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Case Report

Spontaneous coronary artery dissection in a woman undergoing pseudomenopause therapy with leuprorelin: A case report

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ABSTRACT

Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome. SCAD frequently affects women, and may be associated with pregnancy and the peripartum period. Therefore, female sex hormones are thought to play a pathogenetic role. Although pseudomenopause therapy may alter female sex hormone levels similar to those during pregnancy, there are no reported cases of SCAD associated with pseudomenopause therapy. We report the case of a 48-year-old woman who developed SCAD while undergoing pseudomenopause therapy with leuprorelin. This case suggests an association between SCAD and pseudomenopause therapy with leuprorelin.

<**Learning objective:** Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome (ACS). SCAD frequently affects women and is thought to be associated with female sex hormones. Here, we report a case of SCAD in a patient who was undergoing pseudomenopause therapy with leuprorelin to treat uterine fibroids. Young or middle-aged women who present with symptoms suggestive of ACS should be asked about not only pregnancy and menstrual history, but also therapies altering female sex hormones.>

Introduction

Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome (ACS). SCAD commonly presents in young or middle-aged women, and is sometimes associated with pregnancy and the peripartum period [1]. Although pseudomenopause therapy may alter female sex hormone levels similar to those observed during pregnancy, SCAD following pseudomenopause therapy has not been reported. We report a 48-year-old woman who developed SCAD while undergoing pseudomenopause therapy with leuprorelin.

Case report

A 48-year-old woman with a history of hypertension developed occasional episodes of chest pain at rest 3 years previously. She was diagnosed with uterine fibroids 2 months ago, and her obstetrician started pseudomenopause therapy with leuprorelin. On the day of admission, she exhibited severe left-sided chest pain with cold sweat and nausea. She called an ambulance and was delivered to our hospital. Her blood pressure was 104/85 mmHg, and her pulse rate was 57/min and regular. Her respiration and heart sounds were normal. The electrocardiogram on arrival demonstrated ST elevation in the inferior leads and inverted T waves in the other leads (Fig. 1, left panel). Cardiac biomarkers were normal. There was normal left ventricular systolic function and no segmental wall motion abnormalities according to the echocardiogram. In the emergency room, her chest pain gradually improved and spontaneously resolved without medication. The changes on the electrocardiogram also improved (Fig. 1, right panel). We considered ACS or vasospastic angina (VSA), and emergent coronary angiography was performed, which revealed an angiographically normal left main trunk, left anterior descending artery, and left circumflex artery. The proximal-mid portion of the right coronary artery (RCA) exhibited diffuse 50% stenosis and the atrioventricular branch of RCA exhibited 90% stenosis. We found intramural hematoma on

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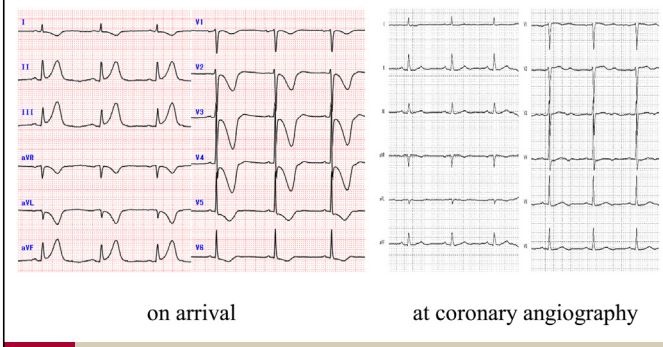

Fig. 1. Electrocardiogram. The electrocardiogram showed ST elevation in the inferior leads and inverted T waves in the other leads on arrival, and these changes on the electrocardiogram spontaneously improved.

intravascular ultrasound (Fig. 2), and diagnosed her with spontaneous coronary artery dissection (SCAD). There was thrombolysis in myocardial infarction grade 3 flow throughout the RCA. Left ventriculogram revealed normal left ventricular systolic function. As her general condition was stable, conservative medical treatment without coronary intervention was selected. She did not have other risk factors for SCAD such as family history, smoking, extreme exercise, intense stress, and migraine. We considered the involvement of VSA for the pathogenesis of SCAD because she had occasional episodes of chest pain at rest, and we started her on diltiazem. After hospitalization, there was no recurrence of chest pain. The peak troponin I level was 764.8 pg/ml (normal range <32.0 pg/ml), but creatine kinase remained within the normal range. She was discharged 6 days after admission. We suggested the obstetrician suspend pseudomenopause therapy, but he and the patient decided to complete the scheduled regimens, and perform surgery for uterine fibroids. After one month of the waiting

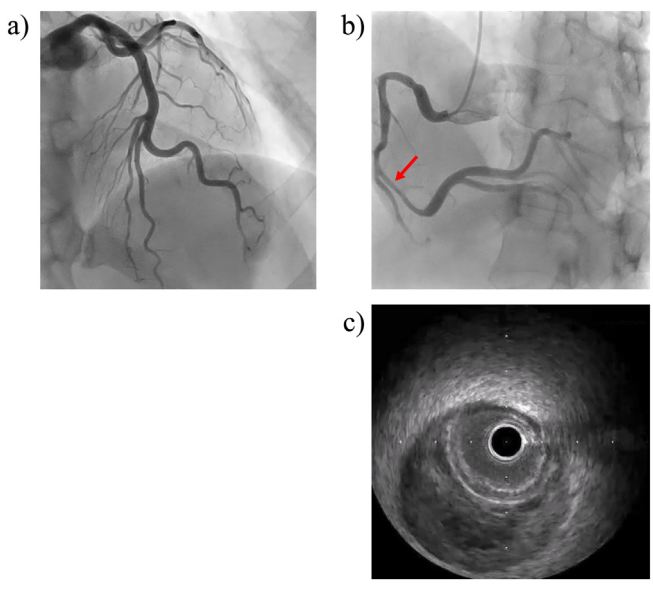

Fig. 2. Coronary angiography and intravascular ultrasound images. (a) Angiography of the left coronary artery was normal. (b) Angiography of the right coronary artery revealed 50% stenosis in the proximal-mid portion and 90% stenosis in the atrioventricular branch. (c) Intravascular ultrasound image at the point indicated by the arrow in (b). There was intramural hematoma in the 2 o'clock to 11 o'clock direction.

period during which she did not complain of chest pain with diltiazem therapy, he restarted pseudomenopause therapy as scheduled. Coronary computed tomography (CT) angiography performed 2 months after discharge demonstrated SCAD to be almost resolved (Fig. 3). We performed whole-body enhanced CT scan concurrently with coronary CT angiography, but any other extra-coronary vascular abnormalities such as aneurysms, dissections, and tortuosity were not present. Thereafter, pseudomenopause therapy was completed as scheduled, and surgery for uterine fibroids was performed. The optimal timing or duration of calcium channel blocker during leuprorelin therapy is unknown. In this particular patient, we will continue to use diltiazem even after the completion of leurporelin therapy, since she has hypertension. Until now, there has been no recurrence of SCAD under the administration of diltiazem.

Discussion

SCAD is a rare cause of ACS. SCAD predominantly affects women who account for 81%–92% of the patients [1]. The prevalence of SCAD has been reported as 0.07%–1.1% of all individuals undergoing coronary angiograms [1]. More recently, diagnostic awareness has become higher and intracoronary imaging has become more prevalent; therefore, the diagnostic rate for SCAD is increasing. Among women, SCAD is the etiology of ACS in as high as 35% of cases [1], and is the most common etiology of myocardial infarction associated with pregnant and postpartum women [1], accounting for 18% of all SCAD cases among women [1]. Pregnancy-associated SCAD (P-SCAD) often occurs in the third trimester and the early post-partum period [2]. Menstruation-associated SCAD (M-SCAD) has also been reported; it more often occurs in the menstrual phase than in the follicular or luteal phase [3]. Moreover, SCAD following the use of oral contraceptives and topical hormone replacement therapy has been noted [4]. Therefore, female sex hormones are thought to play a pathogenetic role. Among the female sex hormones, estrogen has vasodilatory effects. During parturition and menses, estrogen levels are at their lowest, and low estrogen levels are suggested to be the cause of SCAD [5].

Pseudomenopause therapy is a therapeutic option for uterine fibroids, adenomyosis, and endometriosis. For this purpose, gonadotropin releasing hormone (GnRH) agonists are used. Leuprorelin is one GnRH agonist; it binds to the GnRH receptors and transiently raises estrogen levels, and thereafter, induces downregulation of the receptors leading to a decrease in estrogen levels. Thus, pseudomenopause therapy may change estrogen levels similar to those documented during pregnancy. Our patient had been using leuprorelin for 2 months before the onset of SCAD, and therefore we speculated that leuprorelin is associated with SCAD. Unfortunately, we did not measure the concentration of estrogen. A previous paper reported that the change in the concentration of estrogen, but not the absolute value, might be associated with SCAD [3]. To our knowledge, this case is the first to demonstrate the association between pseudomenopause therapy and SCAD, but further investigation is required to clarify this association.

There may be a link between SCAD and VSA. Ueda et al. reported a patient with SCAD who developed chest pain with ST-segment elevation in the inferior leads of her electrocardiogram. After sublingual administration of nitroglycerin, her symptoms and ST elevation were resolved, suggesting that SCAD was associated with VSA [6]. In our case, the patient had occasional episodes of chest pain at rest prior to the onset to SCAD, and VSA may have been involved in the pathogenesis of SCAD. Finally, we think it is important to control other risk factors such as hypertension, dyslipidemia, and smoking, in order to reduce myocardial

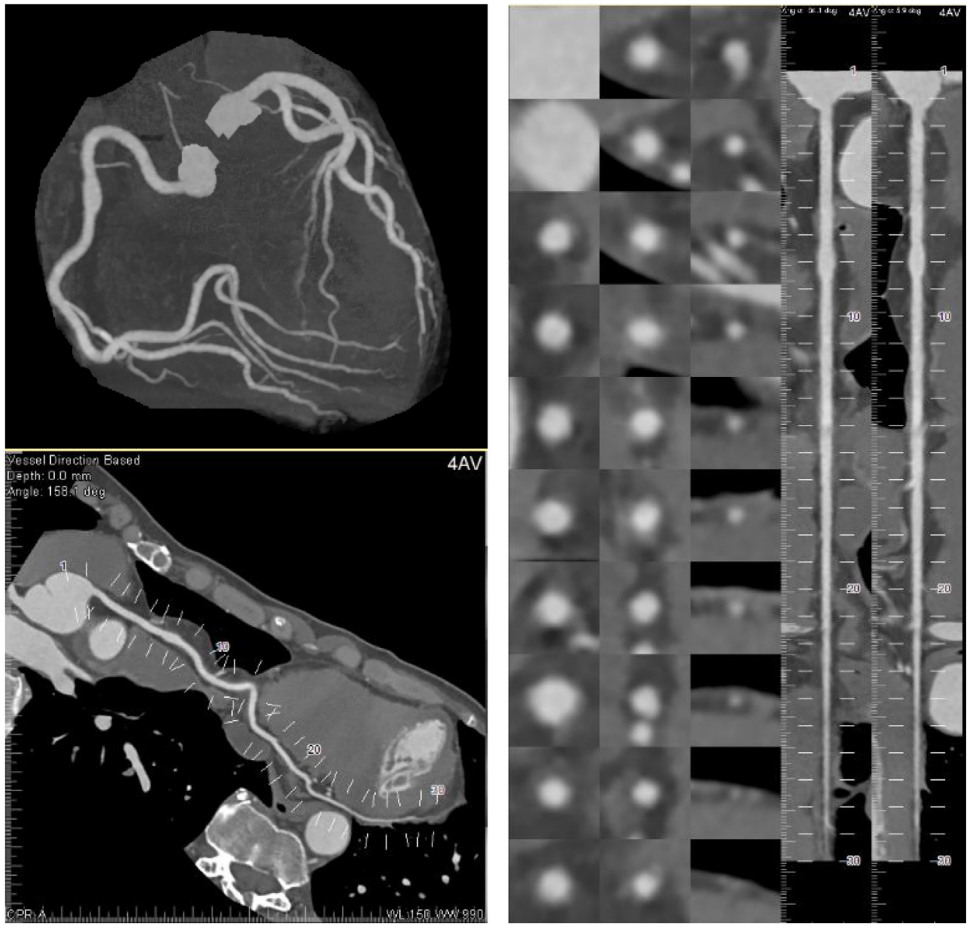

Fig. 3. Cardiac computed tomography angiography at 2 months after discharge. Stenosis due to dissection in the proximal-mid portion of the right coronary artery was healed.

infarction as a complication in patients receiving leuprorelin administration.

Conclusion

Pregnancy and menstruation are well known to be associated with SCAD. We report a case that suggests an association between pseudomenopause therapy with leuprorelin and SCAD. Recognition of the role of female sex hormones in the pathogenesis of SCAD is important for clinicians. Young or middle-aged women who present with symptoms suggestive of ACS should be asked not only about pregnancy and menstrual history, but also about therapies modulating female sex hormones.

Conflict of interest

All of the authors have no conflicts of interest to disclose.

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