Membranous Obstruction of the Inferior Vena Cava Associated with Antiphospholipid Syndrome Presenting with Bilateral Lower Limb Edema: A Case Report

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Abstract

Membranous obstruction of the inferior vena cava (MOIVC) is an infrequent disorder characterized by an acquired intrinsic obstruction of the hepatic portion of the vena cava. Clinical presentation may vary from an asymptomatic state, to a slowly evolving course of lower extremity swelling, ascites, and progressive cirrhosis. MOIVC may rarely be caused by prothrombotic disorders. Herein, we describe a patient with lupus-erythematosus-associated antiphospholipid syndrome (APS) who presented with subacute venous claudication and bilateral lower limb edema while on oral anticoagulation. Cavography confirmed a diagnosis of MOIVC. The patient successfully underwent percutaneous balloon angioplasty for definitive management and remained symptom-free at 4-year follow-up on long-term anticoagulation therapy. To our knowledge, this is the fourth case description of MOIVC associated with APS successfully treated with balloon angioplasty, but the first with a subacute clinical presentation.

Résumé

L'obstruction membraneuse de la veine cave inférieure est une pathologie peu fréquente caractérisée par une obstruction intrinsèque de la portion hépatique de la veine cave. La présentation clinique varie et inclut une absence de symptômes, des signes congestifs progressifs tels que de l’œdème des membres inférieurs, de l’ascite et une cirrhose progressive. L’obstruction membraneuse peut rarement être causée par des états prothrombotiques. Nous rapportons le cas d’une patiente porteuse d’un syndrome des antiphospholipides associé au lupus érythémateux et qui s’est présentée avec de l’œdème subaigu et bilatéral des membres inférieurs sous
Case Report

The patient is a 46-year-old white woman diagnosed 2 years earlier with lupus-erythematous-associated antiphospholipid syndrome (APS) in the setting of femoral venous thrombosis of the left leg and patchy alopecia. During the initial presentation, her laboratory test parameters were the following: hemoglobin 140 g/L (120–160 g/L); white blood count 7.9 × 10^9/L (3.8–10.6 × 10^9/L) with normal lymphocyte count; platelets 96 × 10^9/L (130–400 × 10^9/L); creatinine 83 umol/L (46–92 umol/L) with normal urinalysis, normal complement levels (C3, C4); ANA > 1/320 homogenous and granular; DS-DNA antibodies: 409.4 UI/mL (0–100 UI/mL), aTTP 70 (22–29 s), and normal INR. Thrombophilia workup revealed positive lupus anticoagulant (RVV-confirmed), anticardiolipin IgG (GPL) > 600 (>90 highly positive); anti-beta 2-glycoprotein 1 >100 U/mL (>15 highly positive) which remained positive at 12 weeks. The investigation for other thrombophilic disorders was negative and included: dosage of Protein C, Protein S, and antithrombin III levels; Prothrombin G20210A mutation; and Factor V Leiden. At that time, she was started on long-term oral anticoagulation with warfarin (target INR 2.0–3.0) and hydroxychloroquine 400 mg daily for lupus.

Subsequent review of her medical chart revealed positive ANA and anti-DS-DNA antibodies 7 years before initial presentation.

One year after initial presentation, the patient presented with painful blue toes and arteriography confirmed lower limb vasculitis. Prednisone 50 mg po daily was initiated. Unfortunately, 8 days after the procedure, while on adequate bridging therapy with low-molecular weight heparin and warfarin (INR 2.2), she developed abdominal hematomas with hemodynamic instability requiring resuscitative measures and reversal of anticoagulation. Given the concern for potential abdominal vasculitis, oral prednisone was switched to IV pulsed methylprednisolone at 1 g daily for 3 days followed by oral prednisone 50 mg and cyclophosphamide 100 mg po daily. Anticoagulation was resumed with heparin followed by warfarin (target INR 2.0–3.0) after 10 days of interruption without recurrent bleeding. She was discharged on a course of oral cyclophosphamide, maintained for 6 months, and a slow prednisone taper.

Seven months later, the patient presented complaining of significant bilateral leg discomfort when walking and symmetrical lower limb swelling. Cyclophosphamide and prednisone had been completely weaned and her treatment consisted of hydroxychloroquine 400 mg po daily, mycophenolate mofetil 1 g po twice a day, and warfarin. Physical examination revealed prominent pitting edema of both legs up to the pre-sacral fossa without signs of active lupus or evidence of heart failure. Serum albumin and hepatic function tests were normal; creatinine level was normal without proteinuria. Lower extremity venous doppler ultrasound was negative for deep vein thrombosis. Cardiac echography was normal except for a nonmobile calcified 10 × 7 mm lesion in the inferior vena cava (IVC) near the right atrium. Abdominal doppler ultrasonography showed patent hepatic and portal veins, no ascites, and a tissular density at the cavoatrial junction (Figure 1). MRI confirmed the presence of a tissular, partially calcified lesion within the IVC and no evidence of extrinsic compression, neoplastic mass, or thrombosis. A transfemoral diagnostic cavo gram showed a hemodynamically significant web at the cavoatrial junction with a pressure gradient of 13 mm Hg (normal < 3).

After careful anticoagulation reversal, percutaneous balloon angioplasty of the lesion was performed under local anesthesia and conscious sedation. The right common femoral vein was accessed and a long 10F sheath was inserted. The lesion was crossed and sequential 10 mm, 18 mm, and 22 mm angioplasties were performed. Post-angioplasty, there was minimal residual stenosis and the gradient decreased to 4 mm Hg. The patient had spectacular improvement with complete resolution of leg pain and edema within 48 h. Long-term anticoagulation with warfarin was resumed after the procedure. Mycophenolate mofetil was stopped after 1 year without signs of active lupus, and hydroxychloroquine was continued as a long-term therapy. The patient remains asymptomatic at 4-year follow-up.

anticoagulotherapie orale. La cavographie a confirmé le diagnostic d’obstruction membranuse de la veine cave. La patiente a bénéficié avec succès d’un traitement d’angioplastie par ballon et elle demeure asymptomatique sous anticoagulants après 4 ans de suivi. A notre connaissance, ce cas représente la 4ème description d’obstruction membranuse de la veine cave associée au syndrome des antiphospholipides et traitée par angioplastie, mais la première avec une présentation clinique subaiguë.
Membranous obstruction of the inferior vena cava (MOIVC) is a rare cause of IVC obstruction and is typically located at the hepatic portion of the vena cava. The first description of MOIVC dates back to 1909 in the Japanese literature. It was, thereafter, poorly defined until 1998, when Okuda defined MOIVC as a separate entity from primary Budd-Chiari syndrome with a distinct pathophysiology and prognosis (Table 1). MOIVC is characterized by a fibrotic stenosis of the IVC and with a chronic clinical course, whereas acute clinical presentation caused by thrombosis of the hepatic veins is characteristic of primary Budd-Chiari. Although an iteration of the hepatic vein outflow by MOIVC can ultimately be complicated by acute thrombosis and presents with the Budd-Chiari syndrome, the initial confusion between the two entities, primary Budd-Chiari and MOIVC, represents distinct conditions. MOIVC is more frequently reported in Nepal, Africa, and China where recurrent gastrohepatic infections and pericaval filariasis presumably act as causal factors for the disease. Histopathologic examination of the IVC and hepatic veins in 17 autopsy cases of Budd-Chiari reported by Kage et al., prior to the distinction of MOIVC and primary Budd-Chiari, revealed that organized thrombi of various ages with fibrous tissue and calcification were found in most cases refuting a congenital cause. A recent review of the pathogenesis of MOIVC by Shresta et al., based on several publications looking at cavographic studies, long-term patient follow-up, and autopsy findings was consistent with an acquired microthrombotic process, mainly triggered by recurrent bacterial infections. In a recent study from China exploring the pathogenesis of the occlusive area of the IVA in patients with chronic congestive symptoms and secondary Budd-Chiari syndrome, the authors analyzed clamp biopsies of IVC in 31 patients and found local thrombosis of different stages and fibrosis. The hepatic IVC is more prone

**Discussion**

Membranous obstruction of the inferior vena cava (MOIVC) is a rare cause of IVC obstruction and is typically located at the hepatic portion of the vena cava. The first description of MOIVC dates back to 1909 in the Japanese literature. It was, thereafter, poorly defined until 1998, when Okuda defined MOIVC as a separate entity from primary Budd-Chiari syndrome with a distinct pathophysiology and prognosis (Table 1). MOIVC is characterized by a fibrotic stenosis of the IVC and with a chronic clinical course, whereas acute clinical presentation caused by thrombosis of the hepatic veins is characteristic of primary Budd-Chiari. Although an iteration of the hepatic vein outflow by MOIVC can ultimately be complicated by acute thrombosis and presents with the Budd-Chiari syndrome, the initial confusion between the two entities, primary Budd-Chiari and MOIVC, represents distinct conditions. MOIVC is more frequently reported in Nepal, Africa, and China where recurrent gastrohepatic infections and pericaval filariasis presumably act as causal factors for the disease. Histopathologic examination of the IVC and hepatic veins in 17 autopsy cases of Budd-Chiari reported by Kage et al., prior to the distinction of MOIVC and primary Budd-Chiari, revealed that organized thrombi of various ages with fibrous tissue and calcification were found in most cases refuting a congenital cause. A recent review of the pathogenesis of MOIVC by Shresta et al., based on several publications looking at cavographic studies, long-term patient follow-up, and autopsy findings was consistent with an acquired microthrombotic process, mainly triggered by recurrent bacterial infections. In a recent study from China exploring the pathogenesis of the occlusive area of the IVA in patients with chronic congestive symptoms and secondary Budd-Chiari syndrome, the authors analyzed clamp biopsies of IVC in 31 patients and found local thrombosis of different stages and fibrosis. The hepatic IVC is more prone
In western countries, infectious triggers are virtually absent, and the etiologies of the rare cases of MOIVC are divided between cancers, such as myeloproliferative diseases or hepatocarcinomas, and thrombophilic disorders. By extension from the Budd-Chiari literature, connective tissue diseases and APS could also contribute to MOIVC. Indeed, among 145 patients with the Budd-Chiari syndrome, 25 (17%) had APS. Since 1998, when Budd-Chiari and MOIVC were initially described as distinct entities, the association of autoimmune prothrombotic disorders and MOIVC has been limited to three case reports: one associated with primary APS and two related to lupus erythematosus (SLE)-associated APS. Interestingly, those three cases presented with acute thrombosis of the IVC.

### Table 1. Characteristics of primary Budd-Chiari and membranous obstruction of the inferior vena cava (MOIVC)

<table>
<thead>
<tr>
<th>Primary Budd-Chiari</th>
<th>MOIVC</th>
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<tbody>
<tr>
<td><strong>Epidemiology</strong></td>
<td>Mostly: Western countries</td>
</tr>
<tr>
<td><strong>Etiologies and associated conditions</strong></td>
<td>Mostly: Hypercoagulable conditions • Myeloproliferative disorders • Paroxysmal nocturnal hemoglobinuria • Pregnancy, contraceptives • SLE • Antiphospholipid syndrome • Connective tissue diseases</td>
</tr>
<tr>
<td><strong>Pathophysiology</strong></td>
<td>Thrombosis of the hepatic veins segmental or complete</td>
</tr>
<tr>
<td><strong>Clinical presentations</strong></td>
<td>Acute to subacute onset • Abdominal pain • Hepatomegaly • Ascites, jaundice • Hepatic failure</td>
</tr>
<tr>
<td><strong>Diagnostic imaging</strong></td>
<td>IVC/hepatic venography (gold standard) • Doppler ultrasound • Abdominal MRI or CT with contrast</td>
</tr>
<tr>
<td><strong>Angiographic findings</strong></td>
<td>Complete occlusion of hepatic vein(s) • Intrahepatic collateral veins giving a spider web appearance</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Thrombolysis, if acute thrombosis • Transjugular intrahepatic portosystemic shunt (TIPS) • Treat underlying condition • Long-term anticoagulation when indicated</td>
</tr>
</tbody>
</table>

to microendothelial damage resulting from different factors: constant movement of the diaphragm, turbulence of venous flow from the hepatic veins, and direct exposure to clotting factors produced by the liver which could favor subsequent infection and thrombosis.

In contrast to MOIVC, primary Budd-Chiari caused by thrombosis of the hepatic veins is more frequent in western countries. Its presentation is usually abrupt with the acute thrombotic process at the forefront. MOIVC is very uncommon in the developed world. Old case series from Europe and the United States estimate the incidence of MOIVC to range between c. However, the rate of MOIVC can increase up to 17.3%, in selected Nepalese populations with liver dysfunction.
Membranous obstruction of the inferior vena cava

First therapeutic step but transjugular intrahepatic portosystemic shunt (TIPS) may be needed. In the present case, we opted for endovascular balloon angioplasty and long-term anticoagulation with warfarin as well as hydroxychloroquine to avoid future SLE exacerbations in which inflammation could contribute to increased thrombotic risk.

Conclusion

MOIVC is a rare entity in developed countries. It should nevertheless be considered in patients with unexplained progressive lower limb edema, especially in the context of any thrombophilic disorder. Because of its potentially fatal outcome, from congestive cirrhosis, hepatocellular carcinoma, or secondary acute thrombosis, prompt recognition is important. Diagnosis is usually confirmed by cavography and definitive treatment is achieved by percutaneous balloon angioplasty and anticoagulation.

Author Contributions

Hugues Allard-Chamard, Andrew Benko, and Martine Chamberland were involved in the care of the patient. Hugues Allard-Chamard also designed the case report, and drafted and revised the manuscript. Marco Lefebvre contributed to the writing and revision of the manuscript. Andrew Benko also contributed to the writing of the manuscript, the selection of images, and the revision of the manuscript. Martine Chamberland also contributed to the writing and revision of the manuscript.

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Competing Interests

None.

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1. Okuda K, Kage M, Shrestha SM. Proposal of a new nomenclature for Budd-Chiari syndrome: Hepatic vein thrombosis


