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CASE REPORT

CLINICAL CASE

Isolated Coronary Arteritis Treated With FDG-PET/CT-Guided Immunosuppressant to Break the Vicious Cycle of In-Stent Restenosis

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ABSTRACT

Recurrent in-stent restenosis of the coronary artery is a rare but intractable problem. In this situation, coronary arteritis should be considered as an etiology. This case highlights the use of immunosuppressive drugs, including tocilizumab, and follow-up F-18-fluorodeoxyglucose positron emission tomography/computed tomography to break the vicious circle of recurrent stenosis caused by isolated coronary arteritis of unknown cause. (J Am Coll Cardiol Case Rep 2023;28:102102)

HISTORY OF PRESENTATION

A 71-year-old woman with a history of hypertension and dyslipidemia was admitted with a diagnosis of effort angina. Coronary angiography (CAG) revealed chronic total occlusion of right coronary artery (RCA) and severe stenosis of middle left anterior descending artery (LAD) (**Figure 1**, Video 1). She underwent percutaneous coronary intervention (PCI) at the middle LAD with implantation of a cobalt-chromium sirolimus-eluting stent (Video 2). Intravascular ultrasound (IVUS) findings before stent implantation showed an ambiguous 3-layered vessel structure as well as its outer border at the lesion (**Figure 1B**).

Chest pain recurred 6 months after the first PCI. CAG showed in-stent restenosis (ISR) of the LAD (Video 3A). The second PCI was performed with

LEARNING OBJECTIVES

- To recognize the presence of an isolated coronary arteritis.
- To recognize coronary arteritis as the etiology of recurrent coronary artery stenosis.
- To recognize that IVUS findings are very important in suspecting coronary arteritis.
- To understand the tocilizumab may be effective in the treatment of coronary arteritis with unknown cause or a subtype of Takayasu arteritis, and FDG-PET/CT is useful as a follow-up modality to monitor the response to immunosuppressant.

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ABBREVIATIONS AND ACRONYMS

CAG = coronary angiography

DES = drug-eluting stent(s)

FDG-PET/CT = F-18-fluorodeoxyglucose positron emission tomography/computed tomography

ISR = in-stent restenosis

IVUS = intravascular ultrasound

LAD = left anterior descending artery

LITA = left internal thoracic artery

PCI = percutaneous coronary intervention

QCA = quantitative coronary angiography

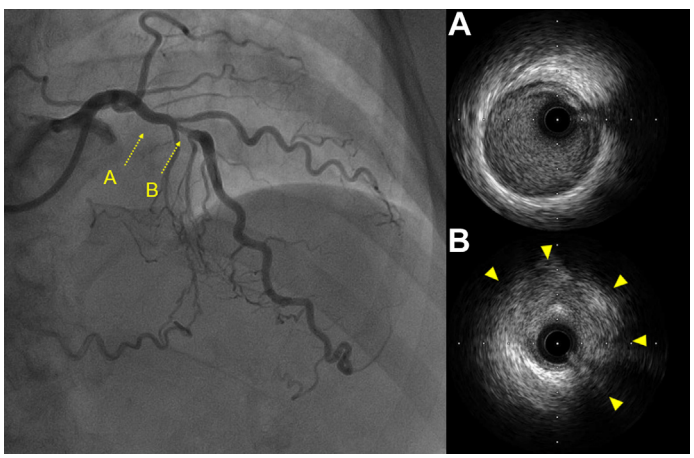
RCA = right coronary artery

excimer laser coronary angioplasty and a paclitaxel-coated balloon (Video 3B). However, unstable angina recurred 3 months after the second PCI (Video 4A). The third PCI was performed with excimer laser coronary angioplasty and a larger-size paclitaxel-coated balloon than used in the previous PCI (Video 4B). Despite aggressive medical management including lipid-lowering therapy and dual antiplatelet therapy, she was readmitted 7 months after the third PCI with effort angina, and CAG showed recurrent ISR. After multidisciplinary discussion, she underwent coronary artery bypass grafting with left internal thoracic artery to LAD, saphenous vein graft to diagonal branch, and saphenous vein graft to distal RCA (Video 5). Unfortunately, 17 months after coronary artery bypass grafting, the distal anastomosis of left internal thoracic artery to LAD and LAD stent were occluded (**Figure 2**, Video 6). A fourth PCI was performed with a zotarolimus-eluting stent (Video 7), and IVUS findings showed marked intimal thickening, as well as an ambiguous 3-layered structure and thickening of adventitia on the outside of the LAD stent (**Figure 2B**).

PAST MEDICAL HISTORY

The patient had a history of catheter ablation for paroxysmal arterial fibrillation.

FIGURE 1 Coronary Angiogram Showed Severe Stenosis of Middle Left Anterior Descending Artery



(A) 3-layered vessel structure with mild atherosclerotic change. (B) An ambiguous 3-layered vessel structure and its outer border in the lesion (yellow arrowheads).

DIFFERENTIAL DIAGNOSIS

Biological, mechanical, and technical factors are potential triggers of ISR with drug-eluting stents (DES). Mechanical and technical factors, such as stent underexpansion, and residual uncovered atherosclerotic plaque were unlikely to be the cause based on IVUS findings. Biological factors such as hypersensitivity reactions associated with metal allergy, systemic inflammatory diseases, and chronic inflammation caused by drugs or polymers associated with DES were considered. In particular, coronary arteritis could be considered as a differential diagnosis based on IVUS findings before stenting.

INVESTIGATIONS

She had no history of metal allergy. In addition, she was also tested for allergy to the metal content of the implanted stent, which was negative. Immunological indexes, such as antinuclear antibody, antineutrophil cytoplasmic antibody, and immunoglobulin G4, were within normal limits. C-reactive protein and erythrocyte sedimentation rate were not elevated. In addition, she was not classified as having any type of collagen disease, including Takayasu aortitis and giant cell arteritis, based on various biochemical tests and computed tomography angiography findings. An F-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) showed increased FDG uptake with maximum standardized uptake value (SUVmax) of 2.6 at the LAD stent site (**Figure 3A**). However, there was no increased FDG activity at RCA occlusion site, carotid arteries and aorta. A possible diagnosis based on the integrated IVUS findings and FDG-PET/CT was isolated coronary arteritis of unknown cause.

MANAGEMENT

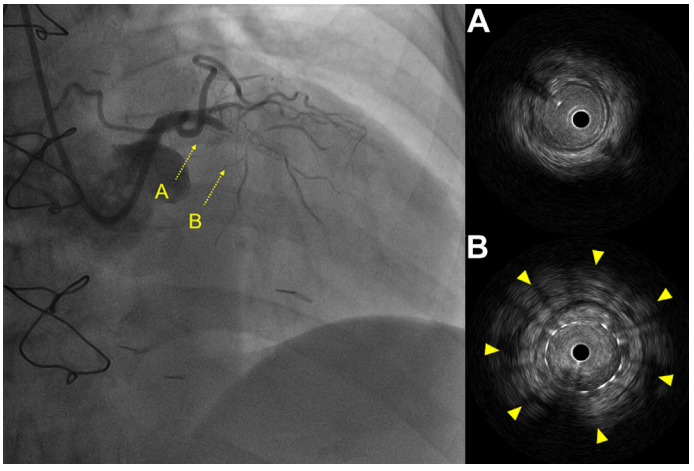
Anti-inflammatory treatment with 30 mg/d of oral prednisolone was started and the dose was gradually reduced. After 3 months of prednisolone therapy, the dose of prednisolone was reduced to 15 mg/d and FDG activity disappeared. CAG showed that the patency of the 2-layered stent was well maintained without stenosis (**Figure 3B**, Video 8A). After 9 months of prednisolone therapy, the dose of prednisolone was reduced to 7.5 mg/d. Increased FDG uptake was confirmed at LAD stent site with SUVmax of 1.7, and CAG showed progression of ISR with 82% stenosis in quantitative coronary angiography (QCA), which was consistent with the FDG-PET/CT findings (**Figure 3C**,

Video 8B). Despite the ISR, she remained asymptomatic, and physiological assessment of LAD was negative for ischemia; therefore, coronary revascularization was deferred and prednisolone was increased to 30 mg/d again.

The strategy of administration and titration of prednisolone alone failed to stabilize the inflammatory state. Therefore, prednisolone was tapered with an addition of tacrolimus 2 mg/d. After 4 months of prednisolone dose adjustment (reduced again from 30 to 12.5 mg/d) and tacrolimus initiation, FDG activity disappeared and CAG showed regression of ISR with 47% stenosis in QCA (**Figure 3D**, Video 9A). However, after 11 months of prednisolone dose adjustment (prednisolone 8 mg/d with tacrolimus 3 mg/d), FDG activity was increased again with SUVmax of 1.7, and CAG showed progression of ISR with QCA of 74% (**Figure 3E**, Video 9B). The strategy of administration and titration of prednisolone with addition of tacrolimus also failed to stabilize the inflammatory state. FDG uptake increased and stenosis progressed when the dose of prednisolone was reduced below 10 mg/d.

Therefore, prednisolone was tapered with an initiation of Tocilizumab 162 mg at 2-week intervals subcutaneously. A total of 11 months after start of tocilizumab, prednisolone was reduced to 4 mg, FDG activity disappeared, and CAG showed regression of ISR with QCA of 52% without symptoms (**Figure 3F**, Video 10).

FIGURE 2 **Coronary Angiogram Showed That Distal Anastomosis of Left Internal Thoracic Artery to Left Anterior Descending Artery and Left Anterior Descending Artery Stent Were Occluded**



(A) 3-layered vascular structure with mild atherosclerotic change. (B) Marked intimal thickening on inside of the stent, as well as an ambiguous 3-layered structure and thickening of adventitia on outside of the stent (yellow arrowheads).

DISCUSSION

In the era of new-generation DES, recurrent ISR is a rare but sometimes intractable problem. In this clinical setting, coronary arteritis should be considered. In practice, however, the diagnosis of coronary arteritis is often difficult, because inflammation caused by DES placement is also known to be an important differential.[1] In this case, the IVUS findings of coronary arteritis, such as ambiguous 3-layered structure and thickening of adventitia, were already identified before initial DES implantation. Because coronary stenting could have led to the vicious cycle of restenosis, the treatment strategy should have been discussed carefully at the beginning.

Coronary arteritis associated with Takayasu arteritis and IgG4-related arteritis are known. FDG-PET/CT is used in clinical practice to diagnose coronary arteritis and to monitor disease status and treatment response.[2,3] In addition, among biologic drugs, tocilizumab, an anti-interleukin-6 receptor antibody, has been reported to be effective in the treatment of refractory Takayasu arteritis.[4] However, in this case, there was no involvement of the aorta and its main branches, which are the most characteristic features of large vessel arteritis. Furthermore, intense FDG uptake was documented only at the LAD stent site. Therefore, we diagnosed isolated coronary arteritis of unknown cause. However, in the present case, IVUS findings were similar to those of coronary involvement in Takayasu's arteritis, so tocilizumab was used.[5,6] This case highlighted that the immunosuppressive drugs such as are effective, and follow-up FDG-PET/CT is useful in monitoring response to immunosuppressive drugs in patients with coronary arteritis even of unknown cause.

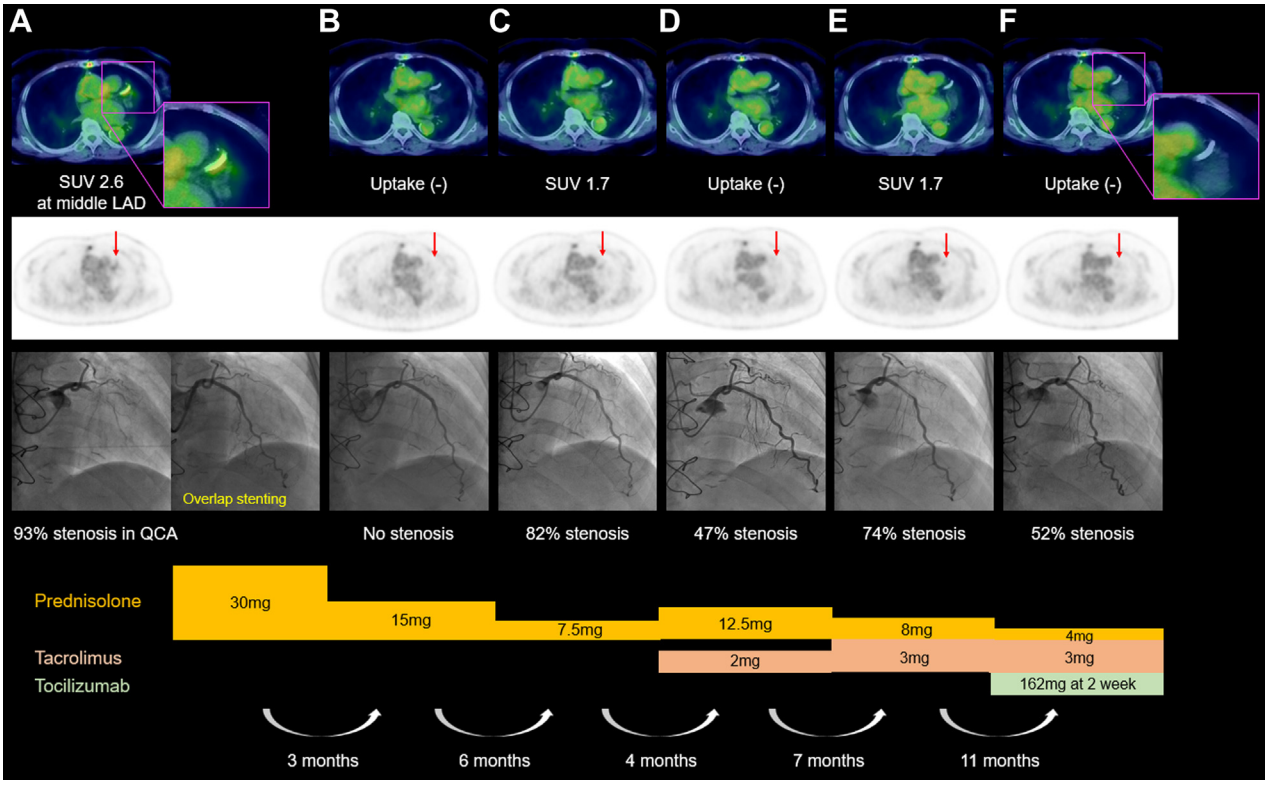
FOLLOW-UP

The patient continued prednisolone 4 mg/d with tacrolimus and tocilizumab and remained asymptomatic over 11 months without coronary arterial revascularization.

CONCLUSIONS

Coronary arteritis should be considered as an etiology of recurrent coronary artery stenosis. Immunosuppressive therapy such as tocilizumab and followed FDG-PET/CT successfully broke the vicious circle of ISR caused by coronary arteritis.

FIGURE 3 A Series of FDG-PET/CT Images and LAD Coronary Angiography



(A) Increased F-18 fluorodeoxyglucose accumulation on positron emission tomography/computed tomography and severe stenosis on quantitative coronary angiography (QCA) at the middle of left anterior descending artery (LAD). After additional stenting, prednisolone was started. (B) After 3 months, fluorodeoxyglucose activity disappeared and the patency of 2-layered stent was well maintained without stenosis. (C) Reduction of prednisolone dosage caused an increased fluorodeoxyglucose uptake and QCA parameter. (D) Additional administration of tacrolimus reduced fluorodeoxyglucose uptake and QCA parameter. (E) Prednisolone reduction caused an increased fluorodeoxyglucose uptake and QCA parameter. (F) Additional administration of tocilizumab disappeared fluorodeoxyglucose uptake and improved QCA parameter. SUV = standardized uptake value.

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KEY WORDS autoimmune, intravascular ultrasound, percutaneous coronary intervention, positron emission tomography, stenosis, stents, treatment

APPENDIX For supplemental videos, please see the online version of this paper.