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A Case of HELLP Syndrome Positive for Anticardiolipin Antibody

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Summary. **We encountered a patient with typical HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) who was positive for anticardiolipin antibody and antinuclear antibody and showed a significantly prolonged activated partial thromboplastin time. This report describes the clinical course of this patient together with the involvement of various autoimmune abnormalities such as positive anticardiolipin antibody in the genesis of HELLP syndrome.**

Key words—anticardiolipin antibody, HELLP syndrome, preeclampsia.

INTRODUCTION

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count), a serious complication of pregnancy, is a multisystem disease form of severe preeclampsia-eclampsia that is characterized by microangiopathic hemolytic anemia, hepatic dysfunction, and thrombocytopenia.[1-3] There are several studies available on the diagnosis and management of HELLP syndrome using a large number of patients;[3,4] there is also a detailed report on the natural history of HELLP syndrome.[5]

The presence of HELLP syndrome is usually recognized by clinical signs and symptoms of hepatic involvement such as epigastric pain, right upper-quadrant tenderness, nausea, vomiting, and malaise. Subsequent laboratory examinations can readily ascertain its diagnosis when the HELLP syndrome occurs in patients with severe preeclampsia. The etiology of HELLP syndrome, however, has not yet been fully elucidated. We here report a case with HELLP syndrome which was positive for anticardiolipin antibody, showing a prolonged activated partial thromboplastin time (APTT) which suggests the existence of lupus anticoagulant.

Recently, autoimmune factors such as antiphospholipid antibodies and lupus anticoagulant have come to be considered etiologic factors for preeclampsia, which has a strong correlation with HELLP syndrome.[6-9] In this context, the clinical course of this patient is described mainly from the viewpoint of autoimmune abnormalities.

CASE REPORT

A 27-year-old primiparous woman was referred to the obstetric ward of Niigata University Hospital on April 19, 1991 with symptoms of epigastralgia, nausea and vomiting and abnormal laboratory findings of elevated liver enzymes and a low platelet count. She was at 33 weeks of gestation and presented no obvious symptoms of preeclampsia. The laboratory data at admission were as follows: platelet count, 3.1×10^4/cmm; GOT, 231 IU/ml; and GPT, 160 IU/ml. Concerning autoimmune examinations, the antinuclear antibody titer was 1: 40 with a speckled staining pattern, and anticardiolipin antibody was 4.24 S.D. (cut-off value; 3.0 S.D.) as measured by a previously reported method of examination.[10] APTT was 48.1 sec (control : 30.0 sec). Ultrasonographic examination revealed a growth retarded fetus with a score of eight points on the biophysical profile scale by Manning's method.[11] Gastrointestinal fiberscopy revealed findings of an acute duodenal mucosal lesion (ADML) accompanied by mucosal edema and redness which was considered to be generated by the thrombosis of a

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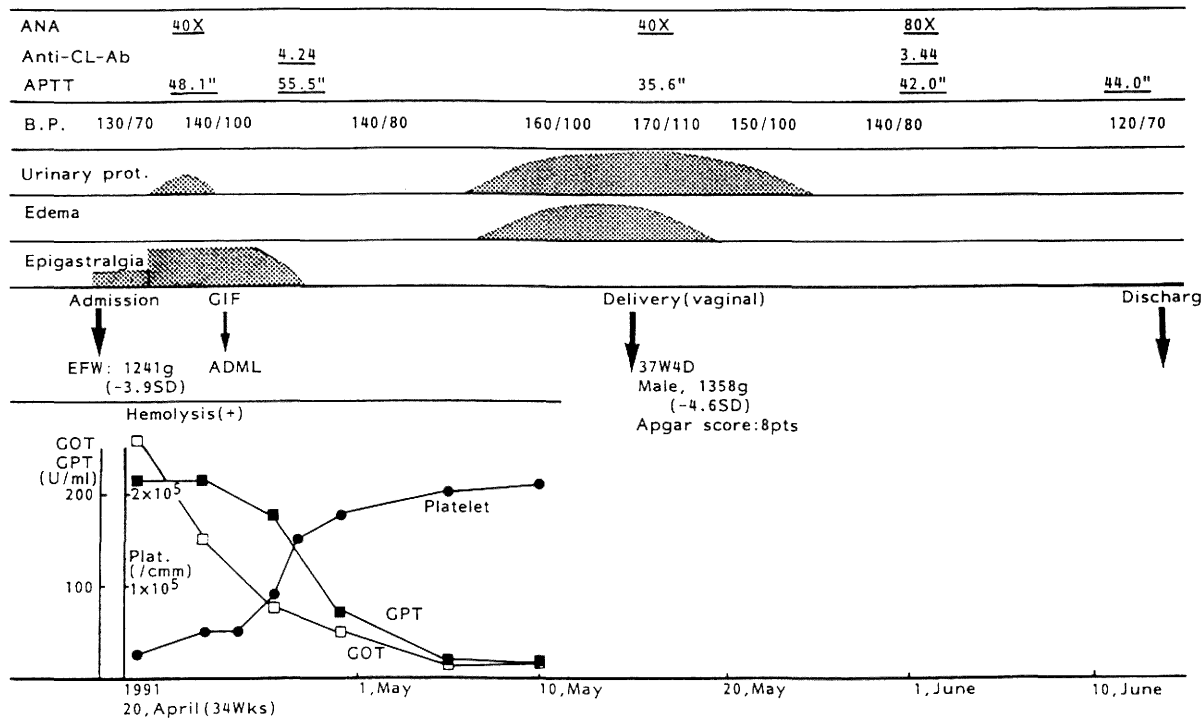

Fig. 1. This figure summarizes the clinical course in this patient. The abbreviations used are as follows: ANA, antinuclear antibody; Anti-CL-Ab, anticardiolipin antibody; APTT, activated partial thromboplastin time; B. P., blood pressure; urinary prot., urinary protein; EFW, estimated fetal body weight; GIF, gastrointestinal fiberscopy, ADML, acute duodenal mucosal lesion. The closed circles represent the number of platelets, the open squares the GOT values, and the closed squares the GPT values. The height of the shaded areas indicates the relative intensity of the symptom. The underlined values of ANA, Anti-CL-Ab and APTT are abnormal values.

feeding artery. Famotidine and perenzepin hydrochloride were used to improve the ADML. Gabexate methylate was also used for suspected thrombosis which was considered to have generated the lesion of the duodenal mucosa. Hemolysis was diagnosed based on the observation of burr cells detected by peripheral blood smear test and elevated serum bilirubin. The symptoms of preeclampsia gradually became manifest (systolic blood pressure and diastolic higher than 170 mmHg and 110 mmHg, respectively, with urinary protein excretion of more than 3.0 g/day), while the symptoms of ADML disappeared and the features of HELLP syndrome improved (Fig. 1). She vaginally delivered a male infant weighing 1358 g (−4.6 S.D. compared with the general mean body weight) in the 37th week of gestation. The offspring presented no major anomalies and his neonatal and infantile course was uneventful with intensive care. The mother's hypertension and proteinuria spontaneously disappeared during the puerperal period, but positivity for anticardiolipin antibody and prolonged APTT persisted throughout the clinical course.

DISCUSSION

In 1982, HELLP syndrome was first described by Weinstein, who presented the clinical course of 29 cases with preeclampsia-eclampsia with the finding of hemolysis (H), elevated liver enzymes (EL), and a low platelet count (LP).[1] Sibai et al. reported the incidence and effects of serious obstetric complications on maternal outcome in pregnancies complicated by HELLP syndrome by analyzing 442 patients; 1.1% maternal mortality rate and a high incidence of disseminated intravascular coagulation (DIC) (21%), abruptio placentae (16%), and acute renal failure (7.7%) were noted in the same report.[4] To date, it is well recognized that HELLP syndrome is a multisystem disease form with severe preeclampsia-eclampsia that is characterized by microangiopathic hemolytic anemia, hepatic dysfunction and thrombocytopenia and which, in the most severe cases, progresses to DIC.[2-5] Although the pathophysiology and the diagnosis of HELLP syndrome were well documented, its

etiology has not yet been fully elucidated.

Our patient showed hemolysis, elevated liver enzymes, and a low platelet count to lead us to consider this case a typical one of HELLP syndrome. Although the severe upper abdominal pain is by far the most striking clinical symptom in HELLP patients, its cause has remained unclear in almost all cases. In this patient, however, an acute duodenal mucosal lesion detected by gastrointestinal fiberscopy was considered to be the cause of the abdominal pain. One very interesting finding in this case was the positive result for autoimmune tests, specifically positive antinuclear antibody, positive anticardiolipin antibody and prolonged APTT. Recently, various autoimmune abnomalities such as positive antiphospholipid antibodies or lupus anticoagulant have been suspected to be implicated in the genesis of preeclampsia and intrauterine fetal growth retardation.[6-8] We disclosed the close relationship between the anticardiolipin antibody and the manifestation of severe preeclampsia in a prospective study of 860 pregnant women.[9] It has also been reported that patients with lupus anticoagulant or antiphospholipid antibodies are at increased risk for thrombotic episodes, and patients revealing a low platelet count, generalized thrombosis, and recurrent fetal wastage with positive antiphospholipid antibodies have been recognized as "antiphospholipid syndrome".[12]

The mechanisms of the generation of thrombosis by antiphospholipid antibodies or lupus anticoagulant have not yet been elucidated, but the proposal with the most empirical suport involves the inhibition of prostacyclin production.[13] A relative increase of thromboxane A2, which is a natural antagonist of prostacyclin, might promote vasoconstriction and platelet aggregation and induce hypertension and local production of thrombosis. The diverse symptoms manifested by this patient, such as preeclampsia, IUGR (intrauterine growth retardation) and ADML might be explained by the function of antiphospholipid antibodies and lupus anticoagulant.

Although the possibility of the involvement of antiphospholipid antibodies in the genesis of HELLP syndrome was pointed out by Gleicher in a discussion of an article by Martin et al.,[5] the obvious involvement of such autoimmune factors is yet unclear. In this context, the examination of the autoimmune background in patients with HELLP syndrome will prove important to elucidate the etiology.

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