Systemic Lupus Erythematous Associated with Extreme Hypertriglyceridemia

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1. Introduction

The concept of autoimmune hyperlipidemia was first proposed by Beaumont in the 1970s.¹,² Only rarely were patients with systemic lupus erythematosus (SLE) reported to develop various types of hyperlipoproteinemia such as type I,³–⁵ type IIB,⁴ type III,⁶ and type V.⁷,⁸ Types I and V hyperlipoproteinemia are associated with a decrease in the ability of lipoprotein lipase (LPL),⁹ which is expressed in the parenchymal cells of several extrahepatic tissues, to hydrolyze the triglycerides (TG) transported in chylomicrons and very-low-density lipoproteins. Several reports have shown that LPL deficiency generally results from gene mutations that may affect physiological activator of LPL.¹⁰,¹¹ In comparison, acquired LPL deficiency is extremely rare.¹²

In this report, we present a girl with SLE complicated with severe hypertriglyceridemia. The persistent hypertriglyceridemia was extremely well tolerated. As a result of steroid treatment, serum triglycerides fell dramatically from a peak of 5601 mg/dL to 75 mg/dL despite the patient switching to a free diet. We considered the presence of an autoantibody to LPL and commenced immunosuppression.

2. Case Report

A 13-year-old girl came to the Ren-Ai Branch of Taipei City Hospital in July 2006 because of newonset low-grade fever (38.0–38.5°C) of 1 week’s duration. Before that, she had gone to the beach in South Taiwan with her family. Due to the scorching sun, she had started to feel uncomfortable.

The patient was 158 cm tall and weighed 44 kg. Blood pressure and heart rate were within normal
ranges. Physical examination revealed butterfly erythema on her cheeks. The erythema had appeared and gradually worsened after the trip to the beach. She also had tenderness and mild bulging over bilateral elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, knees, ankles and the soles of her feet. Laboratory examination revealed pancytopenia (white blood cell count, 3610/µL; red blood cell count, 3.70 × 10⁶/dL; hemoglobin, 13.1 g/dL; hematocrit, 30.9%; platelet count, 114,000/µL). Serologically, antinuclear antibody (2560-fold, homogeneous pattern) and anti-dsDNA antibody (640-fold) were found. All these symptoms and laboratory results met the criteria for SLE according to the American Rheumatism Association. Serum levels of complements did not decrease (C3, 139 mg/dL). Urinalysis results were + for occult blood and negative for proteinuria; the sediment contained 6–8 red blood cells with 0–1 white blood cells per high-powered field. Thyroid, liver and kidney function tests were all normal.

However, chylomicronemia was found on routine biochemical study, and so the patient’s lipoproteins were checked. The results showed that fasting TG was a stunning 3240 mg/dL and cholesterol was 211 mg/dL. Despite the surging numbers, she did not feel any discomfort. In addition, bouts of abdominal pain, xanthomas and hepatomegaly were not detected. The result of ultrasound examination showed normal, but mildly fatty, liver. On the agarose gel electrophoresis of serum lipoproteins, the pre-β and chylomicron fractions were increased (67.9%, normal range 8–29%; 3.1%, normal range 0%, respectively). After being stood in the cold for 24 hours, the plasma contained a creamy layer over a turbid infranatant layer. According to the Fredrickson classification, the patient’s lipoprotein phenotype was type V hyperlipoproteinemia, suggesting defective lipolysis. Her father had mild hypercholesterolemia, but no other abnormalities were present in the family. Secondary causes of hypertriglyceridemia were excluded at the first examination and in the following 3 months, such as hyperglycemia, pregnancy, hypothyroidism and excess dietary fat or alcohol. The presence of an autoantibody to LPL was suspected, and so immunosuppression was commenced. Oral prednisolone (0.7 mg/kg/day) and hydroxychloroquine were started. Fever, erythemas, joint symptoms, pancytopenia and microscopic hematuria abated within a week, but serum TG remained high (3678 mg/dL). The patient was placed on a low-fat diet and followed-up in the outpatient clinic with the speculation of LPL deficiency due to an autoimmune process. We had even reduced the steroids and added a hypolipidemic drug (atorvastatin calcium) for fear of exacerbating her hypertriglyceridemia. However, the dose of steroids had to be increased due to deteriorating hypertriglyceridemia. As a result, serum TG fell dramatically from the peak of 5601 mg/dL to 75 mg/dL (Figure 1), despite the patient having been switched to a free diet. At the same time, serum cholesterol level also decreased and returned to normal (Figure 2). Hypolipidemic drugs were continued until the hypertriglyceridemia was corrected. Prednisolone was tapered to the present dose of 0.05 mg/kg/day. After a few months, TG continues to be within the normal range, and her body weight is 50 kg.

3. Discussion

There have been several previous SLE patients with hyperlipidemia. However, our patient is only the third case of type V hyperlipoproteinemia. To our knowledge, her hypertriglyceridemia was the

![Figure 1](image-url) Following medication with steroids, serum triglyceride level decreased to normal. Since the dose of steroids was tapered, there was no rebound in triglyceride level during several months. *Between August 13 and 16, steroids were reduced to 10 mg/day and a hypolipidemic drug was added for fear of exacerbating hypertriglyceridemia, but steroid dose had to be increased due to deteriorating hypertriglyceridemia.
highest, without any other symptoms, of all existing cases. Previously, hypertriglyceridemia was found prior to the diagnosis of SLE, but this case is the only exception. It is suspected that the patient already suffered from hyperlipidemia but it had not been diagnosed. Paucillo et al reported a hypolipidemic effect of glucocorticoid therapy in a patient with lupus erythematosus.5 In our case, hypolipidemic drugs had no obvious effect. The resurging triglyceridemia due to a reduction in the dose of steroids and the improvement after reintroduction of immunosuppressive therapy strongly suggests an autoimmune origin of this patient’s hypertriglyceridemia.

Borba et al reported that SLE patients had disorders in lipoprotein metabolism, and their LPL activities were nearly half of those of a control group.10 It is also suggested that SLE patients have a lipid profile abnormality that is aggravated by disease activity. The connection between SLE and LPL deficiency has been long debated. Falko et al detected an inhibitor to LPL in the plasma of two SLE patients.4 Kihara et al reported the presence of immune hyperlipoproteinemia caused by autoantibodies against LPL in a patient with idiopathic thrombocytopenic purpura and Grave’s disease.11 Thus, it is supposed that the LPL deficiency in SLE patients is caused by a similar autoimmune process. Pruneta et al identified the presence of an IgG directed against LPL in an autoimmune type I hyperlipidemia patient.12 In vitro, this IgG dramatically reduced the LPL-mediated lipolysis of TG, thereby demonstrating the putative role of this autoantibody in the development of autoimmune hyperlipidemia. In addition to autoantibody formation, inflammation may induce other mechanisms that result in the elevation of TG in SLE patients. Tumor necrosis factor-α, interleukin-1 and interferon-γ have all been shown to decrease LPL enzymatic activity. In lupus patients, there is a strong positive correlation between tumor necrosis factor-α and plasma TG.

Nakane et al supposed that SLE-induced hypertriglyceridemia might be caused by two conditions:8 immunologic damage to vascular endothelium resulting in an inability to synthesize the LPL protein; and presence of an IgG heparin-binding globulin inhibiting the release of LPL on administration of heparin from the vascular endothelium. However, the precise mechanism of the relation between SLE and hypertriglyceridemia is not known and remains to be elucidated in further studies.

References


