Letters to the Editor
disease and/or platelet activation, and may not participate directly in
pathogenesis. We conclude that raised sP-selectin indicates a poor
prognosis among patients with peripheral artery disease. The wide
range of values means that this marker alone is unlikely to be of value in
defining the risk of disease progression in any individual subject.
However, it may be useful as part of a panel of markers that may in-
clude those suggestive of a pro-thrombotic capacity and endothelial cell
dysfunction. If raised sP-selectin is truly a marker of platelet activa-
tion (8, 9), this may provide a new rationale for developing and using
therapy aimed at the platelet. This preliminary finding may be applic-
table to other forms of atherosclerosis (e.g. stroke), and warrants
further attention in larger groups of patients with more diverse dis-
ease(s).

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References

1. Wu KK. Platelet activation mechanisms and markers in arterial thrombosis.
2. Stenberg PE, McEver RP, Shuman MA, Jacques YV, Bainton DF. A plate-
let alpha granule membrane protein (GMP140) is expressed on the plasma
3. Wagner DD. The Wiebel-Palade body: the storage granule for von Wille-
4. Blann AD, Seigneur M, Boisseau MR, Taberner DA, McCollum CN.
Soluble P-selectin in peripheral vascular disease: relationship to the
location and extent of atherosclerotic disease and its risk factors. Blood
5. Chong BH, Murray B, Berndt MC, Dunlop LC, Brighton T, Chesterman
CN. Plasma P selectin is increased in thrombotic consumptive platelet dis-
Toshima H. Soluble form of P-selectin in patients with acute myocardial
Wagner OF, Eichler HG. Elevated circulating P-selectin in insulin depen-
8. Blann AD, Lip GYH. Hypothesis: Is soluble P-selectin a new marker of
Nieuwenhuis HK. The origin of P-selectin as a circulating plasma protein.
Thromb Haemost 1997; 77: 1081-5.
10. Blann AD, Faragher EB, McCollum CN. Increased soluble P-selectin
following myocardial infarction: a new marker for the progression of
11. Palomaki P, Mietten H. Diagnosis of acute myocardial infarction by
MONICA and FINMONICA. Diagnostic criteria in comparison with
12. Hatan S. Experience from a multicentre stroke register. A preliminary
neutrophil adhesion to endothelium by soluble adhesion protein GMP-140.
Adhesion protein GMP-140 inhibits superoxide anion release by human

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Steroid Hormone-responsive Secondary Factor X Deficiency

Dear Sir,

Although more than 30 cases of secondary factor X deficiency have
been reported, very few cases have been treated successfully. Most of
the incidences accompanied monoclonal gammapathy and amyloidosis
(1), with or without multiple myeloma. We experienced a case of factor
X deficiency with monoclonal gammapathy and progressive muscle
hematoma. We treated the patient successfully with prednisone;
bleeding tendency and partial thromboplastin time improved without
any change in the activities of coagulation factors.

A 65-year old Japanese man was admitted to our department be-
cause of back pain. He had been healthy until 3 years before admission,
when he noticed gingival bleeding and subcutaneous purpura. Three
months before admission, he was hospitalized for lumbargo, macro-
escopical hematuria, and massive epistaxis. Laboratory studies at the prior
hospital revealed prolonged prothrombin time (PT, 34.7 s), activated
partial thromboplastin time (aPTT, 64 s) and a reduced level of
coaagulation factor X (4.5%). Although he was administered a total of
33 units of fresh frozen plasma and 4000 units of a plasma factor IX
preparation, which includes factor X, his clinical and laboratory tests
did not improve. The subcutaneous bleeding and hematoma increased,
and he began to complain of severe back pain. He was referred to our
department for diagnosis.

On physical examination, the patient was anemic, with two solid
surface bosalettes in the lumbar-gluteal region and bilateral sub-
cutaneous purpura in the anterior femoral region. His liver was
palpable 4 cm below the right costal margin, but his spleen was not
palpable. His lower limbs showed limited movement because of lumbar
pain. Chest X-ray was normal. Slight splenomegaly and moderate
hepatomegaly were detected by CT.
Laboratory tests revealed the following: hemoglobin, 6.8 g/dl; hematocrit, 22%; platelets, 164000/mm³; and leukocytes, 9000/mm³. Serum urea nitrogen, creatinine, sGPT, lactic dehydrogenase, γ-GTP, and haptoglobin were within normal limits. The alkaline phosphatase level was 623 IU/l (normal, 118-325 IU/l) and the sGOT level was 42 IU/l (normal, 13-29 IU/l). Direct Coomb’s test was negative, and C-reactive protein concentration was 6.3 mg/dl. The PT was 26.9 s (20%), and the aPTT was 61.6 s (normal; 26.2-39.3 s). Coagulation factor X activity was 12%, and the amount of factor X was less than 10% of normal; other coagulation factor (II, V, VII, VIII, IX, XI, XII) activities were not reduced. Mixing studies for circulating anticoagulant were negative, and anticoagulant antibodies could not be demonstrated. Coagulation factors in the patient’s family members were normal. Serum protein electrophoresis revealed an increase in the β- to γ-fraction. Quantitative immunoglobulin determination and immunoelectrophoresis disclosed the following: IgG, 1159 mg/dl (normal, 788-1841 mg/dl); IgA, 1801 mg/dl (normal, 77-437 mg/dl); IgM, 480 mg/dl (normal, 78-552 mg/dl). Serum immunoelectrophoresis revealed IgA κ-type M-protein and urine immunoelectrophoresis revealed κ-type Bence-Jones protein. Bone marrow aspiration disclosed hypocellular marrow with slightly increased (5%) plasma cells without monoclonality. Amyloid deposits were not detected in bone marrow aspirate, rectum, skin, gingiva, or subcutaneous fat tissue. Thus, we diagnosed the patient as having a secondary factor X deficiency with monoclonal gammopathy.

From the first hospital day, the patient was treated with prednisone 60 mg/day, which resulted in rapid improvement in the bleeding tendency. On the third hospital day, his aPTT and PT were shortened to 42.3 s and 24.4 s, respectively (Fig. 1), although the activity of all coagulation factors remained the same. C-reactive protein decreased rapidly and became normal in 2 weeks. The anemia and hematoma improved, and the prednisone was tapered. However, when the dose of prednisone was reduced to 10 mg/day, he showed gingival bleeding and aPTT prolonged to 53.5 s. The dose of prednisone was increased to 60 mg/day and the bleeding tendency, aPTT, and PT again improved. The dose of prednisone was carefully decreased over 40 days and maintained at 15 mg/day. Plasma IgA concentration gradually decreased to 1383 mg/dl and remained approximately the same thereafter. At present, the patient is under close observation as an outpatient, remains on 15 mg prednisone, and is without signs of bleeding.

Our patient developed hematuria and anemia very rapidly, and immediate treatment was required. Since the factor X complementation treatment was not effective, we treated the patient with prednisone, assuming the presence of a circulating inhibitor or antibody against factor X (2) before realizing the presence of the monoclonal gammopathy. The subsequent treatment improved the bleeding tendency; however, we could not demonstrate the inhibitor to factor X in his plasma or urine by laboratory tests such as Western blotting. The reason why aPTT and PT responded to prednisone is unknown. All the coagulation factors remained unchanged throughout the clinical course, including the low plasma factor X level, even after normalization of aPTT. This phenomenon suggests that some unknown steroid-inducible factor might exist as a component or cofactor in the blood coagulation cascade or independent from the cascade. This might explain the hypercoagulability sometimes found in steroid-treated patients. There have been several reports of secondary factor X deficiency, most of which accompany amyloidosis. Only Manabe et al. (3) have described a patient with factor X deficiency and monoclonal gammopathy, and the etiology of factor X deficiency accompanying monoclonal gammopathy has not been determined.

The therapeutic plan for our patient is still under discussion, i.e., whether to employ an additional agent such as melphalan or to treat the patient surgically (4). Fortunately, prednisone treatment did improve the bleeding tendency. However, due to the adverse effect of the treatment, the patient suffered from steroid-induced diabetes mellitus, which is now under control with insulin injection, and he is also at a high risk for osteoporosis. The prognosis in such cases is generally poor, since patients frequently develop systemic amyloidosis or multiple myeloma. Only two cases have been reported that resulted in spontaneous resolution after cessation of melphalan-prednisone therapy (5, 6). We hope that our patient’s monoclonal gammopathy improves spontaneously, and that steroid therapy can be discontinued.

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References


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