Journal of Clinical Lipidology (2016) 10, 1266–1271

Journal of Clinical Lipidology

Ischemic stroke in a young adult with extremely elevated lipoprotein(a): A case report and review of literature

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KEYWORDS:
Lipoprotein(a);
Atherosclerosis;
Carotid stenosis;
Thrombosis

Abstract: Lipoprotein(a) [Lp(a)] is an apolipoprotein(a) molecule bound to 1 apolipoprotein B-100. Elevated levels of Lp(a) are thought to be an independent risk factor for atherosclerosis and to promote thrombosis through incompletely understood mechanisms. We report a 34-year-old man with an ischemic stroke in the setting of an extremely high Lp(a) level—212 mg/dL. He developed severe carotid artery stenosis over a 6-year period and had thrombus formation post-carotid endarterectomy. To our knowledge, this case is unique because the Lp(a) is the highest reported level in a patient without renal disease. Moreover, this is the first reported case of the youngest individual with a stroke presumably related to development of carotid plaque over a 6-year period. The thrombotic complication after endarterectomy may have been related to the prothrombotic properties of Lp(a). Of note, the Lp(a) level did not respond to atorvastatin but did decrease 15% after aspirin 325 mg was added although his Lp(a) levels were variable, and it is not clear that this was cause and effect. This case highlights the need to better understand the relation between Lp(a) and vascular disease and the need to screen family members for elevated Lp(a). We also review treatment options to lower Lp(a) and ongoing clinical trials of newer lipid-lowering drugs that can also lower Lp(a).

Elevated levels of lipoprotein(a) [Lp(a)] are not generally diagnosed until patients experience acute vascular events. Patients having these vascular events are often young and may not have other risk factors for atherosclerosis. We present a 34-year-old man with severe carotid stenosis and ischemic stroke in the setting of extremely elevated Lp(a). We describe the rapid progression of carotid artery stenosis seen in this patient and thrombosis post-carotid endarterectomy. We summarize treatment options for management of elevated Lp(a) and the need for clinical trials with newer lipid-lowering drugs in subjects with elevated Lp(a) levels.

Case report

A 34-year-old man was referred to our lipid clinic after a recurrent stroke. At the age of 27 years, this right-handed man developed sudden onset of "swishing"/ringing in his ears while sitting at his desk at work and eating pizza. He

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Submitted April 1, 2016. Accepted for publication June 30, 2016.

1933-2874/
http://dx.doi.org/10.1016/j.jacl.2016.06.012

felt as if he were going to pass out, had nausea and vomiting, difficulty with forming words and speaking, slurred speech, and unsteady gait. His coworkers walked him outside to fresh air where symptoms improved although he continued to have unsteady gait and intermittent slurred speech. Past medical history was notable only for attention deficit and hyperactivity disorder for which he was taking Adderall 60 mg daily for 4 years. There was no history of diabetes or hypertension. He never smoked, denied cocaine use, and drank 2–4 drinks per week. At admission on January 26, 2009, blood pressure was 167/98 with heart rate of 112. Body mass index was 23.9 kg/m^2. Examination was significant for tremulousness, vertiginous and unable to stand, right hand clumsiness, normal sensation, and intermittent dysarthric speech. Magnetic resonance imaging of the brain showed multiple acute nonhemorrhagic infarcts in the right superior cerebellum, the left parieto-occipital junction, the left inferior parietal lobe, and the left posterior subinsular region. Transesophageal echocardiogram showed no cardiac source of emboli, patent foramen ovale, or valvular abnormalities. Computed tomography angiography (CTA) and magnetic resonance angiography of the head and neck showed no carotid or vertebral artery narrowing or dissection. Transcranial Dopplers were also normal. At admission, blood and urine toxicology screens were negative. C-reactive protein was 5, homocysteine was 8.5, HbA1c was 5.8%, serum creatinine was 0.8 mg/dL, and aspartate transaminase and alanine transaminase were 23 and 21 IU/L, respectively, and thyroid stimulating hormone was 1.8 uIU/mL. On January 27, 2009, total cholesterol was 152 mg/dL, low-density lipoprotein cholesterol (LDL-C) was 81 mg/dL, high-density lipoprotein cholesterol was 60 mg/dL, triglycerides were 55 mg/dL, and fasting glucose was 106 mg/dL (see Table 1). Hypercoagulable workup showed normal levels of antithrombin III, factor V Leiden and anticardiolipin IgG and IgM, and negative lupus anticoagulant. Prothrombin gene mutation studies were normal. Heparin was started and transitioned to warfarin for 3 months. Aspirin was added. Although cardiac telemetry and Holter monitoring showed no arrhythmia, neurology hypothesized that he may have had an arrhythmia as a result of Adderall, which resulted in the strokes; therefore, Adderall was discontinued. Repeat blood pressures as an outpatient were 120/90-96, and lisinopril 5 mg was started 9 months after his initial stroke. Due to cough, he was switched to Norvasc 2.5 mg. He recovered without any residual neurological deficits.

He did well until March 6, 2015, when he developed temporary difficulty with talking and intermittent episodes of numbness and tingling in the right arm for about 48 consecutive hours. He did not seek medical attention. He awoke the next morning with a severe headache, a right facial droop, and garbled speech. At admission on March 7, 2015, blood pressure was 158/107, and body mass index was 24.3 kg/m^2. His sole medication was amlodipine 2.5 mg. Carotid ultrasound on March 7, 2015, indicated severe stenosis (80%–99%) of the left internal carotid artery (ICA) and 0% to 49% right ICA. CTA of the head and neck on March 7, 2015, demonstrated 99% stenosis of the left ICA due to a combination of interval developing soft atherosclerotic plaque in the left carotid bifurcation since 2009 and superimposed presumed plaque rupture with intraluminal thrombus formation, further narrowing the proximal ICA lumen to 1-mm diameter. Free-floating intraluminal

Table 1 Laboratory results

Date	TC (mg/dL)	LDL-C (mg/dL)	HDL-C (mg/dL)	TG (mg/dL)	Lp(a)	Glucose (mg/dL)	ApoB (mg/dL)	Drug
January 27, 2009	152	81	60	55		106		None
January 28, 2009						105		None
February 19, 2009	247	168	44	174		125		None
May 26, 2009	177	110	47	98				None
March 7, 2015	188	132	42	71				None
March 10, 2015	130	77	39	69			88	Atorvastatin 40 mg
March 15, 2015						111		Atorvastatin 40 mg
March 16, 2015						110		Atorvastatin 40 mg
March 17, 2015					152*	117		Atorvastatin 40 mg
May 15, 2015					501†			Atorvastatin 40 mg, niacin 500 mg
May 26, 2015	174	100	35	193	212*	100	99	Atorvastatin 40 mg
May 29, 2015					497†			Atorvastatin 40 mg
November 3, 2015	132	81	26	126	180*	108		Atorvastatin 40 mg and aspirin 325 mg

ApoB, apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); TC, total cholesterol; TG, triglycerides.

*Lp(a) measured in mg/dL—normal <29 mg/dL; multiply by 3.57 to convert to nmol/L.

†Lp(a) measured in nmol/L—normal <75 nmol/L.