Agitation thrombolysis for fresh iatrogenic IVC thrombosis in patients with Budd-Chiari syndrome

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Three patients with Budd-Chiari syndrome (BCS) and fresh inferior vena cava (IVC) thrombosis were treated by agitation thrombolysis as a mechanical thrombectomy procedure and followed up by duplex ultrasonography. Agitation thrombolysis was technically and clinically successful in all patients. Inferior vena cavagrams after the procedure showed complete resolution of the iatrogenic, fresh IVC thrombi without occurrence of pulmonary embolism. Duplex ultrasonography follow-ups after 12, 24, and 28 months, respectively, confirmed complete patency of the IVC without rethrombosis and reobstruction. The results indicate that agitation thrombolysis may be a safe and feasible approach for BCS patients with iatrogenic, fresh IVC thrombosis. (J Vasc Surg 2010;52:782-4.)

Primary Budd-Chiari syndrome (BCS) is a rare form of hepatic venous outflow obstruction at the suprahepatic inferior vena cava (IVC), the hepatic veins, or both. BCS with IVC thrombosis, particularly with acute, fresh thrombosis, is the rarest form. A number of thrombolytic agents, such as the acylated streptokinase-plasminogen complex, urokinase, streptokinase (all three of which are no longer available in the United States), and tissue plasminogen activator have been administered either through a peripheral intravenous route or catheter-mediated through a catheter into the inferior vena cava or hepatic vein, successfully dissolving the fresh clots.1-4 These procedures, however, are slow, time-consuming, and cannot ensure complete resolution of the fresh clots. To overcome the unmet clinical need, we devised a quick and easy thrombolytic approach; that is, agitation thrombolysis for the treatment of BCS patients with iatrogenic, fresh thrombosis. The purpose of our study was to report our preliminary technical and clinical experience with this approach in the treatment of three BCS patients with iatrogenic, fresh thrombosis.

MATERIALS AND METHODS

Patients. Between August 2004 and March 2009, 298 patients with BCS were treated with balloon dilation to reestablish patency and were subsequently followed up by duplex ultrasonography (GE Vivid 7 Pro; GE, Calif) at our hospital. Three of the BCS patients (two men, one woman; mean age 41.67 ± 5.51 years [range, 36-47 years]; see Table) with iatrogenic, fresh IVC thrombosis after failure of rupture of the occluded IVC were treated by agitation thrombolysis prior to balloon dilation. Before treatment start, informed consent had been obtained from each patient, and the study was approved by our local ethics committee.

Agitation thrombolysis procedure. Prior to the procedure, during which the patients were monitored continuously for vital signs and bleeding complications, inferior vena cavagraphy of the right groin revealed the location and size of the thrombus and the occluded section of the IVC (Fig 1a, b). Patients received a bolus of 5000 IU heparin at the start of the procedure, followed by a continuous infusion of 1000 IU/hour to keep the activated clotting time above 300 seconds. Then a J-type Brockenbrough needle (Cook, Inc, Bloomington, Ind) was transfemorally introduced into the distal part of the obstruction, followed by a 5Fr Pigtail catheter (Cook, Inc) inserted into the proximal area of the obstruction by using the right jugular vein as the marker for the needle. Under multiangled fluoroscopy guidance, the angle of the needle was adjusted to ensure that the needle was directed at the catheter at the proximal part of the obstruction. At this point, the obstruction was penetrated slowly.5 After rupture of the IVC membranes, a 5F pigtail catheter was inserted into the IVC with its tip positioned at the level of the fresh IVC thrombosis. A Nipan guide wire (Radifocus; Terumo, Tokyo, Japan) with a helical tip configuration, which
was molded in vitro prior to the procedure, was advanced through the catheter until its tip configured into a helical configuration in the targeted IVC (Fig 1c). The catheter and the guide wire were alternatively rotated clockwise and anti-clockwise or pushed and drawn up and down to agitate and break the thrombosis, while a bolus of 10 to 20 mL mixed urokinase (1.2 \( \times 10^4 \) U) was injected intermittently to dissolve the fresh thrombus. To visualize the status of the IVC thrombus during the procedure, 10 to 20 mL iopromide contrast medium (Ultravist, Berlex Laboratories, Montville, NJ) was injected manually through the catheter.

After completion resolution of the fresh thrombus, a 30-mm balloon catheter (Cook, Inc) was inserted and positioned at the obstructive IVC. Then, the balloon was dilated with the contrast medium to get a full expansion of the IVC. Immediately after the procedure, an inferior vena cavagraphy was performed to confirm complete resolution of the fresh IVC thrombus as well as a satisfactory IVC blood flow (Fig 1d).

To prevent rethrombosis, heparin was given for 48 hours after the procedure, and warfarin (5 mg/day) was administered orally from the beginning of the second day until 3 to 6 months after the procedure. The IVC follow-up protocols were performed at 1 week and 1, 3, 6, and 12 months after the procedure and then annually by duplex ultrasonography (Fig 1c).

RESULTS

Agitation thrombolysis in the IVC was clinically successful and well tolerated without any complications in all three patients. The inferior vena cavagrams performed immediately after the procedure, demonstrated complete resolution of the thrombi and full IVC patency. Duplex ultrasonography follow-ups after 12, 24, and 28 months posttreatment showed full IVC patency, without rethrombosis, restenosis, or reobstruction of the treated IVC. The clinical follow-ups after 16, 30, and 30 months showed full recovery of all patients, without relapse of the clinical symptoms at time of treatment start.

DISCUSSION

We presented agitation thrombolysis as an easy and fast procedure to quickly dissolve iatrogenic, fresh IVC thrombi in three patients with BCS. Agitation thrombolysis was clinically and technically successful in all patients. Inferior vena cavagrams and color Doppler ultrasound results up to 12, 24, or 28 months after the procedure demonstrated complete resolution of the iatrogenic, fresh IVC thrombi. Furthermore, to date, our patients have not experienced any recurrence of clinical symptoms, such as pulmonary embolization.

Fresh clinical thrombosis can occur naturally or iatrogenically. In Asia, membranous obstruction of the IVC or the hepatic vein or both is the most common cause of BCS and accounts for up to 60% to 70% of the total patient number.5-8 In these BCS patients, thrombi are easily formed due to obstruction at the suprahepatic IVC, the slow, turbulent or reverse blood flow in the IVC, and the hypercoagulable blood state. Mostly, IVC thrombosis in the BCS patients presenting in our hospital is already chronic, since onset of the disease is often nonsymptomatic, and the onset time is therefore often difficult to track down. Therefore, we only rarely see BCS patients presenting with natural, fresh IVC thrombosis, whereas cases of iatrogenic, fresh thrombosis are more common.

The causes of iatrogenic thrombosis may be as follows: inferior vena cavography or failure of rupture of occluded IVC; IVC endothelial cell damage by high concentration of contrast medium or manipulation of the catheter, guide wire, or other instruments during the procedure; missed or underdosed anticoagulation therapy after the procedure; or application of antihemorraghic therapy in BCS patients with hemorrhage.

The reasons of iatrogenic IVC thrombosis in our patients were previous failure of rupture of occluded IVC; IVC endothelial cell damage by high concentration of contrast medium or manipulation of the catheter, guide wire, or other instruments during the procedure; missed or underdosed anticoagulation therapy after the procedure; or application of antihemorrhagic therapy in BCS patients with hemorrhage.

Current medication or procedures to treat IVC thrombosis include thrombolytic agents,1 transjugular intrahepatic portosystemic shunts,9 surgical shunts,10 balloon angioplasty, metallic stents,2,3 and retrieval stent filters.4 However, these methods are normally used for only chronic (rather than fresh) thrombosis, and they are complicated to use, expensive, and at high risk of causing bleeding. Continuous injection of thrombolytic agents may be useful; however, the injection duration is long, and complete resolution of the fresh IVC clots cannot be guaranteed. Our agitating thrombolysis procedure has the following advantages: 1) easy and fast to apply; 2) use

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### Table. Demographic and clinical presentation of three BCS patients with fresh IVC thrombosis

<table>
<thead>
<tr>
<th>Pa./age/ gender</th>
<th>Dur. (m)</th>
<th>Symptoms</th>
<th>Thrombosis (mm)</th>
<th>Thrombolysis time (min)</th>
<th>Dosage of urokinase</th>
<th>Duplex ultrasonography follow-up (m)</th>
<th>Follow-up (m)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/47</td>
<td>120</td>
<td>AP, H, S, VT, LE, P</td>
<td>IVC 20 22</td>
<td>20</td>
<td>20 ( \times 10^4 ) U</td>
<td>12</td>
<td>30</td>
<td>Alive</td>
</tr>
<tr>
<td>2/F/36</td>
<td>24</td>
<td>VT, AP, H, S, LE, P</td>
<td>IVC 45 26</td>
<td>20</td>
<td>30 ( \times 10^4 ) U</td>
<td>28</td>
<td>30</td>
<td>Alive</td>
</tr>
<tr>
<td>3/M/42</td>
<td>60</td>
<td>VT, AP, H, S, GB, P</td>
<td>IVC 40 28</td>
<td>20</td>
<td>25 ( \times 10^4 ) U</td>
<td>24</td>
<td>16</td>
<td>Alive</td>
</tr>
</tbody>
</table>

AP: Abdominal pain and distention; Dur, duration of the symptoms; GB, gastrointestinal bleeding; H, hepatomegaly; LE, lower extremity edema; MB, membranous obstruction; P, pigmentation; Pa, patient; S, splenomegaly; VT, varices in thoracico-abdominal and legs.
of less thrombolytic agents; 3) lower risk of pulmonary embolization due to attaining complete thrombus resolution; and 4) additional treatment procedures such as balloon dilation or stent placement can be performed immediately after the procedure, thus avoiding reintervention.

**Study limitations.** Our study is a single-center, short-term case study including only three patients. The long-term efficacy of our agitation thrombolysis procedure for treating fresh IVC thrombosis in BCS patients warrants further investigation in larger, controlled studies.

In summary, our preliminary results indicate that agitation thrombolysis by using a guide wire and a catheter may be a safe and feasible approach in BCS patients with iatrogenic, fresh IVC thrombosis.

**AUTHOR CONTRIBUTIONS**

Conception and design: X-W H
Analysis and interpretation: P-X D, Y-D L
Data collection: G W
Writing the article: P-X D
Critical revision of the article: P-X D, Y-D L, X-W H
Final approval of the article: X-W H
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Overall responsibility: X-W H

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**REFERENCES**


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