2 μg/ml; θ-Dimer, 65.7 μg/ml; antithrombin-III (AT-III), 87%) (Table 1). According to

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**Table 1** Laboratory data on admission.

<table>
<thead>
<tr>
<th>Blood cell count</th>
<th>Biochemistry</th>
<th>Coagulation tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 5600/mm³</td>
<td>CRP 1.2 mg/dl</td>
<td>PT 15.6 s (10–14)</td>
</tr>
<tr>
<td>RBC 173 x 10⁶/mm³</td>
<td>T-bil 0.47 mg/dl</td>
<td>PT-INR 1.77</td>
</tr>
<tr>
<td>Ht 17.1%</td>
<td>D-bil 0.18 mg/dl</td>
<td>APTT 57 s (23–42)</td>
</tr>
<tr>
<td>Hb 5.1 g/dl</td>
<td>BUN 47.0 mg/dl</td>
<td>Fibrinogen 82 mg/dl</td>
</tr>
<tr>
<td>MCV 99 fl</td>
<td>Cr 1.8 mg/dl</td>
<td>AT-III 87%</td>
</tr>
<tr>
<td>MCH 29.5 pg</td>
<td>Na 140 mEq/l</td>
<td>FDP 107.2 μg/ml</td>
</tr>
<tr>
<td>MCHC 29.8%</td>
<td>Cl 113 mEq/l</td>
<td>θ-Dimer 65.7 μg/ml</td>
</tr>
<tr>
<td>Plt 4.4 x 10⁹/mm³</td>
<td>Fe 33 μg/dl</td>
<td></td>
</tr>
<tr>
<td>Reti 50%</td>
<td>Ferritin 192.5 ng/ml</td>
<td></td>
</tr>
</tbody>
</table>

AAA, abdominal aortic aneurysm; DIC, disseminated intravascular coagulation; FDP, fibrin/fibrinogen degradation products; AT-III, antithrombin-III; EVAR, endovascular aneurysm repair; TAT, thrombin–antithrombin complex; PIC, plasmin–α2 plasmin inhibitor complex; t-PA, tissue plasminogen activator; CRP, C-reactive protein; T-bil, total bilirubin; D-bil, direct bilirubin; PT-INR, international normalized ratio of prothrombin time.

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(A) Three-dimensional imaging of enhanced computed tomography showing the presence of a saccular aneurysm of the abdominal aorta. The abdominal aortic aneurysm was composed of two portions, that is, a large upper and a small lower portion. (B) The cross-section imaging of abdominal aortic aneurysm showing large mural thrombosis. The dimensions of the upper and lower portions at the scanned plain were 92 mm and 47 mm, respectively.
Japanese Association for Acute Medicine criteria [5], DIC score was 13 points.

Enhanced computed tomography revealed the presence of a saccular aneurysm of the abdominal aorta, and the AAA was composed of two portions, that is, a large upper and a small lower portion. The dimension of the upper and lower portions at the scanned plain was 92 mm and 47 mm, respectively, and a large mural thrombosis was observed in the lower portion (Fig. 2).

For the investigation of the etiology of anemia and thrombocytopenia, bone marrow aspiration and endoscopic examination were performed, and their results showed no abnormality. The laboratory data led to a diagnosis of DIC, and AAA was the only identifiable cause of coagulopathy. The time course of exacerbation of AAA was consistent with the progression of thrombocytopenia, anemia, and purpura (Fig. 3). Therefore, we concluded from these findings that AAA was the underlying cause of DIC.

To control the condition of DIC, continuous infusion of heparin (12,000 U/day) and nafamostat mesilate (60 mg/day) was initially administered for several days, and AT-III and fresh-frozen plasma were administered for the consumption of coagulation factors. But, the DIC score was unchanged. Thereafter, the administration of nafamostat mesilate was given up, because of hyperkalemia. Instead of nafamostat mesilate, we started to administer camostat mesilate. However, purpura of the lower limbs and her general conditions were exacerbated; therefore, we considered that these drugs did not affect her clinical conditions or coagulopathy (Fig. 4).

DIC in aortic aneurysms is associated with excessive fibrinolysis, which may induce the bleeding tendency. Our case showed bleeding tendency, and we detected markedly elevated levels of FDP and D-dimer. These findings suggested excessive fibrinolysis; therefore, tranexamic acid was administered as anti-fibrinolytic therapy. Two days later, coagulopathy was drastically improved,

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**Fig. 3.** Clinical course before hospitalization. AAA, abdominal aortic aneurysm.

**Fig. 4.** Clinical course after hospitalization. FDP, fibrinogen degradation products.
and the DIC score had decreased to 6 points. Anemia, thrombocytopenia, and purpura became less severe (Fig. 4). Because she was at extremely high-risk of rupture, we proposed endovascular aneurysm repair (EVAR) of AAA to her; however, she refused it. After the improvement in the bleeding tendency, she and her family eagerly desired to go back home. Since the continuous administration of heparin forced the patient to be hospitalized, the intravenous administration of heparin was switched to warfarin carefully. She was discharged after converting from heparin to warfarin therapy.

Discussion

DIC is characterized by systemic activation of coagulation leading to organ failure through the development of fibrin clots that may cause bleeding because of insufficient levels of platelets and coagulation factors. Siebert and Natelson proposed the following criteria for DIC associated with AAA [6] as follows: chronic bleeding, consumptive coagulopathy, reversal of laboratory data after aneurysm repair, and maintenance of the values for 3 months. We did not repair the AAA of the patient reported here; however, the correlation between the time course of exacerbation of AAA with the progression of coagulopathy indicates their association.

Among the characteristics of DIC associated with aortic aneurysm, fibrinolysis is markedly enhanced, and bleeding tendency is prominent. This fibrinolysis-dominant DIC is characterized by the activation of both coagulation and fibrinolysis. The criteria of enhanced-fibrinolytic-type DIC are as follows. (1) Prerequisite: thrombin–antithrombin complex (TAT) \( \geq 20 \mu g/L \) and plasmin–\( \alpha_2 \) plasmin inhibitor complex (PIC) \( \geq 10 \mu g/L \). (2) Laboratory findings – at least two of the following findings: (1) FDP \( \geq 80 \mu g/ml \), (2) fibrinogen <100 mg/dl, and (3) increased FDP/\( \beta \)-dimer ratio (decreased \( \beta \)-dimer/FDP ratio). (3) Reference findings – more severe bleeding is likely with the following findings: (1) decreased platelet count (<50,000/\( \mu \)L) and (2) decreased \( \alpha_2 \) plasmin inhibitor activity (<50%) [7]. In the present case, FDP and fibrinogen were 107.2 \( \mu g/ml \) and 82 mg/dl, respectively. Since tranexamic acid was effective, the process of fibrinolysis played a pivotal role in coagulopathy in the present case; however, the diagnosis regarding fibrinolysis-dominant DIC was incomplete in the present case. In general, the use of tranexamic acid for anti-fibrinolytic therapy is not recommended for patients with DIC. Furthermore, there is the possibility that such therapy could exacerbate the coagulopathy; therefore, it is necessary to consider whether the coagulopathy is primarily caused by fibrinolysis-dominant DIC. To confirm the diagnosis, we should assess the values of TAT and PIC in the present case.

The mechanism responsible for the association of DIC with aortic aneurysm is unknown; however, chronic existence of intraluminal thrombosis might play an important role in the pathogenesis of DIC via an inflammatory process or as a source of proteinases. Regional intravascular coagulation may occur at the site of mural thrombosis of aneurysmal aorta. Although it is not ‘disseminated,’ it may systemically influence the coagulation systems. Recently, Siennicka et al. reported a negative correlation between tissue plasminogen activator (t-PA) and the thickness of intraluminal thrombosis of AAA [8]. On the other hand, Aho et al. reported that there was no relationship between them [9]. Thus, there is still a controversy between plasma t-PA and the mural thrombosis of AAA.

Pathophysiology of DIC in the aortic aneurysm is an important subject to be clarified.

Our patient’s aneurysms were gigantic with diameters greater than 90 mm, and we recognized that she was at an extremely high-risk of rupture. Surgery or EVAR are safe for treating aged patients [10,11]. Because of the aging population, the present patient illustrates the importance of optimizing the treatment of cardiovascular diseases of the aged.

In summary, we presented a case report of an aged Japanese woman with AAA associated with DIC, and anti-fibrinolytic therapy drastically ameliorated her condition. Our experience illustrates the importance of evaluation of the diameter of an aneurysm as well as intraluminal thrombosis, which may play an important role in coagulopathy including DIC. It is necessary to monitor coagulation and fibrinolysis for the follow-up of patients with AAA.

Conflict of interest

The authors declare no conflict of interest.

References