Hyperlipidaemia in patients with hypopituitarism

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Abstract. Five patients with hypopituitarism due to Sheehan’s syndrome showed hyperlipidaemia of various lipoprotein phenotypes. Postheparin plasma lipoprotein lipase activity was subnormal in 4 of the 5 patients and hepatic triglyceride lipase was markedly decreased in all patients studied. After supplementation of both corticosteroid and thyroid hormones, lipoprotein lipase activity was restored to normal within 2 months, while it took longer for hepatic triglyceride lipase to return to normal. Together with the normalization of the two lipase activities, hyperlipidaemia subsided. The findings suggest that reduced activities of the two lipases may, at least in part, account for the development of hyperlipidaemia in hypopituitarism. The study identifies a new group of patients with hyperlipidaemia secondary to a disorder in endocrine function.

Only a few papers have described hyperlipidaemia in hypopituitarism (Jacobs et al. 1961; Summers et al. 1967) and little attention has been paid to it previously. In the present study, we have measured plasma lipid levels and postheparin plasma lipoprotein and hepatic lipase activities in 5 patients with hypopituitarism due to Sheehan’s syndrome. Changes in lipase activities were discussed in connection with the development of hyperlipidaemia. They had low levels of serum cortisol and thyroxine, and none showed a significant increase in plasma TSH in response to iv administration of 500 µg of TRH.

Plasma lipid levels and postheparin plasma lipase activities
Plasma lipids and postheparin plasma lipoprotein lipase (LPL) and hepatic triglyceride lipase (H-TGL) activities were measured before and after hormone replacement therapy. The patients fasted for 14 h. Blood samples were withdrawn before and after iv administration of 10 U of heparin (Novo Industry, Denmark) per kg body weight into tubes containing EDTA, 1 mg/ml of blood. The plasma was separated in a refrigerated centrifuge.

Plasma taken before heparin was used for determination of cholesterol and triglyceride. Plasma apolipoprotein E concentrations were measured (Yamada et al. 1982) in 4 patients. Plasma lipoproteins were also analyzed by an agarose gel electrophoresis (Pol-E Film, Diagnostic Division, Pfizer Inc., NY). Plasma lipoproteins from patient 5 were fractionated by gel chromatography using a column prepared with Bio-Gel A-5m (Bio-Rad Labs., Richmond, Ca, USA) (Sata et al. 1970). Postheparin plasma LPL and H-TGL activities were measured separately by an immunochemical method (Murase et al. 1980).

Results

Plasma lipoproteins
All patients had hyperlipidaemia: 4 had both hypercholesterolaemia and hypertriglyceridaemia, and the remaining one had hypercholesterolaemia with normal triglyceride (Table 1). Plasma apolipoprotein E concentrations were high in 2 of the 4

Materials and Methods

Patients
Five female patients were studied (Table 1). All patients had clinical characteristics of Sheehan’s syndrome in that they had a history of massive post-partum haemorrhage followed by amenorrhoea and hypopituitarism.
Table 1.
Clinical data of the subjects studied.

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<th>Age (years)</th>
<th>Body height (cm)</th>
<th>Body weight (kg)</th>
<th>Duration of illness (years)</th>
<th>Serum hormones</th>
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<th>During treatment</th>
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<td></td>
<td></td>
<td></td>
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<td>Plasma (mg/dl)</td>
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<td>1.5</td>
<td>282</td>
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Normal range

6–17  4.5–12  5 >  130–250  40–150  9.5 ± 1.8

Fig. 1.
Agarose gel electrophoresis of plasma lipoproteins from 5 patients and 2 controls (C). The date when studies were done are shown in parentheses: 770523 denotes May 23rd, 1977.

Fig. 2.
Gel chromatography of whole plasma on a Bio-Gel A-5m column. One ml plasma from a normolipidaemic control subject (a) or from patient 5 (b) was applied to the column (1 × 120 cm) and eluted by ascending flow operation with 0.15 M NaCl at a flow rate of 3 ml/h. Each fraction contains 1 ml (control) or 1.3 ml (patient 5) of the column effluent. Triglyceride (●—●) and cholesterol (○—○) in eluate fractions were determined.
patients examined. On lipoprotein electrophoresis, the patients had various types of lipoprotein abnormalities (Fig. 1). The electrophoretic pattern of patients 1, 2 and 5 showed a dense staining between β and pre-β bands, resembling a broad β type. For further studies, plasma from patient 5 was subjected to gel filtration analysis. Plasma lipoproteins could be fractionated by gel filtration technique into three major elution peaks (Fig. 2a). The large-sized lipoprotein particles eluted first from the column are rich in triglyceride and both medium- and small-size lipoprotein particles are rich in cholesterol. These three lipoprotein fractions presumably correspond to very low density, low density and high density lipoproteins, respectively (Sata et al. 1970). Plasma lipoproteins from this patient showed a quite different elution pattern compared with that of controls (Fig. 2b). Despite a marked increase in plasma triglyceride concentration, the large lipoprotein particles were very scanty and the cholesterol-rich medium-sized lipoproteins contained large amounts of triglyceride.

After supplementation of both corticosteroid and thyroid hormones, plasma lipid levels fell rapidly in all patients, except that in 2 patients who had severe hyperlipidaemia (patient 1 and 2) one or both plasma lipids remained high (Table 1).

Postheparin plasma LPL and H-TGL activities

The LPL activity was subnormal in 4 patients. Following hormone replacement, the low activity increased rapidly and reached normal levels within 2 months (Fig. 3). The H-TGL activity was markedly low in all 5 patients. Corticosteroid hormone replacement alone for 1 week in patient 1 and 4 did not produce any changes in this enzyme activity. Following both corticosteroid and thyroid hormone replacement, the H-TGL activity increased gradually to normal levels in 2–24 months in all patients studied (Fig. 1).

Discussion

The present study together with previous reports (Jacobs et al. 1961; Summers et al. 1967) indicates

![Fig. 3](image)

Postheparin plasma lipoprotein lipase (LPL) (upper) and hepatic triglyceride lipase (H-TGL) (lower) activities before and during the course of treatment with either or both corticosteroid and thyroid hormones in patients with hypopituitarism. Dotted area indicates mean ± SD of normal controls.
that hypopituitarism is frequently accompanied by hyperlipidaemia. A combination of hypercholesterolaemia and hypertriglyceridaemia seems to be common. The observations on lipoprotein electrophoresis suggest that various types of hyperlipoproteinaemia can be produced by hypopituitarism. Patients with hypopituitarism do not seem to have a picture of hyperlipidaemia identical with that of primary hypothyroidism. In our experience, patients with hypopituitarism tend to have lower cholesterol with higher triglyceride levels than those with primary hypothyroidism (unpublished observations). Such a difference could be accounted for by the fact that the pituitary gland secretes many hormones and some of the deficient pituitary hormones might play a role in the development of hyperlipidaemia.

Hyperlipidaemia in hypopituitarism was associated with a marked decline of H-TGL activity. Since the decrease of this enzyme activity is commonly seen in primary hypopituitarism (Krauss et al. 1974; Abrams et al. 1981), such a decrease in hypopituitarism may be due to the accompanying hypothyroidism. On the other hand, as reported previously (Krauss et al. 1974; Abrams et al. 1981), most of the patients with primary hypothyroidism have normal LPL activity. In contrast with this, 4 of the 5 hypopituitary patients in our study had reduced enzyme activity. As for the reduction, some of the deficient pituitary hormones may be a factor. It is also possible that relative or absolute hypoinsulinism contributes to this, because LPL is an insulin-dependent enzyme.

Since LPL is an enzyme which plays a prime role in the catabolism of triglyceride-rich lipoproteins, the low LPL activity in most patients accounts for the increase in plasma triglyceride. The finding that one patient (patient 4) with high LPL activity had normal plasma triglyceride goes along with this view. As for the low H-TGL activity, this may also play a role in the development of lipoprotein abnormalities. Animal experiments suggest a role for this enzyme in the removal of remnant lipoproteins (Murase & Itakura 1981; Goldberg et al. 1982). In the present study, lipoprotein electrophoresis of 3 patients resembled broad β type, 2 of the 4 patients had increased plasma apolipoprotein E levels and 1 patient showed abnormal gel filtration pattern, such findings suggesting a possible presence of remnant lipoproteins in the circulating plasma.

The present study shows that the reduced activi-

ties of both lipolytic enzymes are reversible with hormone replacement therapy. Together with the normalization of the two lipase activities, hyperlipidaemia subsided. Three patients became normolipidaemic, but 2 patients who had shown severe hyperlipidaemia had persistent hyperlipidaemia after adequate replacement therapy. These 2 patients might have an underlying primary hyperlipoproteinaemia, but details of this abnormality could not be defined in our study. Although direct evidence was not available, it is possible that in these patients an underlying defect was accentuated by hypopituitarism, as suggested by Hazzard & Bierman (1972).

References


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