Hyperlipidemia in the Presence of Painless Obstructive Jaundice Secondary to Pancreatic Cancer

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A 61-year-old man presented to our family medicine clinic with acute onset pruritus, 40-lb weight loss over the duration of 3 months, and progressively worsening lethargy and fatigue.

History

He has a medical history of type 2 diabetes, hypertension, controlled hyperlipidemia, and diverticulosis. Prior to the visit, the patient had self-limiting diarrhea, but no other health concerns. The patient denied abdominal tenderness, constipation, nausea, and emesis.

His brother had died from colon cancer, and his mother had died from ovarian cancer. Pancreatic cancer is not present in his family history. He is a nonsmoker, does not consume alcohol, had a routine colonoscopy in 2016, and is adherent with his medications.

Physical examination

Significant findings included scleral icterus, jaundiced skin, hepatomegaly, and a nontender midepigastric solid mass. The patient had weight loss, was hemodynamically stable, and did not have tachycardia. He had no visible clubbing or peripheral edema.

Diagnostic tests

The results of the patient's lipid panel showed fasting-induced hyperlipidemia, with an elevated total cholesterol of 825.0 mg/dL and an elevated low-density lipoprotein (LDL) cholesterol of 738.8 mg/dL (Table). During a previous visit on April 26, 2019, the patient's total cholesterol had been 148.0 mg/dL and LDL cholesterol had been 60.4 mg/dL.

At the time of the current visit on September 23, 2019, hyponatremia was also noted, with a low sodium level of 127 mEq/L. His carbohydrate antigen 19-9 level was significantly elevated at 649 U/mL. His alkaline phosphatase (ALP) level was elevated at 474 U/L, aspartate transaminase (AST) level was elevated at 103 U/L, and alanine transaminase (ALT) level was elevated at 247 U/L (Table).

Results of a computed tomography (CT) scan showed a heterogeneously hyperenhanced 5-cm pancreatic head to uncinate process mass with pancreatic obstruction and intrahepatic and extrahepatic biliary dilation.

Treatment and management

The patient was sent to a local university hospital and was admitted. A sphincterotomy was performed, with a metal stent placed in the common bile ducts region. After the stent placement, the patient's symptoms had resolved.

On November 4, 2019, results of another blood test demonstrated a decrease in total cholesterol, LDL cholesterol, total bilirubin, AST, ALT, and ALP (Table). The patient underwent a Whipple procedure on October 15, 2019, and began postoperative chemotherapy.

The pathology report had determined the patient's pancreatic mass was poorly differentiated carcinoma with clear cell features in the pancreas, invading peripancreatic soft tissue with metastases to 4 out of 18 lymph nodes. More than 1 month after the Whipple procedure, the patient's total cholesterol, LDL cholesterol, total bilirubin, AST, ALT, and ALP levels were stable (Table).

Discussion

There have been reported cases of hyperlipidemia in the presence of chronic cholestasis and liver disease, but few transient cases, especially involving pancreatic cancer, have been reported. In this case, we presented a patient with transient, extreme, hyperlipidemia in the presence of painless obstructive jaundice secondary to pancreatic cancer. The

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Table. Results of the Patient's Laboratory Tests at 4 Time Points

	4/26/19	9/23/19	11/04/19	11/27/19
Triglycerides (reference range, 48-150 mg/dL)	258	286	318	285
Total Cholesterol (reference range, 140-200 mg/dL)	148	825	152	154
High-Density Lipoprotein Cholesterol (reference range, 30-85 mg/dL)	36	29	46	46
Low-Density Lipoprotein Cholesterol (reference range, 0.0-129.0 mg/dL)	60.4	738.8	42.0	51.0
Very-Low-Density Lipoprotein Cholesterol (reference range, 1-50 mg/dL)	5	57	--	57
Protein (reference range, 6.4-8.9 g/dL)	7.2	5.7	5.6	6.2
Albumin (reference range, 3.5-5.7 g/dL)	4.2	3.0	3.0	3.1
Globulin (reference range, 2.0-4.8 g/dL)	3.0	2.6	2.7	3.1
Total Billrubin (reference range, 0.3-1.0 mg/dL)	0.3	14.7	0.6	0.4
Aspartate Transaminase (reference range, 13-39 u/L)	15	103	23	17
Alanine Transaminase (reference range, 7-52 u/L)	18	247	30	19
Alkaline Phosphatase (reference range, 34-180 u/L)	83	474	170	113

patient's pancreatic mass was causing an obstruction of bile flow, leading to a jaundiced appearance.

Obstructive jaundice is characterized by a reduced flow of bile out of the liver due to a narrowed or blocked bile or pancreatic duct.[1] The blockage impedes the normal drainage of bile from the bloodstream into the intestines and causes excess bile and its byproducts to accumulate in the blood.[1] Some theories as to why our patient had experienced wide variations in the degree of hyperlipidemia include decreased plasma lecithin cholesterol acyl transferase (LCAT) activity and the presence of lipoprotein X, an abnormal LDL cholesterol.[2]

Cholestatic liver disease leads to a depression in the esterification of cholesterol with fatty acids, causing an elevation of the abnormal low-density and very-low-density lipoproteins with characteristics similar to those of β very-low LDL cholesterol.[3] LCAT forms cholesterol esters from unesterified cholesterol.[3] These cholesterol esters are then taken into the immature high-density lipoprotein (HDL) cholesterol to create a spherical shape and become mature HDL.[3] The HDL is then brought back to the liver where the cholesterols are excreted into the bile.[3] Decreased LCAT activity increases levels of free and total cholesterol, specifically in obstructive jaundice.[4] Our patient could have had decreased LCAT activity, leading to increased total and LDL cholesterol.

Lipoprotein X comprises phospholipids, cholesterol ester, protein (mainly albumin), and unesterified cholesterol with very little core triglyceride.[2] An abundance of lipoprotein X, and in turn hyperlipidemia, can be attributed to 2 different mechanisms. The first mechanism describes that, although LDL cholesterol is cleared from the blood via hepatic uptake, clearance of lipoprotein X relies on the reticuloendothelial system. Therefore, lipoprotein X cannot apply a negative feedback effect on β-hydroxy β-methylglutaryl-CoA (HMG-CoA) reductase, the rate-limiting enzyme of cholesterol biosynthesis.[2] Additionally, increased concentrations of lipoprotein X rev HMG-CoA reductase activity in the liver, leading to increased hepatic cholesterol synthesis.[5]

The second mechanism involves regurgitation of bile salt micelles from bile, which are rich in phospholipids, back into the plasma compartment during cholestasis. When the bile salts are diluted in the plasma compartment below their critical micelle concentration, the bile salt micelles spontaneously rearrange and form lipoprotein X particles.[4] In-vitro studies show that when bile lipoproteins are incubated with serum or albumin, lipoprotein X particles appear. This suggests that reflux of bile into the plasma compartment during cholestasis causes the formation of lipoprotein X.[4] The degree of the transient malignant hyperlipidemia expressed in our patient's case could be from an increase in lipoprotein X leading to an increase in LDL.[6]

Patient outcome

The patient's transient malignant hyperlipidemia had resolved after the biliary obstruction had been surgically removed. Our deductions of a specific mechanism remain inconclusive due to insufficient laboratory capabilities. Further research is required to determine the possible causes of transiently increased LDL cholesterol in cholestatic disease.

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