Journal of Cardiology Cases (2011) 3, e29–e32

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journal homepage: www.elsevier.com/locate/jccase

Case Report

Multiple spontaneous coronary artery ruptures and cardiac tamponade in vascular Ehlers-Danlos syndrome

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Received 1 August 2010; received in revised form 15 September 2010; accepted 24 September 2010

KEYWORDS
Ehlers-Danlos syndrome;
Carotid-cavernous fistula;
Coronary arterial rupture;
Cardiac tamponade;
Procollagen

Abstract We report a case of a 45-year-old woman with Ehlers-Danlos syndrome (EDS) type IV, the vascular type, who presented with multiple coronary artery ruptures causing cardiac tamponade. She had sudden onset of chest pain soon after transarterial embolization for right carotid-cavernous fistula. Transthoracic echocardiography confirmed cardiac tamponade and hypokinetic inferolateral wall. Enhanced CT and transesophageal echocardiography ruled out aortic dissection. Coronary angiography showed contrast extravasation from multiple sites of the right coronary artery and left circumflex coronary artery. We suspected EDS type IV, and a skin biopsy for DNA and RNA analysis was done after taking written informed consent. Polymerase chain reaction (PCR) and sequencing of the PCR product showed a heterozygous missense mutation of codon 85 in the *COL3A1* gene, which converted glycine to aspartic acid, and thus a diagnosis of EDS type IV was established. To our best knowledge, this is the first case of EDS type IV causing multiple coronary artery ruptures.

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doi:10.1016/j.jccase.2010.09.002

Introduction

Spontaneous coronary artery rupture (SCAR) is a rare cause of cardiac tamponade and cardiogenic shock with a high mortality. Computed tomography (CT) is useful to rule out the aortic dissection which often causes cardiac tamponade. At coronary angiography, a definitive diagnosis of SCAR can be made by the observation of extravasation of contrast material anywhere in the coronary arteries. In contrast to naturally occurring coronary artery rupture, which happens in conjunction with blunt chest trauma, atherosclerotic disease, aneurysm, localized infection, and iatrogenic complications of percutaneous coronary intervention, SCAR may occur in patients with Ehlers-Danlos syndrome (EDS) type IV. EDS type IV, the vascular type, is a life-threatening autosomal dominantly inherited disorder of connective tissue, caused by mutation of the type III procollagen gene (*COL3A1*) [1]. EDS type IV causes severe fragility of connective tissues with arterial and intestinal ruptures. SCAR in patients with vascular EDS is rare, and there is only one case in the literature [2]. Furthermore, multiple SCARs associating with myocardial infarction have not been reported. We report here the first case of multiple SCARs complicating myocardial infarction in a 45-year-old female with EDS type IV.

Case

On May 25th in 2009, a 45-year-old woman was transferred to the emergency room from another hospital for suspected ST-segment elevation myocardial infarction (STEMI). She had sudden onset of chest pain soon after transarterial embolization for right carotid-cavernous fistula (CCF). Fifteen years before admission, she underwent transarterial embolization for left carotid-cavernous fistula (CCF). Since then, she had been regularly followed-up in out-patient clinic. On fourteen days before admission, she presented to the hospital with headache and tinnitus, and MRI revealed the right CCF. On May 25th, she underwent transarterial embolization for it. Although embolization was completed uneventfully, she developed chest pain in the recovery room when she became conscious after systemic anesthesia. ECG showed ST-segment elevation in II, III, aV_F, and V_4-V_6 leads suggesting acute myocardial infarction. Then, she was transferred to the catheter laboratory in our hospital. She had no classical risk factors for coronary artery disease. There was no family history of cardiovascular disease or sudden death.

On admission to our hospital, her blood pressure was 65/41 mmHg. Her pulse was 115/min and regular, and her body temperature was 36.3 °C. Arterial blood gas evaluation on O_2 2 l/min nasal showed pH 7.3; PaO_2 161.1 mmHg; $PaCo_2$ 23.7 mmHg; HCO_3^- 14.1 mmol/l; BE −9.4. She had a tendency of easy bruising, thin and translucent skin, atrophic scars of both knees, and hypermobility of metatarsophalangeal (MTP) joints of toes (data not shown).

An electrocardiogram (ECG) showed sinus tachycardia with ST-segment elevation in leads II, III, aV_F, and V_4—V_6 suggesting acute inferolateral (MI) (Fig. 1A). Total serum creatine kinase (CK) was 179 IU/l (reference range < 216 IU/l). Plasma troponin I was 4.71 ng/ml (reference range < 0.1 ng/ml). Transthoracic echocardiography confirmed cardiac tamponade and hypokinetic inferolateral wall. Computed tomography (CT) scanning with contrast agent (Fig. 1B) and transesophageal echocardiography ruled out aortic dissection. Stabilization was achieved with pericardiocentesis and blood transfusion. Surprisingly, coronary angiography (CAG) showed extravasation of contrast material from multiple sites in distal segments of the left circumflex artery (Fig. 2A) and right coronary artery (Fig. 2B). Vessels with ruptured sites were markedly spastic. Left ventriculography showed hypokinesis of inferolateral wall and no rupture of the ventricle.

Because blood oozing was barely detected by CAG performed at 30 min after the initial CAG, and because ECG showed that ST-segment almost returned to the baseline, we did not attempt to terminate bleeding at the ruptured sites. On the second hospital day, we confirmed no bleeding by CAG. The drain of pericardial cavity was removed uneventfully on the third day. Serum creatine kinase (CK) finally rose to a peak of 635 IU/l, and then returned to baseline within 3 days. The patient was discharged in good condition on the fifth day on calcium channel blocker and angiotensin-converting enzyme (ACE) inhibitor for secondary preventive medication.

Characteristic physical findings, thin and translucent skin, atrophic scars of both knees, and hypermobility (MTP) joints of toes, together with her clinical history of bilateral CCF, led us to the clinical diagnosis of vascular EDS. To confirm vascular EDS, a skin biopsy was performed. Informed consent was obtained from the patient for the DNA analysis before a skin biopsy.

To generate complementary DNA (cDNA), reverse transcription was performed using reverse transcription-polymerase chain reaction (RT-PCR) according to manufacturer's protocol. Sequencing of the PCR product including the 3.3 kb-pair of exons encoding the triple-helix domain of type III collagen was performed as previously described [3]. The results of the sequencing revealed a heterozygous missense mutation of codon 85 in the *COL3A1* gene, which converts codon GGT for glycine to codon GAT for aspartic acid (Fig. 3A, B and C), and thus a diagnosis of EDS type IV was established. To our best knowledge, this is the first case of EDS type IV causing multiple spontaneous coronary artery ruptures.

Discussion

The estimated prevalence of the EDS varies between 1/10,000 and 1/25,000 with no ethnic predisposition, and EDS type IV accounts for approximately 5—10% of all EDS [4]. The clinical diagnosis of EDS type IV is made based on the finding of at least two of four clinical criteria: easy bruising, thin skin with visible veins, characteristic facial appearance, and rupture of arteries, uterus, or intestines, but biochemical and molecular studies are required for confirmation [5]. The systemic arteries, which are rich in type III procollagen, may undergo dissection, aneurysm, or rupture. An arterial rupture may be preceded by either an aneurysm, arteriovenous fistula, or a dissection, but may also occur spontaneously. The *COL3A1* gene encodes 1467 amino acids, of which 1029 are located within the triple-helical domain