Resolution of Thrombocytopenia in a Patient with Lupus Anticoagulant Who Received Warfarin Therapy

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Although thrombocytopenia is a characteristic clinical finding in patients with anti-phospholipid antibody syndrome (APAS), neither the etiology nor the treatment of thrombocytopenia is clear [1]. We report the case of a 37-year-old Japanese man with APAS, whose thrombocytopenia was improved by oral warfarin. The patient had experienced multiple cerebral infarctions in 1984, at which time he was found to have thrombocytopenia ($98 \times 10^7/l$) and was given 200 mg/day of ticlopidine without effect on his thrombocytopenia. In 1987, he came to our hospital to consult for his early-onset cerebral infarction and thrombocytopenia. Several assays for lupus anticoagulant (LA), including kaolin clotting time (KCT), tissue thromboplastin inhibition test (TTI), and rabbit brain phospholipid neutralization procedure (RBNP) were performed as previously described [2-4]. Based on the results of these tests, he was diagnosed to have LA and was given mini-dose aspirin (40 mg/day), which was followed by a transient slight increase in his platelet count. In 1988, he developed venous thrombosis of the right lower limb and was thus readmitted to hospital. On admission, clinical and laboratory investigations revealed mild thrombocytopenia ($85 \times 10^9/l$) and mild renal dysfunction (blood urea nitrogen 25 mg/dl and serum creatinine 1.2 mg/dl), but electrolytes and hepatic function were normal. Antinuclear antibody (ANA) and anti-DNA antibody were positive. A false-positive result was obtained on the VDRL test. Anticardiolipin antibody (ACA)-IgG was 48 U/ml (normal < 10), and ACA-IgM was below 5 U/ml (normal < 10). Anti-platelet antibody was negative but platelet-associated IgG (PA-IgG) was slightly elevated (23 ng/10⁷ cells). PT was normal but APTT was prolonged (12.7 and 52.2 s., respectively). Plasma fibrinogen was normal. Antithrombin III, plasminogen, α_2 -plasminogen inhibitor and protein C activity was normal. Although plasma thrombin-anti-thrombin III complex (TAT) and prothrombin fragment 1+2 (F1+2) were slightly elevated (3.8 ng/ml and 1.8 nmol/l, respectively), fibrin/fibrinogen degradation products (FDP), cross-linked fibrin degradation products (XDP), protein S, and plasmin- α_2 -plasmin inhibitor complex (PIC) were normal. The presence of LA was demonstrated by mixing tests based on KCT, the RBNP test, and the TTI test. From these findings, systemic lupus erythematosus (SLE) with APAS was diagnosed. 5 mg/day of warfarin was added to low-dose aspirin for recurrent thrombosis. His platelet count immediately

normalized ($134 \times 10^7/l$) without disappearance of LA or decrease in ACA-IgG, but plasma levels of FI+2 decreased from 2.3 to 0.5 nmol/l.

For the assessment of his renal insufficiency, a renal biopsy was performed without administration of warfarin and aspirin, and his platelet count fell ($89 \times 10^7/l$) following cessation of treatment. After the renal biopsy, the same warfarin and aspirin dosages were reinstituted, resulting in an immediate significant increase in platelet count to $234 \times 10^7/l$; the platelet count has remained stable for 5 years. In December 1993, it was still normal ($253 \times 10^7/l$) although the LA had not disappeared and the ACA-IgG remained at the same level (fig. 1).

The mechanism by which platelet count increased in our patient is not clarified. However, the observations that warfarin decreased plasma TAT and FI+2, sensitive markers of the hypercoagulable state, but remained ineffective on PA-IgG, ACA and LA suggest that the increase in platelet count resulted from the improvement of hypercoagulability and a decline in platelet consumption.

To the best of our knowledge, no other cases in which a reduced platelet count was corrected by warfarin have been reported. The etiology of the resolution of thrombocytopenia is not clear in this case. Further investigations in more patients need to be performed.

Pts ($\times 10^7/l$) 200 A

Cerebral infarction

Diagnosis of Lupus anticoagulant

100-

0-i

*84

Ticlopidine 200mg/day

*85

'86

'87

Aspirin 40mg/day

Ar

"88

Pts

($\times 10^7/l$) 200-

Renal biopsy Occurrence of DVT *

100

Warfarin 5mg/day ·

Warfarin 5mg/day\

Aspirin 40mg/day

Aspirin 40mg/day

Fig. 1. Clinical course and evolution of platelet count. DVT = Deep vein thrombosis.

'88

Nov.

Dec.

'89

Jan.
Feb.
93 Dec.

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