anticoagulation in a patient with secondary APS. Lupus. 2003;12:851–3.
5. Deák M, Bocskai M, Burcsár S, Dányi O, Fekete Z, Kovács L. Non-thromboembolic risk in systemic lupus erythematosus associated with antiphospholipid syndrome. Lupus. 2014;23:913–8.
6. Gouya H, Cabanes L, Mouthon L, Pavie A, Legmann P, Vignaux O. Severe mitral stenosis as the first manifestation of systemic lupus erythematosus in a 20-year-old woman: the value of magnetic resonance imaging in the diagnosis of Libman-Sacks endocarditis. Int J Cardiovasc Imaging. 2014;30:959–60.
7. Vinales KL, Gopalan RS, Lanza LA, Lester SJ, Chaliki HP. Unusual case of nonbacterial thrombotic endocarditis attributable to primary antiphospholipid syndrome. Circulation. 2010;122:e459–60.
8. Nishioka N, Morimoto N, Yoshida M, Mukohara N. Left ventricular vegetations: a rare manifestation of Libman-Sacks endocarditis. J Thorac Cardiovasc Surg. 2013;145:e26–8.

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Development of deep vein thrombosis during treatment with plasmapheresis☆

Desarrollo de trombosis coincidiendo con la realización de plasmaféresis

Dear Editor,

In primary focal segmental glomerulosclerosis (FSGS) the response to drug treatment is 30–70%, depending on factors such as histological type, degree of proteinuria, presence of kidney failure or degree of resistance to steroid treatment.[1,2] Plasmapheresis is used as rescue therapy when there is no response to drugs, results are variable and there are, frequent relapses.[3,4] Plasmapheresis, accompanied by immunoadsorption in post-transplant relapse of FSGS, achieves good results with minimal complications.[5]

Here we report a case of venous thrombosis that occurred while performing plasmapheresis on a patient with FSGS. The patient is 26-year-old man with severe nephrotic syndrome (NS) due to FSGS, a cellular variant, diagnosed 10 months earlier. The patient received treatment with steroids, cyclophosphamide, cyclosporine and mycophenolate, with no response, maintaining a proteinuria of 15–33 g/day. He was admitted the Hospital on 3 occasions for extreme generalised oedema, with ascites, effusion in the testicular region, no pleural effusion, and during the last admission the patient required ultrafiltration for oedema and oligoanuria, with no response to an intravenous albumin infusion. Four months later, he was re-admitted due to a new episode of extreme generalised oedema, with Cr 2.3 mg/dl, proteinuria 49.2 g/day, serum albumin 1.6 g/dl and total protein 3.7 g/dl. Plasmapheresis was performed through a right femoral transient venous catheter, performing 3 sessions, extracting 3300 ml of plasma and infusing 1800 ml of 5% albumin and 1500 ml of fresh frozen plasma (FFP) every other day. Anticoagulation was performed with 3500 IU of subcutaneous bemiparin every 24 h. The patient maintained diuresis and had no episodes of hypotension. On the third day, the patient noticed pain in the left thigh, together with an increase in its volume of the extremity; the Doppler ultrasound showed bilateral iliofemoral venous thrombosis. The coagulation study showed D-dimer 14,895 ng/ml, fibrinogen 8.9 mg/dl, prothrombin activity at 77%, antithrombin III at 49% and platelets 534,000/mm^3. Proteinuria rose to 71.3 g/day during admission, and serum albumin initially rose to 2.2 g/dl and then decreased rapidly and remained at 1–1.3 g/dl. Antithrombin III (1000 IU/day) was administered for 10 days, achieving serum antithrombin III levels around 70% by discharge. The venous catheter was removed after the third round of plasmapheresis; the patient was anticoagulated with 7500 IU of subcutaneous bemiparin/day and discharged on acenocoumarol. Creatinine stayed at 1.6 mg/dl. Nine months later, the Doppler ultrasound was repeated, showing the complete permeability of

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the iliac and femoral axis. Plasmapheresis did not affect the subsequent changes in proteinuria. Rituximab and tacrolimus were subsequently administered, but, 13 months later, the patient entered the haemodialysis programme due to severe kidney failure (Cr 12.2 mg/dl), with no changes in proteinuria (25 g/day).

It has been postulated that the most important predictive factor for the development of thrombosis in NS is a degree of proteinuria[6,7] at which hepatic synthesis can no longer compensate; this entails an imbalance between coagulation-regulating proteins and fibrinolysis.[8,9] Plasmapheresis would theoretically allow restautration of the balance this imbalance, in addition to removing the postulated permeabilising agent that mediates the podocyte lesion in FSGS. The curious nature of our case lies in the fact that the thrombosis coincided with the performance of plasmapheresis, an observation that we have not found described in the literature.

Several factors may have facilitated the thrombosis. Ultrafiltration can cause haemoconcentration, which may have raised levels of procoagulant factors; this could have promoted the thrombosis by a similar mechanism as in children following dehydration.[10] Replacement of FFP with plasmapheresis provides all the coagulation factors, as well as antithrombotic factors (antithrombin III, proteins C and S), while with 5% albumin we could increase serum albumin levels slightly, and so the thrombotic risk should be reduced.[9] However, we observed that the antithrombin III levels during thrombosis were low; it is therefore possible that plasma infusion in cases of severe NS does not completely restore the coagulation/fibrinolysis imbalance. There is nothing in the literature describing how coagulation factors change after plasma replacement.

Our case provides several interesting and practical reflections. First, should specific preventive anticoagulation be used when plasmapheresis is to be performed in a case of nephrotic syndrome? The dose of LMWH may need to be higher than that normally used if there is no nephrotic syndrome, given the low levels of antithrombin III, coupled with elevated procoagulant factors, plus the loss of LMWH via the kidneys compared with heparin sodium. Antithrombin III levels should be monitored before starting plasmapheresis and after each session, since it may not normalise, despite plasma infusion, as happened in our case. We do not know whether a LMWH with a higher molecular weight or with a longer half-life would be more effective or suitable for preventing venous thrombosis in cases with severe NS.

REFERENCES

1. Chun MJ, Korbet SM, Schwartz MM, Lewis EJ. Focal segmental glomerulosclerosis in nephrotic adults: presentation, prognosis, and response to therapy of the histologic variants. J Am Soc Nephrol. 2004;15:2169–77.
2. Thomas DB, Franceschini N, Hogan SL, Ten Holder S, Jennette CE, Falk RJ, et al. Clinical and pathologic characteristics of focal segmental glomerulosclerosis pathologic variants. Kidney Int. 2006;69:920–6.
3. Mitwalli AH. Adding plasmapheresis to corticosteroids and alkylating agents: does it benefit patients with focal segmental glomerulosclerosis. Nephrol Dial Transplant. 1998;13:1524–8.
4. Haas M, Godfrin Y, Oberauer R, Yilmaz N, Borchhardt K, Regele H, et al. Plasma immunadsorption treatment in patients with primary focal and segmental glomerulosclerosis. Nephrol Dial Transplant. 1998;13:2013–6.
5. Kandus A, Ponikvar R, Buturović-Ponikvar J, Bren AF, Oblak M, Mlinšek G, et al. Plasmapheresis and immunoadsorption for treatment and prophylaxis of recurrent focal segmental glomerulosclerosis in adult recipients of deceased donor renal grafts. Ther Apher Dial. 2013;17:438–43.
6. Kerlin BA, Blatt NB, Fuh B, Zhao S, Lehman A, Blanchong C, et al. Epidemiology and risk factors for thromboembolic complications of childhood nephrotic syndrome: a Midwest Pediatric Nephrology Consortium (MWPNC) study. J Pediatr. 2009;155:105–10.
7. Robert A, Olmer M, Sampol J, Gugliotta JE, Casanova P. Clinical correlation between hypercoagulability and thrombo-embolic phenomena. Kidney Int. 1987;31:830–5.
8. Kanfer A. Coagulation factors in nephrotic syndrome. Am J Nephrol. 1990;10 Suppl 1:S63–8.
9. Rabelink TJ, Zwaginga JJ, Koomans HA, Sixma JJ. Thrombosis and hemostasis in renal disease. Kidney Int. 1994;46:287–96.
10. Ozanne P, Francis RB, Meiselman HJ. Red blood cell aggregation in nephrotic syndrome. Kidney Int. 1983;23:519–25.

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