Case Report

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A Case of Dilated Cardiomyopathy with Massive Left Ventricular Thrombus after Use of a Sibutramine-Containing Slimming Product

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Sibutramine, which acts as an anti-obesity drug by inhibiting reuptake of serotonin and norepinephrine, has now been banned due to cardiovascular adverse effects. However, despite being banned, it is not uncommon for people to purchase products with sibutramine or its analogues used as adulterants in non-prescription slimming products or health foods available on the internet. Sibutramine has been associated with rare but serious adverse reactions such as cardiac arrhythmia including QT interval prolongation, myocardial infarction, and cardiomyopathy, as well as increases in blood pressure and pulse rate. Here, we report a case of a 32-year-old male who presented with dilated cardiomyopathy with massive left ventricular thrombus after taking unauthorized sibutramine-containing slimming pills sold over the internet. **(Korean Circ J 2013;43:632-635)**

KEY WORDS: Sibutramine; Cardiomyopathy, dilated; Anti-obesity agents.

Introduction

A variety of non-prescription slimming products are now readily available on the market, which are often advertised to contain purely natural ingredients, hence assumed to be harmless. However, these products may contain prescription weight-loss agents or banned pharmaceutical analogues that are not mentioned on the pack or in the patient information leaflet, and therefore may result in significant toxicities and even mortality.[1)2)] Sibutramine, which has now been banned due to cardiovascular adverse effects, is one of the most commonly encountered illicit adulterants in non-prescription slimming pills.[2)]

We describe a rare case of dilated cardiomyopathy with massive left ventricular (LV) thrombus in an otherwise healthy 32-year-old man who was taking sibutramine-containing slimming products.

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Case

A 32-year-old man was admitted with progressively worsening dyspnea on exertion of 1 month duration. The patient was not known to have hypertension, diabetes or any other medical illness. He reported having taken the unauthorized health product, "Slim-30", for the last 7 months and had stopped taking it 2 weeks ago. Several medicines regulatory authorities are warning that this product contains an undeclared pharmaceutical ingredient, N-desmethyl sibutramine, an analogue of sibutramine, which has now been banned because of cardiovascular adverse effects. When the drug was first started, his body mass index was 26.3. From the outset the patient presented higher blood pressure and palpitation, therefore he had taken the pill at intervals of about 2 to 3 days. On admission, initial vital signs were as follows: blood pressure of 110/80 mm Hg, pulse rate of 130 beats/min, respiration rate of 20 breaths/min, and body temperature of 36.5°C. Upon physical examination, pitting edema in both lower extremities was noted and a S3 gallop sound was audible. Chest X-ray showed cardiomegaly (cardiothoracic ratio was 0.60) and no pulmonary edema (Fig. 1). The electrocardiogram showed sinus tachycardia with diffuse non-specific ST segmental changes. The cardiac enzymes were within the normal range with a Troponin-T level of 0.023 ng/mL (normal ≤0.100) and creatine kinase-MB level of 1.86 ng/mL (normal ≤4.94). However, pro-B-type

natriuretic peptide level was elevated to 5404 pg/mL (normal ≤88). A complete blood cell count, coagulation profile, and thyroid function test were within normal limits. Liver enzymes were elevated with an aspartate aminotransferase level of 80 IU/L and alanine transaminase level of 120 IU/L. The transthoracic and transesophageal echocardiogram revealed dilated LV (end-diastolic diameter of 6.5 cm) with severely impaired systolic function {ejection fraction (EF) of 23%} and multiple hyperechoic, pedunculated masses attached to the LV apical wall, of which the largest measured 4.6×1.5 cm in size (Fig. 2). In the presence of severe LV systolic dysfunction, the mass-like lesions were suspected of thrombi. The patient was started on diuretics, angiotensin-converting-enzyme inhibitor (ACEI) and parenteral unfractionated heparin. He had a good clinical resp-

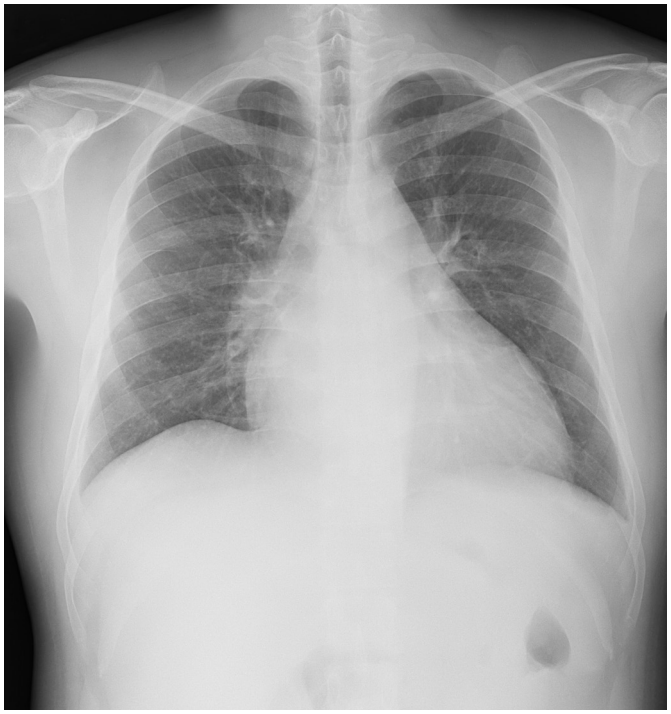

Fig. 1. Chest X-ray shows cardiomegaly and no pulmonary edema.

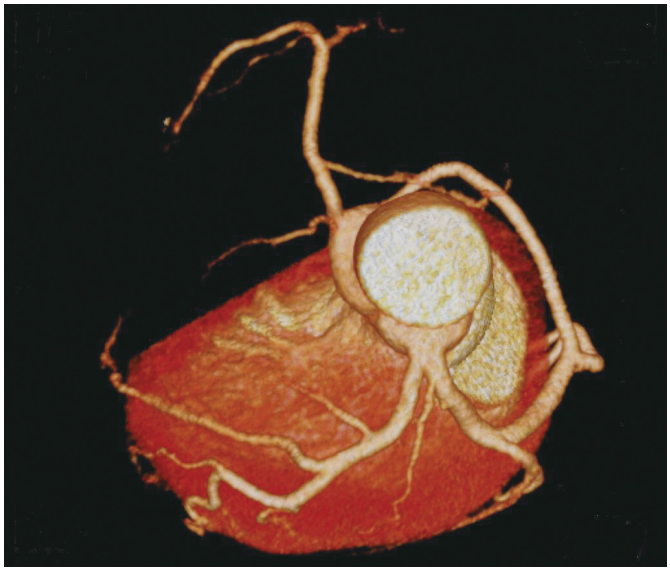

Fig. 3. Multi-detector computed tomography shows no intraluminal narrowing in coronary artery.

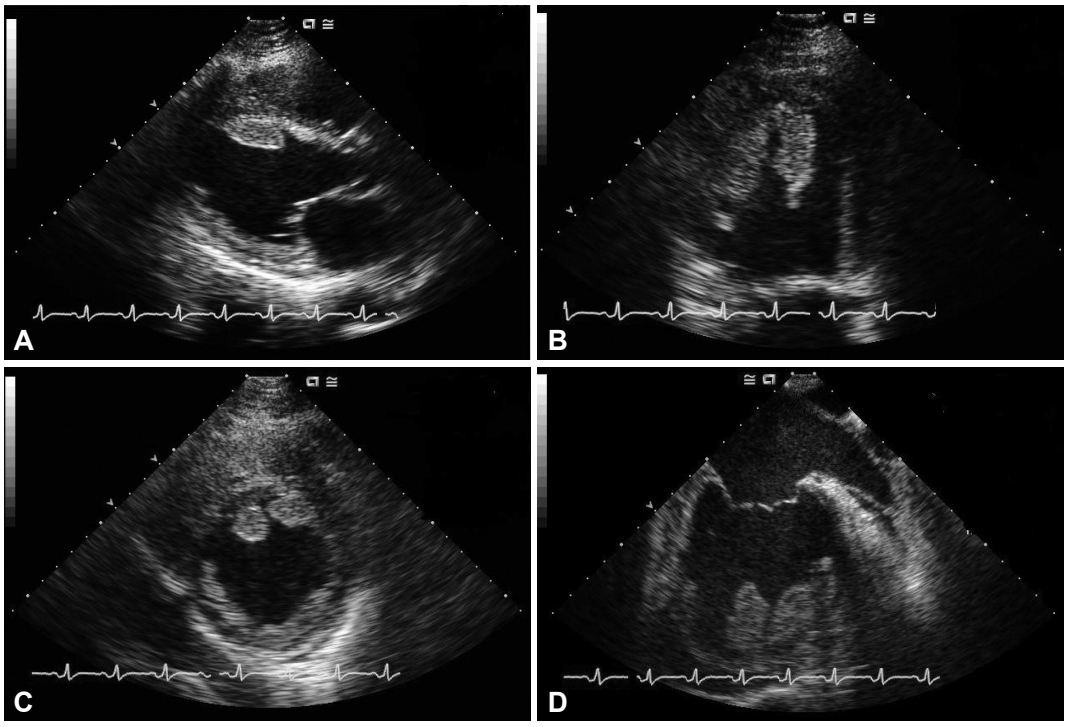

Fig. 2. Initial transthoracic (A, B and C) and transesophageal (D) echocardiograms show severe LV systolic dysfunction and dilatation with multiple, pedunculated thrombi attached to LV apical wall. LV: left ventricle.

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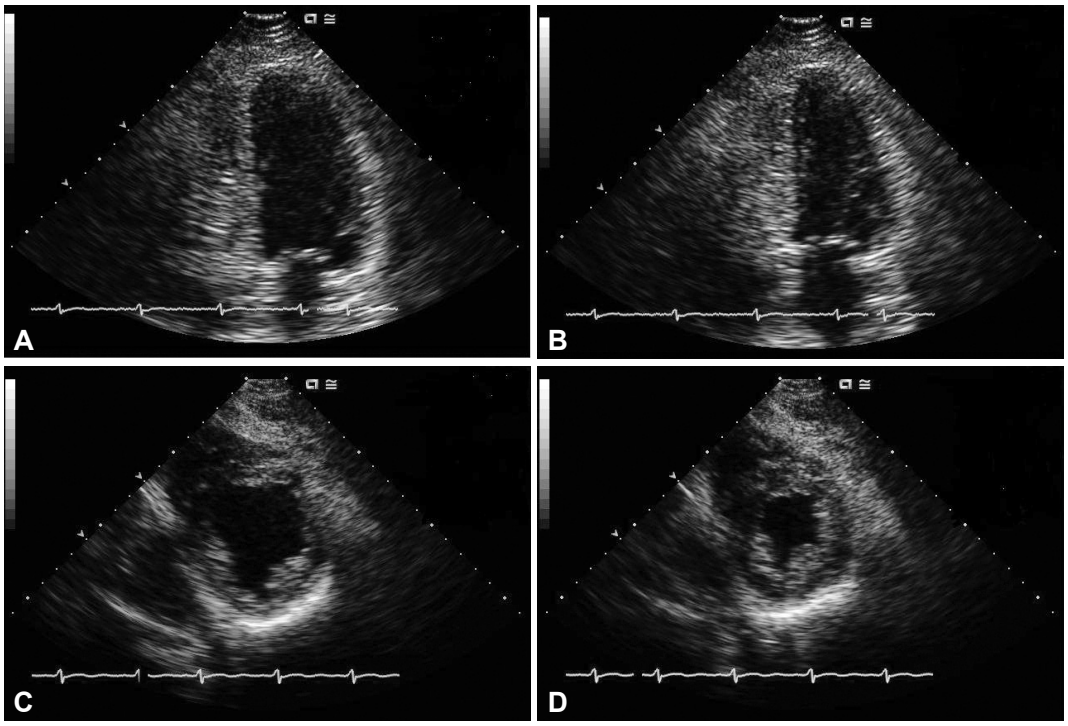

Fig. 4. Follow-up transthoracic echocardiogram demonstrates significantly improved LV systolic function and dilatation together with complete resolution of LV thrombus. A: end diastolic period on apical 4-chamber view. B: end systolic period on apical 4-chamber view. C: end diastolic period on PSAX mid-ventricular view. D: end systolic period on PSAX mid-ventricular view. LV: left ventricle, PSAX: parasternal short axis.

onse to treatment and subsequent echocardiogram performed 10 days later showed that LV thrombi had nearly dissolved, although there was only a slight improvement in LV dilatation and contractility. Multi-detector computed tomographic coronary angiography, which was performed before discharge, showed normal a coronary artery (Fig. 3). He was discharged in a stable condition and prescribed a beta blocker, ACEI, and oral warfarin. At 1 month follow-up, echocardiogram demonstrated complete resolution of LV thrombi and markedly improved LV systolic function (EF of 45%) and dilatation (end-diastolic diameter of 5.6 cm) (Fig. 4). The patient is currently doing well and is being followed up via the outpatient department.

Discussion

Sibutramine (Meridia®, Reductil®, Ectiva®, Abbott Laboratories, Abbott Park, IL, USA) was approved by the U.S. Food and Drug Administration in 1997 and was approved for use in the European Union (EU) in 1999 for the long-term (12 months) management of obesity. Sibutramine and its two active metabolites, N-desmethyl and N-bisdesmethyl sibutramine, act centrally to inhibit serotonin and noradrenaline (norepinephrine) reuptake leading to satiety and act peripherally to increase metabolic rate, thermogenesis, and energy expenditure by stimulating β3-adrenergic receptors.[3] Such sympathomimetic activity of sibutramine causes a modest increase in heart rate and blood pressure,[4)5)] which can potentially increase the risk of adverse cardiovascular outcome in susceptible patients. Since 2002, serious adverse events including cardiac arrhythmia (QT interval prolongation), myocardial infarction (MI), and death had been reported in sibutramine-treated patients.[6-12] This led to a contraindication of the use of this drug in patients with established coronary heart disease, previous stroke, heart failure, or cardiac arrhythmias. In the sibutramine cardiovascular outcomes trial, subjects with pre-existing cardiovascular disease who were receiving long-term sibutramine treatment (5 years) had an increased risk of nonfatal MI and nonfatal stroke but not of cardiovascular death or death from any cause.[5)13)] On the basis of this trial, sibutramine was withdrawn from the EU in January 2010 and subsequently withdrawn from parts of Asia and the U.S. market in October 2010.[14-16] However, sibutramine has still been found in adulterated non-prescription slimming products or natural herbal products.[1)17)] These products, of which ingredients are not declared, are usually found to contain N-desmethyl sibutramine in concentrations far above the maximum daily dose (5 to 15 mg).[1)17)] The unperceived use of this substance may be even more hazardous and lead to unpredictable complications and even mortality for individuals without any cardiovascular risk factor. Therefore, more effective and proactive measures are required to guard against illicit use of slimming products containing N-desmethyl sibutramine or other banned pharmaceutical ana-

logues such as N-nitrosofenfluramine.

One case has been reported of reversible cardiomyopathy possibly associated with sibutramine.[18] However, cases of patients who presented with dilated cardiomyopathy with massive intracardiac thrombus secondary to sibutramine use have not been reported. In our case, the patient did not have any attendant cardiovascular risk factors and another culpable agent was not identified. We excluded other etiologic causes of reversible cardiomyopathy such as alcohol abuse, abnormal thyroid function, and coronary heart disease. The chance of myocarditis seemed to be very low due to cardiac enzymes within the normal range and no history of viral infection. The patient had been making a remarkable recovery with the discontinuation of the agent. This strongly suggested that sibutramine use was responsible for his dilated LV with severely impaired contractility, thereby causing intracardiac thrombus formation.

We report a rare case of an otherwise healthy man who presented with dilated cardiomyopathy with massive LV thrombus secondary to the use of sibutramine-containing slimming pills. This case highlights the emerging threat posed by adulteration of non-prescription slimming products with undeclared, banned pharmaceutical analogues. When investigating the secondary cause of dilated cardiomyopathy with unknown etiology, physicians should be vigilant to the possibility of over-the-counter weight-loss agents or dietary supplements with undeclared ingredients.

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