

Lupus anticoagulant-hypoprothrombinemia in healthy adult

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The presence of lupus anticoagulant is associated with an elevated risk of venous and arterial thrombosis, and recurrent miscarriages as well. For some cases, this disease can present with bleeding as a consequence of lupus anticoagulant-hypoprothrombinemia (LAHPS). LAHPS is a rare disease and it is reported to be most frequent in young females with/without systemic lupus erythematosus or in healthy children who are suffering with a viral infection. In such cases, steroid therapy is usually effective in normalizing the biological abnormalities and controlling the bleeding problems.

A 34-year-old previously healthy man was admitted to our department because of his prolonged coagulation times; these abnormalities were discovered before performing orthopedic surgery. The prothrombin time (PT) was 15.2 sec, and the activated partial thromboplastin time (APTT) was 37.7 sec. A 1:1 dilution of patient plasma with normal plasma nearly corrected the PT, but this failed to correct the APTT. Evaluation of the clotting factors revealed decreased levels of factors II, V, VIII, IX and XI. The presence of LA was demonstrated by the dRVVT test, and the patient was diagnosed with LAHPS. He was successfully treated with corticosteroid before performing the orthopedic surgery.

Key Words: Lupus anticoagulant; Bleeding; Hypoprothrombinemia

INTRODUCTION

The most common clinical presentation of patients with lupus anticoagulant antibody is arterial or venous thromboembolism¹⁾. Hemorrhage is much less common and this is usually attributable to the associated thrombocytopenia, a platelet dysfunction, a prothrombin deficiency or other underlying coagulopathies^{2,3)}. Lupus anticoagulant-hypoprothrombinemia (LAHPS) is a rare syndrome. In many cases, steroid is required to treat patients' hemorrhages, and steroid has been noted to promptly correct the hypoprothrombinemia and control bleeding events⁴⁾.

Herein, we report on a 34-year-old previously healthy man with LAHPS. He was referred to our hospital because of his prolonged coagulation time, which was discovered during his lab work-up for an orthopedic operation. The laboratory studies showed LAHPS with microscopic hematuria; however, any viral

infection or other systemic disease was not found. He was successfully treated with corticosteroid before undergoing orthopedic surgery.

CASE REPORT

A 34-year-old-man was admitted to another hospital for an orthopedic operation. The coagulation studies showed a prolonged prothrombin time (PT) and an activated partial thromboplastin time (APTT). He was treated with fresh frozen plasma, but without success. After 2 weeks, the patient was referred to our hospital. He was not taking any medication, and especially, any anticoagulant and antiplatelet agents. He had no personal or family history of any bleeding disorder. The physical examination was non-specific except for signs of ligament

•Received: November 3, 2006

•Accepted: February 9, 2007

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*This study was supported by research funds from Chosun University, 2006

Table 1. Results of the Serial Coagulation Studies and the Treatment

	28 Oct 04	16 Dec 04	27 Dec 04	10 Jan 05	23 Feb 05
PT (sec)	15,2	12,2	10,7	10,9	12,5
APTT (sec)	37,7	26,9	23,2	23,5	28,6
Factor II (%)	29	67		92	
Factor V (%)	24	62		81	
Factor VII (%)	82	113		114	
Factor VIII (%)	3,4	49		81	
Factor IX (%)	5,8	51		103	
Factor X (%)		104		98	
Factor XI (%)	1,2	31		78	
Factor XII (%)		108		91	
Prednisone (mg/day)	-	60	40	30	-

The date of administering prednisone: 8 Dec 04

rupture. The initial laboratory tests showed a leukocyte count of $8,200/\text{mm}^3$, a hemoglobin of 14.7 g/dL and a platelet count of $226,000/\text{mm}^3$. The PT was 15,2 sec (normal values (NV): 10,0-13,0 sec), the APTT was 37,7sec (NV: 27,5-34,7 sec). Evaluation of the clotting factors revealed decreased levels of factors II, V, VIII, IX and XI (Table 1). A 1:1 dilution of patient plasma with normal plasma nearly corrected the PT, but this failed to correct the APTT. The diluted Russell's viper venom time (dRVVT, American Diagnostica,) was positive. The anticardiolipin antibodies IgG and IgM were positive. The tests for antinuclear antibodies and anti-double stranded DNA antibodies were negative; the C3 and C4 complement levels were low. The patient denied any symptoms that would be suggestive of SLE, and there was no family history of bleeding or connective tissue disease. An extensive infectious disease workup ruled out hepatitis A, B and C, cytomegalovirus and Epstein-Barr virus. Finally, we diagnosed the patient as having lupus anticoagulant-hypoprothrombinemia (LAHPS). However, he displayed only microscopic hematuria and he was without SLE or any underlying disease. So, we closely followed the patient's laboratory findings and clinical symptoms for 2 months. He did not show any symptoms or signs of bleeding, yet the abnormal laboratory findings were sustained. We decided to try corticosteroid treatment to prepare the patient for orthopedic surgery and then 2 weeks later, the coagulation studies were significantly improved. He successfully underwent the operation and was discharged. At present, he hasn't any symptoms or signs of thrombosis, hemorrhage and SLE.

DISCUSSION

Lupus anticoagulant (LA) is an antiphospholipid antibody that causes prolonged in vitro coagulation times. This may be associated with a hypercoagulable state together with thromboembolic events¹. A bleeding diathesis is a rare manifestation

of lupus anticoagulant, and when it occurs, it was nearly always due to thrombocytopenia or Factor II deficiency^{2, 3}.

Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare clinical malady that can occur in association with SLE, transient viral infections, drug reactions or even in healthy individuals^{5, 6}. It mostly occurs in young females, and only rarely in those adults who are without systemic lupus erythematosus, an underlying disease or a preceding illness².

The clinical findings are generally asymptomatic, but there can be severe hemorrhagic symptoms such as brain hemorrhage, gastrointestinal bleeding and diffuse muscular hemorrhage. These patients may present with severe life threatening bleeding diathesis if the Factor II level is very low (i.e., usually under 10%)². In our case, the Factor II level was 29% and only microscopic hematuria was observed.

Simel et al. have reported on a case of LAHPS for which the patient did not respond to replacement therapy, and the patient showed a significant response to immunosuppressive drugs⁷. Most of the cases previously reported in the literature have responded well to administering only prednisone treatment⁴. A few cases needed an additional immunosuppressive drug such as cyclophosphamide or azathioprine^{7, 8}. Corticosteroid therapy is the treatment of choice for LAHPS associated with SLE; it normalizes the abnormal coagulation times, including the PT, the APTT and the clotting factors. For those cases associated with viral infection, the LAHPS spontaneously reverses itself when the infection has been resolved, and so steroid therapy is not necessary. Our patient had only microscopic hematuria without SLE or any underlying disease. Therefore, we followed up the laboratory findings and clinical symptoms for 2 months; during this time, he did not display any symptoms and signs of bleeding. However, the abnormal laboratory findings were sustained. We decided to institute corticosteroid treatment for getting him ready for orthopedic surgery; 2 weeks later, the coagulation studies were significantly improved. He successfully received the operation and was discharged. At present, he has

no signs or symptoms of thrombosis, hemorrhage and SLE. Prompt, close follow up of these patients is crucial because they may develop, at any time, the full clinical syndrome of SLE and thrombosis because of the presence of LA.

REFERENCES

- 1) Cuadrado MJ, Hughes GR. *Hughes (antiphospholipid) syndrome: clinical features*. *Rheum Dis Clin North Am* 27:507-524, 2001
- 2) Vivaldi P, Rossetti G, Galli M, Finazzi G. *Severe bleeding due to acquired hypoprothrombinemia-lupus anticoagulant syndrome: case report and review of literature*. *Haematologica* 82:345-347, 1997
- 3) Bernini JC, Buchanan GR, Ashcraft J. *Hypoprothrombinemia and severe hemorrhage associated with a lupus anticoagulant*. *J Pediatr* 123:937-939, 1993
- 4) Hift RJ, Bird AR, Sarembok BD. *Acquired hypoprothrombinemia and lupus anticoagulant: response to steroid therapy*. *Br J Rheumatol* 30:308-310, 1991
- 5) Follea G, Coiffier B, Viale JP, Dechavanne M. *Antiprothrombinase and factor II deficiency in a non SLE patient*. *Thromb Haemost* 46:670, 1981
- 6) Bajaj SP, Rapaport SI, Fierer DS, Herbst KD, Schwartz DB. *A mechanism for the hypoprothrombinemia of the acquired hypoprothrombinemia-lupus anticoagulant syndrome*. *Blood* 61:684-692, 1983
- 7) Simel DL, St Clair EW, Adams J, Greenberg CS. *Correction of hypoprothrombinemia by immunosuppressive treatment of the lupus anticoagulant-hypoprothrombinemia syndrome*. *Am J Med* 83:563-566, 1987
- 8) Lillquist KB, Dyerberg J, Krogh-Jensen M. *The absence of Factor II in a child with systemic lupus erythematosus*. *Acta Paediatr Scand* 67:533-536, 1978