Lipoprotein Lipase Deficiency

Mutations in the *LPL* gene resulting in deficiency of LPL synthesis or function lead to increased circulating chylomicron and VLDL particles and severe hypertriglyceridemia. Homozygous LPL deficiency is rare. It manifests in childhood with triglyceride levels higher than 1000 mg/dL. Heterozygous LPL deficiency occurs in 2% to 4% of the population and usually requires a precipitating factor, such as uncontrolled diabetes or estrogen therapy, to manifest the phenotype. These individuals have moderate hypertriglyceridemia (250 to 750 mg/dL) that can increase to levels greater than 1000 mg/dL with secondary factors. This can result in the chylomicronemia syndrome, which is characterized by marked hypertriglyceridemia (>1000 to 2000 mg/dL), pancreatitis, eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly. Visual inspection demonstrates lipemic plasma. After refrigeration for 12 hours, a creamy top layer (increased chylomicrons) or turbid plasma infranatant (increased VLDL), or both, can be demonstrated. Documentation of diminished LPL activity confirms the diagnosis. A diet low in fat (<10% of total calories or 20 to 25 g/day) is the primary treatment. Secondary factors such as uncontrolled diabetes and alcohol use should be addressed, and VLDL-lowering agents (e.g., fibric acid derivatives, niacin) may be needed to prevent severe hypertriglyceridemia.

Apolipoprotein C-II Deficiency

Apo C-II is an activating cofactor for LPL. Deficiency of apo C-II is a rare autosomal recessive disorder that leads to increased chylomicrons and VLDL particles in the circulation, resulting in severe hypertriglyceridemia. Clinical manifestations are similar to those of LPL deficiency, including hypertriglyceridemia (>1000 mg/dL) and symptoms of pancreatitis, eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly. Treatment recommendations include appropriate management of secondary factors such as diabetes and hypothyroidism, dietary fat restriction (<10% of calories), and drug therapy (e.g., fibric acid derivatives). For severe hypertriglyceridemia, plasma transfusion (with apo C-II) can be considered.

Familial Hypertriglyceridemia

Familial hypertriglyceridemia is an autosomal dominant disorder that is characterized by overproduction of hepatic VLDL. The exact defect or mutation is unknown. Secondary factors that increase VLDL, such as diabetes, alcohol ingestion, and estrogen therapy, appear to exacerbate this condition. Low HDL associated with familial hypertriglyceridemia is related to increased catabolism. Individuals with this condition have hypertriglyceridemia (200 to 500 mg/dL) and low HDL-cholesterol (<35 mg/dL) at presentation. This diagnosis is considered in individuals who have a family and personal history of hypertriglyceridemia, CHD, and normal LDL levels. Cloudy infranatant after overnight refrigeration of plasma identifies a disorder of VLDL metabolism. Treatment starts with management of secondary factors that may exacerbate the condition. Dietary fat restriction (<10% of calories) and drug therapy with fish oil, niacin, and fibric acid derivates should be initiated if target goals are not achieved.

For a deeper discussion on this topic, please see Chapter 206, "Disorders of Lipid Metabolism," in Goldman-Cecil Medicine, *25th Edition.*

SUGGESTED READINGS

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