Budd-Chiari syndrome in a young patient with anticardiolipin antibodies: need for prolonged anticoagulant treatment

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Abstract

The case of a 20 year old woman is reported with Budd-Chiari syndrome in whom lupus anticoagulant and anticardiolipin antibodies were shown; treatment with oral anticoagulants induced a considerable improvement. This treatment was interrupted after one year; interruption was followed by redevelopment of ascites. Further treatment with anticoagulants was continued for five years with noticeable improvement. When treatment with oral anticoagulants was stopped because of pregnancy, the patient redeveloped ascites and had a spontaneous miscarriage. Subsequently, treatment with oral anticoagulants was reintroduced and again resulted in noticeable improvement. In conclusion patients with Budd-Chiari syndrome should be tested for lupus anticoagulants and anticardiolipin antibodies, Budd-Chiari syndrome resulting from this cause may have a good response to treatment with oral anticoagulants; this treatment should be maintained permanently, and pregnancy in such patients may initiate serious difficulties.

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Hepatic venous outflow block or Budd-Chiari syndrome is a severe liver disease with a three year survival rate of 50%.¹ Several conditions have been implicated as a cause of Budd-Chiari syndrome, including myeloproliferative disorders,² paroxysmal nocturnal haemoglobinuria,³ the presence of lupus anticoagulant,⁴⁻⁶ oral contraceptives,⁷ pregnancy,⁸ and others.^{9,10} In a small number of cases Budd-Chiari syndrome is associated with the presence of lupus anticoagulant.⁴⁻⁶ Anticardiolipin antibodies are similar to lupus anticoagulant antiphospholipid antibodies, which have been described in patients with recurrent arterial and venous thrombosis, thrombocytopenia, fetal loss or miscarriage. This syndrome has been called the antiphospholipid antibody syndrome.¹¹ We report a case of Budd-Chiari syndrome in a young woman with both lupus anticoagulant and anticardiolipin antibodies, who responded to oral anticoagulation and remained well for five years. When the patient became pregnant, however, and oral anticoagulants were stopped she redeveloped ascites and intra-uterine fetal death occurred.

Case report

A 20 year old woman was well until two weeks before admission, when she developed right upper abdominal pain, vomiting, and fever. She had been taking oral contraceptives for several years. On admission, she had a normal blood pressure, body temperature of 38°C, and tenderness in the right upper abdomen, no signs of ascites were noted. Laboratory examination showed the following values: haemoglobin 5.9 mmol/l; packed cell volume 40%; white blood cell count $6.4 \times 10^9/l$; platelet count $1.8 \times 10^9/l$; reticulocytes 5%; prothrombin time 13.0 s (control, 11 s); activated partial thromboplastin time (aPTT) 41 s (control 30-39 s), serum alanine aminotransferase 18 U/ml (N<30) alkaline phosphatase 41 U/l (N=120), γ -glutamyl-transferase 57 U/l (N<30), total bilirubin 37 μ mol/l.

Ultrasonography showed a thickened gall bladder wall, which was tender.

On the probable diagnosis of acalculous cholecystitis, a laparotomy was performed. The gall bladder was normal. The right liver lobe was red and swollen, the spleen slightly enlarged, there was no ascites. A biopsy specimen was taken from the right lobe of the liver, which showed only dilated sinusoids.

Two weeks later she developed ascites with a protein content of 2 g/l. During venous angiography of the hepatic veins, only the vein of the caudate lobe could be visualised. The inferior cava was patent, the free hepatic venous pressure was 14 mm Hg, wedged hepatic venous pressure 30 mm Hg, and right atrial pressure 14 mm Hg. By magnetic resonance imaging the left and middle hepatic vein and a collateral vessel draining the right liver lobe

T² weighted (TR 2000, TE 90) section at the level of the hepatic veins entering the inferior caval vein. The left and middle hepatic veins (arrows) and a collateral vessel (open arrow) draining the right liver lobe are visualised as bright structures. The right hepatic vein is obliterated.

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were visualised. The right hepatic vein was obliterated (Figure).

Further investigation of the cause of the Budd-Chiari syndrome was performed. Antibodies against extractable nuclear antigen, antinuclear antibodies, rheumatoid factor, and *Treponema pallidum* haemagglutination antibodies could not be detected. The direct and indirect Coombs' test and Ham's test were negative. Antithrombin III, protein S and C concentrations were normal. The prothrombin time was normal, while aPTT was slightly raised. Lupus anticoagulant and anticardiolipin antibodies were found. Culture of bone marrow with and without erythropoietin showed a normal growth pattern. We concluded that this patient had a Budd-Chiari syndrome because of lupus anticoagulant and anticardiolipin antibodies. Ascites was successfully treated with paracentesis and diuretics. Coumarin treatment was started. After six months, the diuretics were stopped without recurrence of ascites. After one year we decided to stop the oral anticoagulants.

Within a month she redeveloped ascites. After the oral anticoagulation treatment and diuretics were started again, she remained well for another five years. Repeat magnetic imaging showed no progression of the Budd-Chiari syndrome. She then wanted to have a baby despite having been informed of the risk of deterioration of the Budd-Chiari syndrome and obstetrical complications.

After several months, she returned because of an amenorrhoea of four weeks' duration. The oral anticoagulants were stopped; heparin 7500 IE twice daily subcutaneously was started. Fourteen days later she had the same complaints as at the first admission five years previously. On physical examination no abnormalities were found. Laboratory investigation showed several abnormalities. Haemoglobin, 6.7 mmol/l; packed cell volume, 45%; white blood cell count, $2 \times 10^9/l$; platelet count $5.6 \times 10^9/l$; prothrombin time, 13 s; aPTT, 43 s; fibrinogen 4.6 g/l; fibrin degradation products, 200 µg/l. The lupus anticoagulant test was positive, IgG anticardiolipin antibodies were positive 98 IU/l (normal 0–31) as were IgM anticardiolipin antibodies 26 IU/l (normal 0–12); ultrasonography showed a uterus of six weeks pregnancy with no signs of fetal heart action. Treatment with intravenous heparin and prednisone 80 mg daily was started. Ascites was successfully treated with diuretics. In the following days spontaneous miscarriage occurred. Within six weeks all laboratory results returned to normal. Two months after the miscarriage, she was well. Platelet count was $140 \times 10^9/l$ with 25 mg prednisone daily, a reduction to 20 mg daily was followed by an acute drop of the platelet count to $43 \times 10^9/l$, which became normal after treatment with 60 mg prednisone daily. At 12 months after the miscarriage she did not have ascites, although she had stopped using diuretics, and platelet count was $141 \times 10^9/l$ (with 5 mg prednisone daily). The patient still had high concentrations of IgG anticardiolipin antibodies 81 IU/l and IgM anticardiolipin antibodies 17 IU/l.

Discussion

The aetiology of the Budd-Chiari syndrome can be classified in five groups according to the mechanism of obstruction, namely primary lesions of the main hepatic veins, benign or malignant invasion of the hepatic veins, obstruction of the inferior vena cava, and veno occlusive disease.^{12 13}

In our patient computed tomography and magnetic resonance imaging showed thrombosis of two hepatic veins. Thrombosis of the hepatic veins can result from an underlying primary myeloproliferative disorder,² the use of oral contraceptives,⁷ pregnancy,⁸ postpartum state,¹⁴ paroxysmal nocturnal haemoglobinuria,³ the presence of lupus anticoagulant, and several miscellaneous disorders such as connective tissue diseases.^{9 10} A myeloproliferative disorder was excluded by a normal bone marrow aspirate and normal colony formation of the erythroid cells in an erythropoietin poor medium. A normal acid Ham's test, normal coagulation parameters apart from a prolonged aPTT and negative rheumatoid and lupus erythematosus serology in our patient excluded paroxysmal nocturnal haemoglobinuria, diffuse intravascular coagulation, and rheumatic disorders.

In our patient two possible causes for the hepatic vein thrombosis were found, namely the use of oral contraceptives and the presence of lupus anticoagulant and anticardiolipin antibodies. Longterm use of oral contraceptives increases the risk of venous thrombosis by exacerbating an underlying thrombogenic condition such as paroxysmal nocturnal haemoglobinuria or a myeloproliferative disease.^{2 7 15} As mentioned such abnormalities were not found in this patient. The most likely cause in our patient is therefore the lupus anticoagulant and anticardiolipin antibodies. Lupus anticoagulant and anticardiolipin antibodies are both antiphospholipid antibodies.^{11 16 17}

Antiphospholipid antibodies are associated with venous and arterial thrombosis and recurrent miscarriage.^{11 17}

Lupus anticoagulant is an immunoglobulin of IgG or IgM class with a tendency to adhere to the phospholipid portion of the prothrombin activator complex resulting in prolongation of the aPTT. At presentation and during pregnancy our patient had a prolonged aPTT, with detectable lupus anticoagulant and anticardiolipin antibodies.

Anticardiolipin antibodies are of the IgM, IgG, or IgA classes and can be quantified by a radioimmunoassay. Anticardiolipin antibodies are also associated with arterial and venous thrombosis, cerebral thrombosis, thrombocytopenia, recurrent miscarriages, endocardial lesions in systemic lupus erythematosus, and giant cell arteritis.^{18 19} In 70% of the patients both lupus anticoagulant and anticardiolipin antibodies are present. High concentrations of anticardiolipin antibodies are closely correlated with severe complications such as thrombosis, thrombocytopenia, and a variety of obstetrical problems.^{11 20}

Tests for anticardiolipin antibodies are possibly of greater value than tests for lupus

anticoagulant, because they are more sensitive and less subject to interobserver errors or variations in methodology than tests for lupus anticoagulant.^{11 20-25}

The treatment of choice in patients with Budd-Chiari and the presence of lupus anticoagulant and anticardiolipin antibodies is coumarin anticoagulation.^{4 6 22} Our patient was successfully treated by coumarin anticoagulation; ascites was treated by paracentesis and diuretics. It was possible to stop the diuretics after six months of treatment.

The longterm prognosis of patients with the Budd-Chiari syndrome resulting from lupus anticoagulants is not well known. Several reports with long survival after the diagnosis have been described; however, rapid deterioration and death have also been reported.⁴⁻⁶

Pregnancy is a risk factor for the development of Budd-Chiari syndrome; but, on the other hand, several cases of successful pregnancy in patients with the Budd-Chiari syndrome have been reported.²⁶ The presence of lupus anticoagulant and the high concentrations of anticardiolipin are associated with venous and arterial thrombosis, increased fetal loss or recurrent miscarriage.^{11 17 20} Despite being warned about the risks our patient became pregnant and despite subcutaneous heparin the patient had a miscarriage at six weeks of pregnancy and developed ascites and severe thrombocytopenia.

High concentrations of IgG anticardiolipin antibodies are closely correlated by recurrent fetal loss, thrombocytopenia, and thrombosis and have a high predictive value of renewed problems in subsequent pregnancies.^{11 23} Our patient has high IgG anticardiolipin antibodies, suggesting again problems in another pregnancy. To prevent complications in patients with lupus anticoagulant and high concentrations of anticardiolipin antibodies some have advocated aspirin, heparin, and corticosteroids.^{20 23 24 27 28} The role of corticosteroids in the treatment of this condition is not clearly defined.^{20 22 24 28}

The good clinical response to oral anticoagulants in our patient illustrates the importance of testing patients with Budd-Chiari syndrome for anticardiolipin antibodies and lupus anticoagulant, and, if positive, of giving prolonged oral anticoagulation.

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