

Two Cases of Type V Hyperlipoproteinemia and Eruptive Xanthomas associated with Diabetes Mellitus

Hyun Jin Mo, M.D., Jong Yuk Yi, M.D., Chul Jong Park, M.D., Hyun-shik Son, M.D.*

Departments of Dermatology and Internal Medicine, Uijongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Uijongbu, Korea.*

We report two cases of type V hyperlipoproteinemia and eruptive xanthomas associated with diabetes mellitus in a 44-year-old woman and a 25-year-old woman. They had asymptomatic, diffuse, erythematous yellowish papules on the extremities and buttocks. The laboratory studies showed increased serum blood glucose, total cholesterol, triglyceride, increasing pre- β and chylomicron bands on electrophoresis of lipoprotein. Histopathologic findings of erythematous yellowish papules on the thigh and buttock revealed aggregation of foam cells in the dermis. They have been treated with diet control, hypoglycemic agent (gliclazide) and hypolipidemic drug (gemfibrozil), and are under continued supervision.

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Hyperlipoproteinemia is a disorder that abnormal accumulation of lipoproteins in the plasma results from excessive production, defective removal or decrease in catabolism of lipoproteins, or a combination of both mechanisms¹. The disorder may be seen either as primary manifestation of specific genetic disorders or as an associated phenomenon secondary to specific underlying diseases, such as diabetes, biliary cirrhosis, hypothyroidism, or pancreatitis¹. Xanthomas are usually cutaneous clues to these disorders, although they may be attributable to other disorders². Since 1970 WHO classification³ of hyperlipoproteinemia into six types on the basis of electrophoretic patterns has been used. Type V hyperlipoproteinemia results from the accumulation of triglyceride (TG)-rich lipoproteins, very

low-density lipoproteins (VLDL) and chylomicrons^{3,5}. To our knowledge, one case of type V hyperlipoproteinemia and eruptive xanthomas associated with diabetes mellitus has been reported in the Korean literature⁶. Herein we report two additional cases of type V hyperlipoproteinemia and eruptive xanthomas secondary to diabetes mellitus in a 44-year-old woman and a 25-year-old woman.

CASE REPORTS

Case 1.

A 44-year-old woman presented with asymptomatic, multiple, progressive, yellowish papules on the elbows and buttocks for 1 month (Fig. 1A). Her past medical history was not contributory. In family history, her brother had a history of diabetes mellitus and no hyperlipoproteinemia. On laboratory studies, complete blood cell count was normal, but blood chemistry revealed that fasting blood sugar was 168mg/dL (normal range, 70 to 110mg/dL), total cholesterol 890mg/dL (normal range, 120 to 220mg/dL), triglyceride 3550mg/dL (normal range, 30-160mg/dL), HDL-cholesterol 35mg/dL (normal range, 30-70mg/dL). Electrophoresis of lipoproteins revealed increased pre-beta and chy-

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Reprint request to : Jong Yuk Yi, M.D. Dep. of Dermatology Uijongbu St. Mary's Hospital The Catholic University of Korea

65-1, Kumoh-dong, Uijongbu, Kyonggi-do, 480-130, Korea

Tel. (031) 820-3123, Fax. (031) 846-4799

Fig. 1. Case 1. Diffuse, yellowish papules on the buttock(A) and lipoprotein electrophoresis : increased pre-beta and chylomicron bands(B).

lomicron bands and no “floating beta band” (Fig. 1B). The pattern of this lipoproteins is typical for type V hyperlipoproteinemia according to WHO classification³. A biopsy specimen from the buttock showed the characteristics of xanthomas (Fig. 2). After 3 months of treatment with diet control, oral hypoglycemic agent (gliclazide), and hypolipidemic drug (gemfibrozil), the serum glucose and triglyceride were reduced to near normal level.

Fig. 2. Case 1. Large clusters of foam cells throughout the dermis(H & E stain, $\times 400$).

Fig. 3. Case 2. Erythematous papules on the lower extremities(A) and increasing pre-beta and chylomicron bands on electrophoresis of lipoprotein(B).

The skin lesions of the elbows and buttocks showed a marked improvement.

Case 2.

A 25-year-old woman presented with asymptomatic, diffuse, small, erythematous to brownish papules on both lower extremities and buttocks for 9 months (Fig. 3A). In past history, she had had a 2-year history of diabetes mellitus and had been treated with diet control and hypoglycemic agent (gliclazide). There was no specific family history. The laboratory findings showed serum blood glucose was 252mg/dL, total cholesterol 319mg/dL, triglyceride 1702mg/dL. There were increasing pre-beta and chylomicron bands on electrophoresis of lipoprotein (Fig. 3B). This pattern was also suggestive of type V hyperlipoproteinemia³. Histopathologic findings of the thigh lesion revealed large clusters of foam cells in the dermis but no Touton type giant cells. After 2 months of additional treatment with hypolipidemic agent (gemfibrozil), the serum level of glucose was 159mg/dL and that of triglyceride was 854mg/dL. She had mild improvement of the skin lesions of the legs and buttocks.

DISCUSSION

Hyperlipoproteinemia is a disorder that abnormal accumulation of lipoproteins in the plasma occurs¹. According to WHO³ classification, the disorder is divided into six types on the basis of electrophoretic patterns: type I, excess chylomicrons; type IIa, excess β -lipoproteins (low-density lipoproteins, LDL); type IIb, excess β -lipoproteins with slightly elevated VLDL; type III, increased intermediate-density (remnant) lipoproteins; type IV, increased pre β -lipoproteins (VLDL); type V, increased pre β -lipoproteins and chylomicrons². Type V hyperlipoproteinemia is due to accumulation of TG-rich lipoproteins, VLDL and chylomicrons^{3,5}. This pattern has now been recognized with a variety of conditions, including alcoholism, uncontrolled diabetes, nephrosis, hypothyroidism. In all of these instances type V hyperlipoproteinemia is considered "secondary" and the plasma lipoprotein pattern returns to normal if the underlying disorder is successfully treated^{1,5}. However, in some cases that no underlying cause is found, they are considered as "primary" type V hyperlipoproteinemia³. In our cases, type V hyperlipoproteinemia was considered

"secondary" associated with uncontrolled diabetes mellitus. Clinical features of type V hyperlipoproteinemia include eruptive xanthomas, episodes of abdominal pain, peripheral neuropathy, and emotional lability⁵. Our patients were showing eruptive xanthomas and no abdominal pain, peripheral neuropathy, emotional lability. Xanthomas are composed of masses of lipid-containing histiocytes forming papular, nodular, and plaque-like lesions in the skin, tendons, and sometimes internal organs¹. Xanthomas are important clinical findings as they often evolve in the presence of elevated blood lipids, lipoproteins, atherosclerosis, and fatal cardiovascular disease¹. As shown in our patients, eruptive xanthomas are discrete yellow-orange to reddish brown papules with white centers often surrounded by a red halo which appear in crops over the entire body^{1,2,4}. Buttocks, flexor surfaces of the arms and thighs, knees, inguinal and axillary fold, and oral mucosa are various favored locations². These occur in association with markedly elevated triglycerides^{1,2,4}. In our patients, plasma triglyceride of one case was 3550mg/dL and that of the other case was 1702mg/dL when eruptive xanthomas developed.

The diagnosis of type V hyperlipoproteinemia relies on clinical examination and appropriate laboratory measurements⁴. Lipids and lipoproteins should be measured in the fasting state. If hypertriglyceridemia is present, lipoproteins should be measured by ultracentrifugation or serum lipoprotein electrophoresis⁴. If type III hyperlipoproteinemia is excluded, plasma stored overnight at 4°C showing creamy layer overlying a turbid infranatant layer is diagnostic³. Type V pattern may be imitated in two situations. One is a type I pattern with enough VLDL to impart faint turbidity to the infranatant layer. The Chol/TG ratio is usually below 0.15 in type I and usually above this in type V. The other situation is type III. Here the Chol/TG ratio is often close to 1 but may be as low as 0.3³. In our cases, type I and III hyperlipoproteinemia were excluded in that the Chol/TG ratio was 0.25 of one case, 0.19 of the other case, and both the cases showed increasing pre- β and chylomicron bands on the electrophoresis, and creamy layer overlying a turbid infranatant layer on the stored plasma overnight at 4°C.

The management of patients with type V hyperlipoproteinemia consists of weight reduction, very

low fat diet (<10 percent of total calories as fat) and medication to lower TG levels in an effort to prevent pancreatitis^{4,7}. The risk for acute pancreatitis rises sharply when TG levels exceed 2000mg/dL. At this TG level, eruptive skin xanthomas also commonly appear⁷. Type V patients may also be at increased risk of atherosclerotic coronary artery disease (especially in the presence of diabetes and low HDL-cholesterol), and they commonly manifest peripheral arterial disease⁷. Medications to lower TG levels include nicotinic acid, fibric acids (e.g., gemfibrozil)^{4,7}. Our patients were treated with diet control, weight reduction, hypoglycemic agent (glizalide), and hypolipidemic drug (gemfibrozil). After treatment, blood sugar and lipid levels were reduced, and skin lesions of both the cases showed improvement.

In conclusion, our cases showed typical type V hyperlipoproteinemia and clinical and histopathological findings of eruptive xanthomas, which occurred secondary to uncontrolled diabetes mellitus, and skin lesions showed marked or mild improvement according to blood sugar and lipid levels.

REFERENCES

1. Parker F: Abnormalities in lipid metabolism. In Moschella SL, Herley HJ: *Dermatology*. 3rd ed, WB Saunders Co, Philadelphia 1642-1658, 1992.
2. Arnold HL, Odom RB, James WD. *Andrews' disease of the skin*. 8th ed., Philadelphia: WB Saunders, Philadelphia 599-608, 1990.
3. WHO Memorandum: Classification of hyperlipidemias and hyperlipoproteinemias. *Circulation* 45: 501-508, 1972.
4. Norman RA, Arlington DO, Jenest J, et al: Tubero-eruptive xanthomas: Unusual presentation of type V hyperlipoproteinemia. *Cutis* 43:169-171, 1989.
5. Greenberg BH, Blackwelder WC: Primary type V hyperlipoproteinemia. *Ann Intern Med* 87:526-534, 1977.
6. Chang JH, Lee SH, Lee SJ, et al: A case of type V hyperlipoproteinemia and xanthoma eruptivum associated with diabetes mellitus. *Kor J Dermatol* 38:561-563, 2000.
7. Sanchez JL, Ackerman AB: Xanthomatoses and lipoprotein disorders. In: Fitzpatrick TB, Freedberg IM, Eisen AZ, Wolff K et al, eds. *Dermatology in general medicine*, 5th ed. New York: McGraw-Hill Book 1804-1811, 1999.