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Case Report

The Culprit of Coronary Artery Spasm: Atherosclerosis Evidenced by OCT and a Provocation Test: A Case Report

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Abstract

We reported the case of vasospastic angina unresponsive to lifestyle modifications and intense medical treatment, in which symptoms improved after coronary stent placement. The patient had episodes of ST-segment elevation. Vasospasm was induced by a provocation test and relieved by nitroglycerin, leading to a diagnosis of Coronary Vasomotion Disorders. Optical coherence tomography showed vasospasm only in segments with atherosclerotic lesions. This case underscores the importance of early intervention for atherosclerotic lesions, since acute coronary syndrome (ACS) can occur without significant stenoses. Interventional treatment should be considered for drug-resistant vasospasms unresponsive to optimal medical therapy to improve outcomes.

Keywords

coronary artery spasm; provocation test; optical coherence tomography; atherosclerosis

Introduction

Vasospastic angina (VSA) is caused by spasms in the wall of the coronary artery leading to reduced blood flow and resulting in episodes of myocardial ischemia. The exact cause of vasospastic angina is not fully understood, but it is believed to involve factors such as increased reactivity of vascular smooth muscle cells, endothelial dysfunction, imbalances of vasomotor tone, and genetic variations [1]. These elements contribute to vasoconstriction and may lead to serious complications such as arrhythmias, myocardial infarction, or sudden cardiac death. Conventional treatments include nitrate esters, calcium channel blockers (CCBs), anti-platelet agents, and statins, which can relieve most symptoms. However, some patients continue to face significant risks despite these therapies. Invasive provocative testing was considered to be the major criterion for diagnosing coronary artery vasospasm [2]. VSA occurs more frequently in non-obstructive atherosclerotic lesions. Optical coherence tomography (OCT) with high imaging resolution can help to identify the link between vasospasm and atherosclerosis. These investigations allow clinicians to tailor the most appropriate therapy [3]. We present a patient who underwent a coronary intervention with the guidance of intracoronary imaging and provocation testing for recurrent VSA refractory to medical treatment.

Case Presentation

A 71-year-old male was initially sent to the hospital because of chest pain, diaphoresis. His symptoms progressively worsened, occurring not only at rest but also during exertion. He has a history of hypertension and an acute cerebral infarction. He had smoked one pack of cigarettes daily for 40 years and did not consume alcohol. Physical examination showed no abnormalities. His electrocardiogram (ECG) showed sinus bradycardia with a heart rate of 41 beats per minute, with no ST-T segment changes. The Holter monitor revealed sinus bradycardia, with a total of 71,262 heartbeats over 24 hours, a minimum heart rate of 33 beats per minute, and a maximum heart rate of 77 beats per minute. There was a 0.05 mm ST-segment depression observed in leads II, III, aVF, and V4–V6. The transthoracic echocardiogram (TTE) showed an ejection fraction (EF) of 72%, without any valvular dysfunction or abnormalities in cardiac structure. Computed tomography angiography showed widespread mild to moderate narrowing of the coronary arteries. All laboratory results, including troponin levels, were within normal range. He was prescribed aspirin (100 mg per day), clopidogrel (75 mg per day), atorvastatin (20 mg per day), and amlodipine (2.5 mg per day) and was free from angina at the time of discharge. One month later, he was admitted to the hospital with recurrent chest pain. Coronary angiography (CAG) showed a severe blockage involving the proximal posterior descending branch, and mild to moderate blockages were present in other parts of the right coronary artery (RCA). The left coronary artery was free of disease. The forward TIMI flow in all vessels was grade 3. The blockage did not significantly improve with intracoronary nitroglycerin, so the pa-

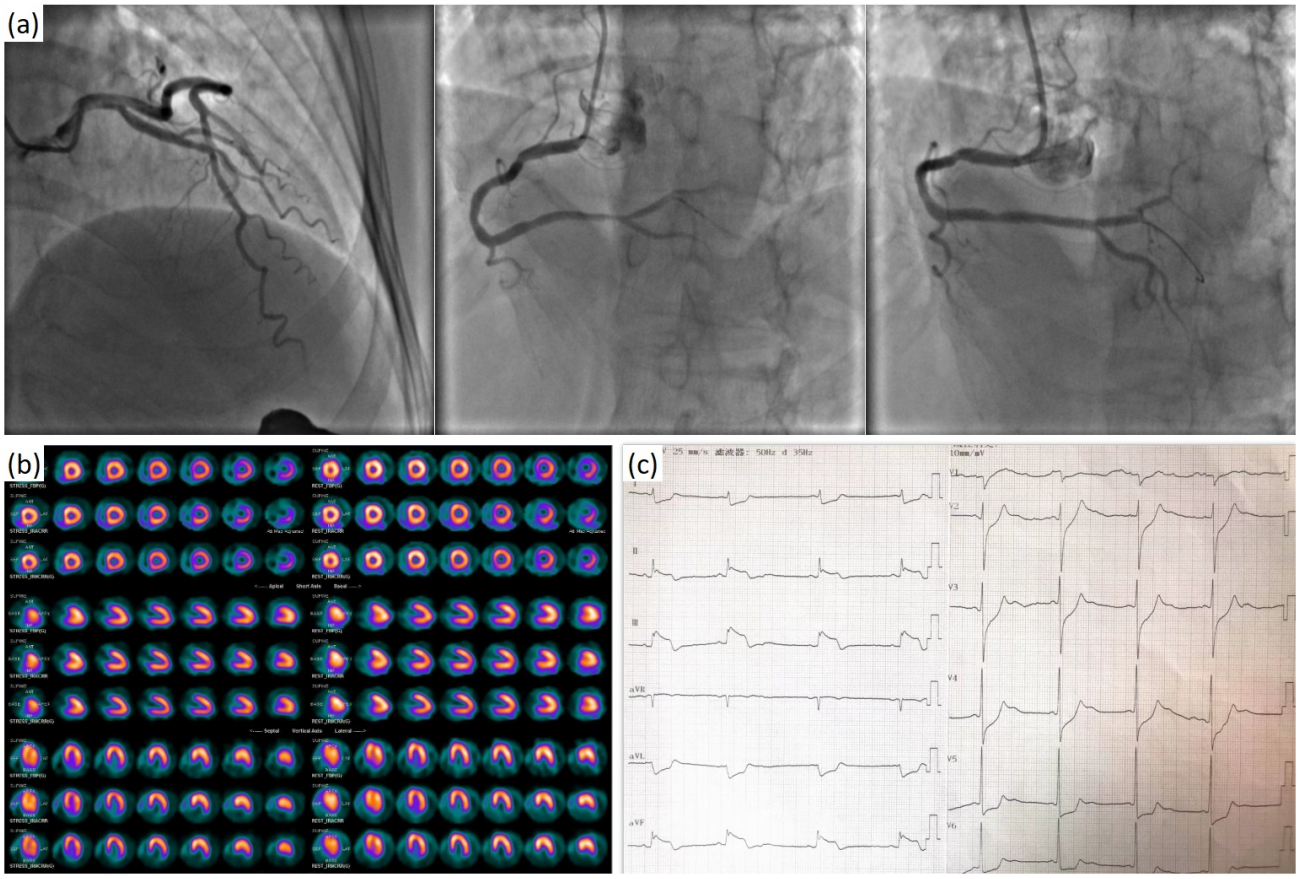

Fig. 1. First cardiac catheterization therapy of the patient, radionuclide stress test, and Electrocardiogram. (a) The coronary angiogram shows significant stenosis around the ostium of the posterior left ventricular branch and implantation of a Sirolimus stent 2.75/23 mm. (b) Radionuclide stress test results show no evidence of ischemia throughout the left ventricular wall. (c) Electrocardiogram shows ST-segment changes during angina.

tient underwent implantation of a Sirolimus stent measuring 2.75/23 mm (Fig. 1a). Isosorbide mononitrate (60 mg per day) was added, and he was discharged with no symptoms. However, the patient experienced similar chest pain 45 days later, leading to another admission. During this admission, myocardial perfusion imaging with radionuclide was performed, and the results ruled out microvascular disease (Fig. 1b). The next morning, he developed chest pain, and the electrocardiogram revealed significant sinus bradycardia with ST-segment elevation in leads II, III, and aVF, along with reciprocal ST depression in leads I, aVL, and V1–V6 (Fig. 1c). His symptoms resolved with sublingual nitroglycerin. Cardiac enzymes were unremarkable. The patient was diagnosed with coronary spastic angina. Based on the result of the previous study [4], amlodipine (2.5 mg per day) was replaced with benidipine (4 mg per day), in addition to diltiazem (90 mg per day) and nicorandil (15 mg per day). One month later, he returned with recurrent angina symptoms. Coronary angiography revealed that the severity of the lesion had not changed, and the stent was patent (Fig. 2a). OCT revealed mild stenosis caused by the formation of fibrous and lipid plaques along with the accumulation of macrophages from the distal to proximal segments of the base of the RCA (Fig. 2b). A temporary pacing electrode was implanted before the ergometrine provocation test. Provocative testing with 20 μg of ergonovine was performed on the RCA, which revealed diffuse spasm except in the segment of the stent and the proximal part of the RCA which had no atherosclerosis (Fig. 3a). Simultaneously, the ECG showed ST-segment elevation in leads II, III, and aVF. OCT revealed luminal irregularities due to diffuse thickening of the intimal layer, localized within the areas of atherosclerosis (Fig. 3b). The patient experienced relief from VAS after receiving a 200 μg dose of intracoronary nitroglycerin, and the electrocardiogram returned to normal. Three stents were deployed sequentially in the right coronary artery to treat the atherosclerotic stenotic lesions, from the distal to proximal segments (Sirolimus stent, 3.0/30 mm, 3.5/36 mm, 3.5/18 mm). Post-dilation was performed, and the immediate result appeared satisfactory on angiography (Fig. 4a) and OCT evaluation (Fig. 4b). Provocative testing conducted after the stenting showed no epicardial spasm, and the patient was symptom free. Five days following the implantation, the patient was discharged

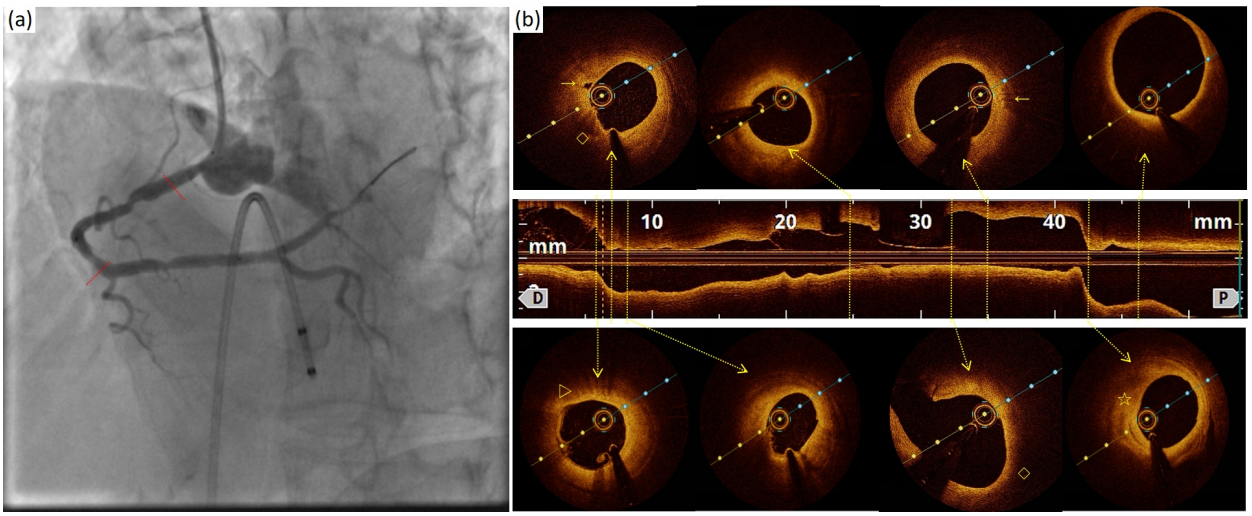

Fig. 2. Baseline coronary angiogram and optical coherence tomography (OCT) images before provocation test. (a) Coronary angiography showed lesion severity had not changed compared with the first intervention and the former stent with no restenosis. (b) OCT shows diffuse atherosclerosis with thin-cap fibroatheroma, layered plaque, macrophage infiltration, cholesterol crystal, and microchannel. ◇: thin-cap fibroatheroma; ▷: macrophage infiltration; ☆: layered plaque; ← : cholesterol crystal; → : microchannel.

free of any chest pain. During a 15-month follow-up, no additional coronary events were observed. The timeline of the patient's treatment and clinical events is presented in Table 1.

Discussion

Vasospastic angina (VSA) usually occurs at rest, accompanied by temporary electrocardiogram changes while maintaining normal exercise capacity. VSA can present in various clinical situations, including acute coronary syndrome, arrhythmias, syncope, or sudden cardiac death. It most frequently occurs between the ages of 50 and 60 years and has a male predominance [5]. According to the Coronary Vasomotion Disorders International Study Group (COVADIS), a definitive diagnosis can be made if the patient presents with classical clinical manifestations of VSA, transient ischemic changes on the electrocardiogram, and coronary artery spasm [6]. We present a typical VSA case that experienced recurring angina with ST-segment elevation and subtotal diffuse spasm of the RCA during the provocation test.

Coronary artery vasospasm results from a transient abnormal or hypersensitive reaction of the affected segment to various stimuli. The pathohistological and morphological characteristics of the involved coronary segments are not yet fully understood [7]. Although the areas of spasm can be normal or mildly narrowed, atherosclerosis can almost always be detected at spasm sites using intracoronary imaging [8]. Coronary atherosclerosis typically leads to endothelial dysfunction and abnormal vasomotor function, which makes the target lesion more prone to coronary spasm. High-resolution OCT can detect angiographically undetectable plaque and visualize detailed structures in the coronary arterial walls [9], and helps to understand the underlying mechanisms of spasm. In this case, the OCT found a diffuse atherosclerosis plaque in the spastic lesion, characterized by a thin fibrous cap overlying a lipid-rich plaque, a layered plaque, macrophage infiltration, and intraplaque microchannels reflecting active and ongoing inflammation. Layered plaque is considered a healing process of thrombosis. A previous study showed that layered plaque, macrophage, and microchannels were frequently observed in lesions associated with coronary spasm, suggesting links between coronary spasm, thrombosis, and inflammation [9]. Inflammation, by exacerbating endothelial dysfunction, increases oxidative stress, and promotes the abnormal response and proliferation of vascular smooth muscle cells (VSMCs), making coronary artery spasm more likely to occur. Coronary artery spasms can trigger or exacerbate thrombus formation, especially when it occurs on a background of atherosclerotic plaques, leading to the formation of layered plaques. This interaction could culminate in acute coronary events. Another study suggested that coronary spasms induce plaque erosion [3]. Erosion could be induced by vessel spasms through increased shear stress on the endothelial surface, and is typically seen in a more severe atherosclerotic lesion compared to the lesion seen in our patient. There is known to be an interplay between spasm and atherosclerosis; spasm enhances atherosclerosis, and in turn, atherosclerosis can trigger spasm [10]. Most importantly, during coronary spasm, as seen in this case, the luminal irregularity is mainly caused by the contraction of quadrants with atherosclerosis, which further implicates the pathophysiological link between coronary spasm and atherosclerosis.

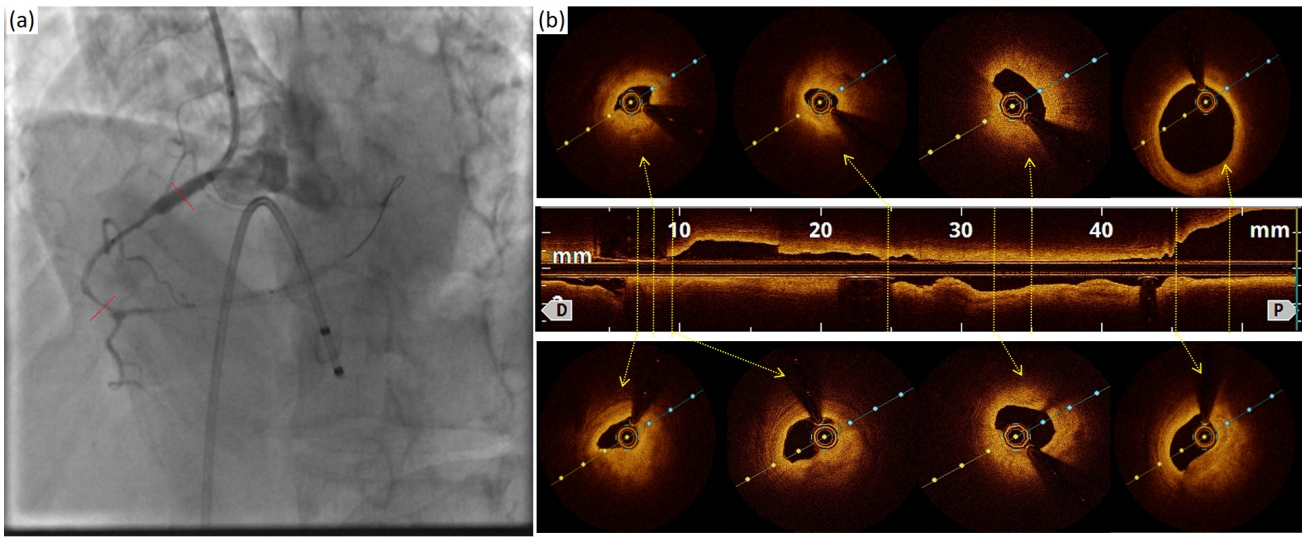

Fig. 3. Coronary angiogram and OCT images during the provocation test. (a) Coronary angiography showed subtotal occlusion with diffuse spasm except in the proximal part of the right coronary artery (RCA) without atherosclerosis. (b) OCT shows luminal irregularity mainly caused by the contraction of quadrants with atherosclerosis in the same segment mentioned before.

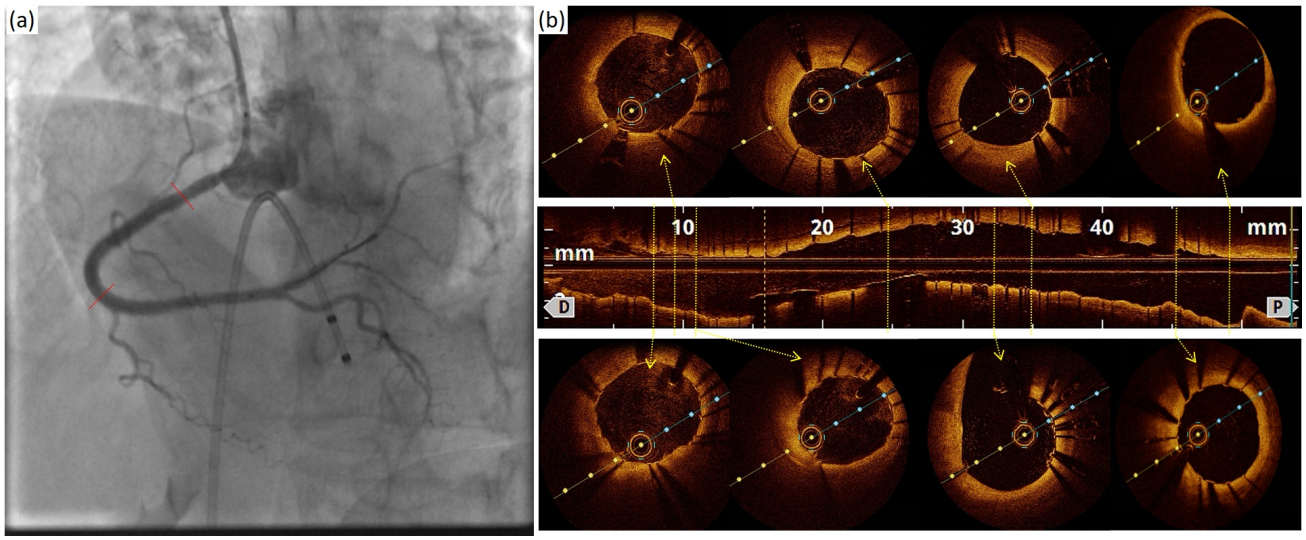

Fig. 4. Coronary angiogram and OCT images after stent implantation. (a) Coronary angiography showed no spasm after stent implantation with ergonovine provocation. (b) OCT shows full coverage of spasm segments with stents, no tissue prolapses, and excellent expansion.

Current guidelines recommend cardiovascular risk factor control and lifestyle change, especially smoking cessation, to avoid coronary atherosclerosis. Calcium channel blockers (CCB) and long-acting nitrates are considered first-line therapy for preventing VSA [11]. Despite optimal medical therapy at maximally tolerated doses, our patient experienced recurrent angina. Intracoronary provocative testing with ergonovine was undertaken to identify the site and mode of spasm, which was a subtotal occlusion of the RCA with diffuse spasm in atherosclerosis segments. Stent implantation is a technically viable option for patients with drug-resistant VSA [12]. The stent can prevent spasms, address organic stenosis, and reduce elastic recoil; however, there are concerns regarding early recurrences in the segments adjacent to the stent resulting in restenosis, as noted in previous reports [13]. This is usually due to the incorrect identification of the spasm sites that leave segments of spasm uncovered and results in mismatched stents [13]. Therefore, a thorough assessment should be done before proceeding with this technique. Our patient suffered from refractory angina even after intensive medication, so we combined intracoronary imaging and provocation testing to accurately definite the etiology and mode of the coronary artery spasm and further optimized treatment with coronary stenting.

Table 1. Timeline.

Week 1	The patient was first admitted to hospital with chest pain. CTA revealed diffuse mild stenosis of the coronary artery. He was prescribed aspirin (100 mg/d), clopidogrel (75 mg/d), atorvastatin (20 mg/d), amlodipine (2.5 mg/d) and free from any symptoms at the time of discharge.
Week 5	He re-experienced chest pain and was taken to hospital. CAG revealed severe stenosis in the ostium of the posterior descending branch and was treated by implantation of a Sirolimus stent 2.75/23 mm. Isosorbide mononitrate (60 mg/d) was added, and he was discharged with no symptoms.
Week 11	The patient complained of chest pain and was again admitted to the hospital. Myocardial perfusion imaging with radionuclide shows normal. Electrocardiography exhibited severe sinus bradycardia with ST-segment elevation in leads II, III and aVF and reciprocal ST depression in I, aVL and V1–V6 during chest pain in in the early morning. Coronary spastic angina was diagnosed. Based on lifestyle adjustment, Amlodipine (2.5 mg/d) was replaced with benidipine (4 mg/d), union diltiazem (90 mg/d), and nicorandil (15 mg/d) was prescribed.
Week 15	He visited the hospital again and frequently experienced chest pain in the early morning and rested. CAG showed the lesion severity had not changed, and the former stent had no restenosis. OCT examined the morphological characteristics of the RCA, and provocative testing showed diffuse spasm except in the segment of the stent and the proximal part of the RCA without atherosclerosis. Three stents were deployed from the distal to the proximal portion of the RCA (distal to proximal: Sirolimus stent, 3.0/30 mm, 3.5/36 mm, 3.5/18 mm).
Follow up	During a 15-month follow-up, no additional coronary events were observed.

Abbreviation: CTA, Computed Tomography Angiography; CAG, Coronary Angiography; OCT, Optical Coherence Tomography; RCA, Right Coronary Artery.

Conclusion

This case demonstrates that spasm is closely linked with atherosclerosis, and that stent placement guided by intracoronary imaging and functional tests can be an effective therapeutic option for patients with vasospastic angina (VSA) that is refractory to aggressive medical therapy. It highlights the importance of addressing atherosclerotic lesions in clinical practice, with early intervention, as acute coronary syndrome (ACS) events can occur even without significant stenosis. Furthermore, while optimizing medical therapy is fundamental for managing vasospastic angina, interventional treatment should also be considered for patients with drug-resistant vasospasms to achieve better outcomes. Adherence to the CARE guidelines ensures that this case report meets the highest standards for clarity and completeness. The checklist is provided in the supplementary materials for reference (**Supplementary Fig. 1**).

Availability of Data and Materials

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Author Contributions

FFZ and HLL designed and performed the research study. YTX and FFZ were responsible for data analysis and writing of the manuscript. YD helped gather information on the cases, review the full text and provided comment. All authors read and approved the final manuscript. All authors contributed to the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Hebei General Hospital (2021-11). The patient signed an informed consent form.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7891.

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