Case Report

Primary antiphospholipid antibody syndrome with membranous obstruction of the inferior vena cava—successful PTA and thrombolytic therapy

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Introduction

The primary antiphospholipid antibody syndrome is a thrombophilic disorder in which the combination of recurrent venous or arterial thrombosis and antiphospholipid antibodies (anticardiolipin antibodies and/or lupus anticoagulant) occurs in patients without the characteristic features of systemic lupus erythematosus (SLE) [1–3]. The thrombosis can affect vessels of all sizes, the most consistent histopathological lesion being a bland thrombus without inflammation [4].

The mechanism of thrombosis is unknown. Recent studies have shown that a subset of phospholipid antibodies reacts with the complex of phospholipid and serum β2-glycoprotein 1, the cofactor that inhibits factor XII and platelet activation, and prothrombinase activity [5]. The membrane, a web or shelf of tissue occluding the inferior vena cava, is seen in various pathological states, such as myeloproliferative disorders, disorders due to oral contraceptives, antiphospholipid antibody syndrome, SLE, Bechter’s syndrome, pericaval filariasis, visceral thrombophlebitis migrans [6], and paroxysmal nocturnal haemoglobinuria [7].

The membranous obstruction of the inferior vena cava is generally associated with Budd–Chiari syndrome, since the outflow of venous hepatic blood is generally obstructed in some way at various sites within the inferior vena cava [8], whereas acute renal failure (ARF) is not usually present.

Renal involvement is also relatively infrequent in patients with antiphospholipid antibody syndrome without SLE and it may be due to renal thrombotic microangiopathy and glomerular necrosis [9], renal artery stenosis [10] or thrombosis [11], renal vasculitis [12], renal infarction [13], or renal vein thrombosis [14].

Case

A previously healthy 42-year-old caucasian male was referred to our hospital for ARF. He had been well until about 7 days earlier, when he first experienced a transitory episode of low back pain; 3 days before his admission he experienced another but severe episode of low back pain with nausea and vomiting during light work. His blood pressure was 110/70 mmHg. The results of ECG and ambulatory abdominal ultrasound were normal. The patient was therefore admitted to a district general hospital where non-oliguric ARF was diagnosed (serum creatinine concentration = 7.93 mg/dl). The result of an ultrasound investigation of the abdominal organs was normal. The patient was then transferred to our renal Unit. He complained of mild abdominal pain and nausea. His body temperature was 36.5°C, pulse rate 90 b.p.m., and blood pressure 130/70 mmHg. Tenderness and oedema were found in the right leg. Examination of the lungs, heart, and abdomen was unremarkable.

The patient’s past medical history included hyperbilirubinaemia caused by Gilbert syndrome.

The results of the laboratory evaluation are shown in Table 1. Twenty-four hour urinary protein excretion was 0.5 g, and the patient presented microhaematuria. He did not meet the criteria for SLE. Lupus anticoagulant was positive and high levels of IgG anticardiolipin antibodies were detected. Colour-Doppler abdominal ultrasonography showed thrombosis of the superficial femoral, common femoral, external and common iliac right veins, as well as of the inferior vena cava just above the renal and just below the hepatic veins. The renal arteries were normal. Intravenous heparin therapy (1500 U/h) was started. After 7 days of treat-
Antiphospholipid antibody syndrome with membranous obstruction of the IVC

Table 1. Laboratory evaluation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day of admission</th>
<th>Day of discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (mg/dl)</td>
<td>7.12</td>
<td>0.95</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>23.5</td>
<td>25.7</td>
</tr>
<tr>
<td>Whitecell count (per mm³)</td>
<td>7200</td>
<td>3900</td>
</tr>
<tr>
<td>Platelet count (per mm³)</td>
<td>142 000</td>
<td>269 000</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.1</td>
<td>1.29</td>
</tr>
<tr>
<td>Conjugated</td>
<td>3.27</td>
<td>0.31</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/l)</td>
<td>47</td>
<td>27</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/l)</td>
<td>74</td>
<td>35</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/l)</td>
<td>246</td>
<td>144</td>
</tr>
<tr>
<td>Lactate dehydrogenase (U/l)</td>
<td>273</td>
<td>221</td>
</tr>
<tr>
<td>Prothrombin activity (%)</td>
<td>77</td>
<td>40</td>
</tr>
<tr>
<td>INR</td>
<td>1.18</td>
<td>2.04</td>
</tr>
<tr>
<td>Partial-thromboplastin time (s)</td>
<td>28</td>
<td>92</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>637</td>
<td>449</td>
</tr>
<tr>
<td>ANA</td>
<td>+(1:40)</td>
<td>+(1:80)</td>
</tr>
<tr>
<td>Ab anti-DNA</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>ANCA</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ab anticardiolipin-IgM (U-MPL)</td>
<td>2.8*</td>
<td>6*</td>
</tr>
<tr>
<td>Ab anticardiolipin-IgG (U-GPL)</td>
<td>36.8**</td>
<td>48**</td>
</tr>
<tr>
<td>LAC</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Antithrombin III (activity)</td>
<td>104%</td>
<td></td>
</tr>
<tr>
<td>Sucrose haemolysis test</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

*Control value <11 U-MPL; **control value <23 U-GPL.

After 14 days of treatment, a venacavogram revealed a complete acute thrombosis of the inferior vena cava (Figure 1), whereas the renal veins were patent. Thrombolytic therapy was started with a local infusion of urokinase (200 000 U/h) into the clot and intravenous heparin therapy (1500 U/h). After 4 days of treatment, a further venacavogram showed the complete dissolution of the thrombus and partial patency of the inferior vena cava with a membranous septum (Figure 2). The pressure gradient across the caval stenosis was 10 mmHg.

Thrombolytic therapy was subsequently discontinued and repeated sessions of percutaneous transluminal balloon angioplasty (PTA) were started (with increasing balloon diameter: 10–12–15 mm).

Following this last procedure, the venacavogram showed a complete resolution of the stenosis and a normal patency of the inferior vena cava (Figure 3). After dilatation, the pressure gradient decreased to 1 mmHg. The patient was started on anticoagulant and antiplatelet therapy, and discharged. The laboratory evaluation is shown in Table 1.

A follow-up venacavogram after 1 month confirmed the normal patency of the inferior vena cava, as did colour-Doppler imaging, at 6, 12 and 24 months.

Discussion

ARF is a rare complication of primary antiphospholipid antibody syndrome, a recognized cause of the membranous obstruction of the inferior vena cava, and it is due to thrombotic complications of the renal vessels.

We here present the case of a patient affected by membranous obstruction of the inferior vena cava due to antiphospholipid antibody syndrome with ARF that was successfully managed by means of angioplasty and thrombolytic therapy.

The ARF was probably a haemodynamic complication of the inferior vena cava acute thrombosis, as we found no thrombosis in the renal veins or arteries. However, the concomitant presence of another renal pathology cannot be excluded without performing a renal biopsy. The rapid improvement in renal function and proteinuria supports the hypothesis of haemodynamic damage.

In our case, appropriate thrombolytic therapy and angioplasty probably avoided the proximal extension of the thrombus and the onset of Budd–Chiari syndrome, which has a high incidence of mortality. Local thrombolytic therapy completely dissolved the thrombus, and the venacavogram showed a membranous septum of the inferior vena cava.

There are few data in the literature concerning the use of thrombolytic therapy for thrombosis of the inferior vena cava [7,15,16].

Direct application of the thrombolytic agent into the clot through a catheter seems likely to be effective,
Fig. 2. Partial membranous obstruction of the inferior vena cava.

and has previously been claimed to be superior to systemic infusion in superior vena cava syndrome [17].

The lytic agent should ideally be administered before the organization of thrombus, otherwise the lysis of the thrombus is less likely to succeed. The main thrombolytic agents used are urokinase, streptokinase, and tissue-type plasminogen activator. No studies have addressed the relative efficacy of these agents for the thrombosis of the vena cava, and the choice of an agent for a specific patient depends on physician preference and costs. Haemorrhagic risks are minimized by direct application, because a lower dose than that used in systemic therapy can be administered.

The cause of the acute thrombosis of the inferior vena cava in our patient was the membranous obstruction of the inferior vena cava due to antiphospholipid antibody syndrome. It is still unknown whether the membranous obstruction of the inferior vena cava is congenital or acquired. Although there is a lack of convincing data supporting a congenital origin, there is evidence showing that the webs are a result of the natural resolution of a thrombus. Histologically, the occlusive tissue has been found to be muscular and elastic, similar to organized thrombi in other sites [18]. All of the three layers of the vessel wall are present at autopsy, thus suggesting normal initial development and a subsequent thrombosis leading to a web [19].

Fig. 3. Complete resolution of the stenosis and normal patency of the inferior vena cava.

The web of our patient was below the hepatic veins, and there was a large pressure gradient across it. Possibly the web could be a previous thrombus at this site, now organized, with partial obstruction of blood flow.

Conclusion

Aggressive therapy is warranted for patients with acute membranous obstruction of the inferior vena cava due to antiphospholipid antibody syndrome in order to avoid the onset of Budd–Chiari syndrome. Thrombolytic therapy and angioplasty seem to be the most logical combination because they are directed at the site and cause of obstruction.

The risk of recurrent thrombosis in patients with the antiphospholipid antibody syndrome is high [20], and so long-term anticoagulation therapy is advisable.

References
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