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Case Report

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Alirocumab Lowers Lipoprotein (a) Levels, Improving Symptoms of Primary Biliary Cholangitis: Case Report

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Abstract

A 46-year-old female with a history of high cholesterol was diagnosed with primary biliary cholangitis (PBC). Limited research has indicated that inhibiting proprotein convertase subtilisin kexin 9, e.g. alirocumab, may reduce lipoprotein (a) levels, but none have been used in patients with PBC. This case highlights the potential for alirocumab to reduce lipoprotein (a) levels, thereby improving symptoms of primary biliary cholangitis.

Keywords: Case report; Alirocumab; Lipoprotein (a); Primary biliary cholangitis

Introduction

Primary Biliary Cholangitis (PBC) is an autoimmune cholestatic liver disease that results from a combination of genetic factors, environmental factors, and epigenetic regulation **[1].** Cellular disease mechanisms characterized by multilineage immune dysregulation. Lipid metabolism abnormalities due to cholestasis are more common in patients with PBC **[2].** Inhibition of Proprotein Convertase Subtilisin Kexin 9 (PCSK9) has been demonstrated to play an important role in lipid-lowering therapy (especially low-density lipoprotein cholesterol (LDL-C)); it works by blocking PCSK9 binding to the LDL-C receptor, and a consequent reduce in circulating LDL-C **[3].** Alirocumab, an anti-PCSK9 monoclonal antibodies, is indicated for second-line treatment for high cholesterol adults whose LDL-C is not controlled by the diet and statin. To the best of our knowledge, no experience with Alirocumab for PBC has been reported **[4].**

Case Presentation

In 2019, a 46-year-old woman underwent gastroscopy due to malodorous belching, loss of appetite, and dry stools lasting for over a month. The procedure revealed the presence of bile reflux gastritis. Omeprazole was prescribed by the attending physician, but it did not provide any relief of the symptoms. Laboratory examinations indicated positivity for antinuclear (ANA, 1:320), Antimitochondrial Antibody-M2 (AMA-M2), and 2-oxo glutarate dehydrogenase complex (anti-3E-BPO). The patient received a diagnosis of PBC and was promptly prescribed rsodeoxycholic acid (UDCA) as treatment. Unfortunately, the patient experienced diarrhea on the same day of taking the medication, with over 10 watery stools per day. After that, the patient ceased taking UDCA after 1 week of intermittent use. Despite discontinuing medication, gastrointestinal symptoms of hiccups, nausea, and loss of appetite persisted. The patient has no record of chronic non-communicable diseases including hypertension or diabetes mellitus, nor has the patient had any contagious infections such as hepatitis or tuberculosis. The patient has regular menstrual cycles, one pregnancy resulting in a healthy delivery, and a healthy daughter. The patient has no reported family history of genetic or infectious diseases. Physical examination revealed no yellowing of the skin or mucous membranes or haemorrhage. There were no palpable superficial lymph nodes, and the abdomen was soft with no pain on palpation. The liver and spleen were non-enlarged, and bowel sounds were normal. The patient was readmitted to the hospital on 27 July 2020 and was back on UDCA with no further symptoms of diarrhea. Laboratory tests indicated normal liver function and Low-Density Lipoprotein Cholesterol (LDL-C) levels of 3.57 mmol/L (normal range 0 to 3.64). The ultrasound results for the upper abdomen showed no apparent abnormal sound images of the liver, gallbladder, spleen, or pancreas. Magnetic resonance imaging of the pancreatic and biliary ducts (MRCP) revealed a lack of visualization of the gallbladder, and the cystic duct and the lower part of the common hepatic duct up to the upper part of the common bile duct were not clearly observed. As for follow-up, while the symptoms of hiccups and retching showed slight improvement, belching, nausea, loss of appetite, and aversion to fatty foods persisted.

On 1st February 2021, the patient was admitted to the hospital for review with LDL-C levels at 3.97 mmol/L and lipoprotein a [Lp(a)] levels at 918 mg/L. Following examination, a nightly dose of 10 mg rosuvastatin was prescribed despite persisting gastrointestinal symptoms. On May 20th 2021, the patient was followed up with a LDL-C level of 2.28 mmol/L and Lp(a) of 1009 mg/L. The first alirocumab treatment was given on May 25th, resulting in the patient's gastrointestinal symptoms disappearing after one week and enabling consumption of meat. The second treatment was given on June 25th and the changes in lipid indices pre and post alirocumab treatment are summarised in Table 1. After receiving two rounds of anti-treatment with Alirocumab, the patient's digestive symptoms were completely resolved and there was a significant decrease in their lipid levels, particularly Lp(a).

Table 1: Dynamics of the patient's glycaemic lipids.

	TG mmol/L	TC mmol/L	HDL-C mmol/L	LDL-C mmol/L	Lp (a) mg/L
Before treatment (2020/07/27)	1.14	5.47	1.69	3.57	——

Before treatment (2021/02/01)	1.43	6.07	1.81	3.97	918
Oral Rosuvastatin for 3 months (2021/05/20)	1.23	4.20	1.59	2.28	1009
Alirocumab 1 week after first injection (2021/06/02)	1.10	3.27	1.75	1.48	800
Alirocumab 1 week after second injection (2021/07/01)	0.92	3.49	1.73	1.60	736

Note: TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein a

Discussion

This report suggests that alirocumab reduces Lp(a) levels in patients with PBC associated with hyperlipidemia and improves digestive symptoms in PBC. Previous literature and clinical evidence suggest that Lp(a) is closely associated with cardiovascular disease **[5,6],** but commonly used lipid-lowering drugs such as statin and ezetimibe have limited improvement in Lp(a) levels. Some studies even suggest that statins may increase Lp(a) levels **[7]** (like our report), while alirocumab may improve the prognosis of cardiovascular disease by reducing Lp(a) **[8].** The case report suggests a significant symptomatic improvement with alirocumab in a patient with PBC. Alirocumab has been shown to improve hyperlipidemia and systemic oxidative stress levels in rats with biliary cirrhosis, based on the results of only one animal study **[9].** Due to the long history of this patient, the symptomatic improvement of alirocumab in PBC cannot be denied.

In conclusion, our case provides a reference model for the treatment of PBC combined with hyperlipidemia, and a large number of RCTs or cohort studies are still needed to demonstrate that alirocumab reduces Lp(a) levels and improves PBC symptoms.

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